ADOLESCENT MEDICINE

1 IRON STATUS OF ADOLESCENT FEMALE ATHLETES: Robert T. Brown, Susan M. McIntosh, Vicki R. Seabolt, William A. Daniel, Jr., Univ. of AL., Sch. of Med., Dept. of Peds., Birmingham, AL.

A literature review failed to support the suggestion that adolescent female athletes routinely should take iron supplements. Therefore, female high school track athletes were compared to non-athlete controls from the same schools. Medical and nutrition history, anthropometrics, hemoglobin (Hgb), hematocrit (Hct), mean corpuscular volume, transferrin saturation, and serum ferritin (SF) level were obtained. All participants were menstruating regularly. Recent or current illness, recent transfusion, excessive menstrual or other bleeding, and current medication or iron supplement use were reasons for exclusion. Results showed that 2 of 33 subjects (6%) and 1 of 37 controls (3%) were anemic (i.e., low Hgb.). 14 of 33 subjects (40%) and 9 of 37 controls (30%) had low SF's. There was no difference between the two groups on any of these measures by χ^2 analysis and, for SF, by use of Wilcoxon's Rank Sums Test. An unexpected finding showed significantly more black girls (subjects and controls) had low SF's than white girls ($p=0.005$) even though there was no difference in the number who were anemic or in the mean Hgbs. of the two groups. We conclude that female high school athletes are in no more need of iron supplementation than are non-athletes. Screening for iron status should be done by using SF as well as Hgb. or Hct. We did not address whether low iron stores without anemia adversely affect athletic performance. Black girls may be at greater risk for iron deficiency, though we did not rule out the importance of socioeconomic factors.

2 BONE DEMINERALIZATION IN LACTATING ADOLESCENTS. Gary M. Chan, Nonie Ronald, Patricia Slater, Rita Thomas, (spon. by Lowell Glasgow), University of Utah School of Medicine, Department of Pediatrics, Salt Lake City.

Lactation may cause bone demineralization in animals and humans. To study the effect of lactation on adolescent bone mineral status, we compared 12 nursing teenagers (17.0±0.2 yrs, M±SE) with 11 non-nursing teenagers (16.4±0.3 yrs), 8 nursing adults (25.4±1.1 yrs) and 11 nulliparous teen controls (15.9±0.4 yrs). At 2 and 16 weeks post partum, serum calcium (Ca), phosphate (P), alkaline phosphatase (AP), and 25-OH vitamin D (D) levels were drawn. Bone mineral content (BMC) was measured by photon absorptiometry on mothers and teen controls. Dietary intake was recorded on all mothers and controls. At 2 and 16 weeks, there were no differences in serum Ca, P, AP, D, or BMC among the 4 groups. However, there was a decrease in BMC between 2 and 16 weeks in the nursing teenagers, 1.049±0.088 vs. 0.877±0.054 gm/cm (Wilcoxon Signed Rank, $p<0.02$). There was no change between 2 and 16 weeks in BMC in the non-nursing teenagers (0.975±0.076 vs. 1.05±.07 gm/cm) or nursing adults (0.981±0.079 vs. 1.04±0.06 gm/cm). During the study, there were no differences among the groups in dietary intakes of calories, proteins, fats, carbohydrates, or vitamin D. However, only 3 of 10 nursing teenagers met recommended dietary allowance (RDA) for Ca or P, while 6 of 7 nursing adults, 8 of 10 non-nursing teenagers, and 7 of 10 teen controls met RDA for Ca or P (χ^2, $p<0.05$). We conclude that nursing teenagers are at risk for bone demineralization which may be due to low dietary Ca or P intakes.

3 THE EFFECTS OF TEENAGE PREGNANCY ON NEONATAL BEHAVIOR. Cynthia Garcia Coll. (Sponsor William Oh). Brown Univ. Women & Infants Hosp., Dept. of Ped., Providence, RI

This study assessed the impact of adolescent pregnancy on newborn behavior in 2 cultural settings. The Brazelton Scale was administered during the first 3 days to 148 term newborns born in Florida (38 of mothers ≤17 yrs.) and 155 born in Puerto Rico (42 of mothers ≤17 yrs). Stepwise Multiple Regression was used to analyze the additive effects of maternal age and obstetric factors on 7 clusters of neonatal behavior. Puerto Rican infants of older, married mothers with higher gestation and Ponderal Index had higher habituation scores ($p<.001$). Higher scores for regulation of state were found for infants of older mothers, higher gestation and less obstetric risk ($p<.009$). Infants of older mothers with lower obstetric risk and drug score and higher Ponderal Index had higher scores on autonomic regulation ($p<.02$). In Florida, infants of older mothers with a lower drug score and higher Ponderal Index had higher motor scores ($p<.03$). Higher range of state scores were found in infants of older mothers with lower drug score and higher gestation ($p<.001$). Higher regulation of state scores were related to older mothers, lower drug score and higher apgar scores ($p<.02$). Infants of older mothers with lower drug scores, lower obstetric risk and higher Ponderal Index had higher autonomic regulation scores ($p<.02$). These data suggest that teenage pregnancy and obstetric factors have an additive adverse effect on newborn behavior. Furthermore, teenage pregnancy and other high risk factors affect the Brazelton clusters differently in the two cultures, suggesting an additional role of ethnicity on the effects on neonatal behavior.

4 PREDNISONE TREATMENT OF INFECTIOUS MONONUCLEOSIS (IM). Marjeanne Collins, Samuel Fager and Gary Fleisher, University of Pennsylvania Medical School, Children's Hospital of Philadelphia, Department of Pediatrics, Phila., PA.

A double blind, placebo (P) controlled study of a 6 day course of steroid (S) therapy for IM was undertaken to ascertain (1) the clinical response to S and (2) the effect of S on the antibody response to Epstein-Barr virus (EBV). College students with IM caused by EBV, who did not have tonsillar obstruction, were evaluated clinically and serologically [IgG and IgM anti-VCA, anti-EA(D/R), anti-EBNA] at 0,1,2,4,12, and 24 wks. Thus far, 14 pts have been followed at least 4 wks (mean 14 wks): 7 on P and 7 on S. There was no difference in the resolution of (a) clinical symptoms (dysphagia, fatigue, anorexia), (b) physical signs (fever, adenopathy, pharyngitis) or (c) days of school missed. On the Beck depression test, 0/14 pts were initially depressed, but 3/7 S were post steroid. 2/7 S pts had complications: a peritonsillar abscess and diabetes mellitus. IgG anti-VCA decreased in 3/5 S and 5/6 P pts. 4/7 S and 3/6 P pts had anti-EA (D). This persisted in 4/7 S pts at 4 wks, 2/4 at 12 wks and 1/5 at 24 wks. Only 1/7 P pts had anti-D titers at 4 wks and 0/7 thereafter. 3/7 S and 2/7 P pts have not yet developed anti-EBNA. Comparing the geometric mean titers (Table), the fall of IgG anti-VCA and anti-EA(D) may be slower in S pts. In these pts, S had no short term benefit. Long term clinical outcome, complications of S and their effect on the response to EBV need further study.

	0		4 wks		12 wks		24 wks	
	G-VCA	EA(D)	G-VCA	EA(D)	G-VCA	EA(D)	G-VCA	EA(D)
S	207	40	320	24	320	16	240	20
P	254	25	285	10	201	<10	160	<10

5 TESTICULAR VOLUMES OF ADOLESCENTS: William A. Daniel, Jr., Ronald A. Feinstein, Patricia N. Howard-Peebles, Univ. of AL Schl. of Med., Dept. Peds., B'ham, AL.

Macro-orchidism is a clinical predictor of the "fragile-X"syndrome,an X-linked disorder of mental retardation with an identifiable structural"fragile"site, fra (X)(q27),on the X-chromosome. Testicular volumes were determined at an adolescent clinic on a random sample of 348 normal healthy boys 12-18 yrs. of age of whom 221 were black & 127 were white. Measurements of the greatest width & length of each testicle with the subject standing were made by one of the investigators using a transparent straight-edged ruler. Volumes were calculated with the formula for an elipsoid, $\frac{\pi}{6} L \cdot W^2$. Race, wt., ht., age & sex maturity ratings (SMR) were recorded for each subject. Least squares analysis showed that combined volume of the testes (t.v.) is more closely correlated with pubic hair or genital maturity ratings than with race, age, ht.,wt.,or any combination thereof; $p < .0001$ for correlation with the SMR for pubic hair or for genitalia. There was no significant statistical difference in the mean volumes between the races at any SMR. Though the genital rating correlated slightly better than the pubic hair rating with the t.v.,the difference was not significant & mean SMR's were used for graphic purposes. Mean combined testicular volumes in cm^3 with ± one standard deviation were: SMR I. 10.05 ± 6.44; SMR II. 13.49 ± 6.79; SMR III. 29 ± 11.17; SMR IV. 40.25 ± 11.53; SMR V. 58.56 ± 17.15.

A representative sample of adolescent boys in special education classes at school were also measured & there was no significant statistical difference in t.v.'s when compared with those of normal boys.

6 INDICATIONS FOR FLEXIBLE FIBEROPTIC BRONCHOSCOPY IN ADOLESCENTS. Sherahe Fitzpatrick, Bernard Marsh, Dennis Stokes (spon. by Felix Heald)Dept of Ped/Otol, Johns Hopkins Hospital, Balto;MD

Although the availability of the flexible fiberoptic bronchoscope (FFB) has been a major advance in adult pulmonary medicine, the role of FFB in ped. & adolescent patients (pts) has remained less well defined. Therefore, a 2 yr retrospective study was undertaken to determine the indications for FFB in adolescents. Twenty-six teenagers ($\bar{X}$=16.7 yrs) underwent 32 FFB procedures in either an OR or ICU setting. Topical anesthesia with supplemental sedation was given in 54% of cases. A transnasal approach with an Olympus 4.9mm scope was utilized in 72% of cases. Rigid bronchoscopy was done concomittantly in 6% of cases. Diagnostic procedures during FFB included: transbronchial lung biopsy(9), bronchial brushings(5), bronchial lavage(2), localized bronchogram(1) & biopsy of endobronchial lesion(2). Indications for FFB included abnormal chest xray [18-atelectasis(5), hilar adenopathy(2), abscess(1), mass(1) & other(9)]; evaluating airway in tracheostomy pts(5); hoarseness(2); chronic cough(2); tracheal injury(2); airway obstruction(1); failed extubation(1) & hemoptysis(1). Presumptive diagnosis (dx) was confirmed in 66% of cases but was revised in 18%. In 16% of cases, preop. dx was uncertain but was obtained by FFB. Overall, specific dx was made in 91% of cases. A lower airway disorder was noted in 88% of pts. while 12% had an upper airway abnormality. A minor complication rate of 3%(transient hypoxia) was observed with no major complications. This study demonstrates the safety & value of FFB in selected teenagers when performed by skilled endoscopist in an optimal setting

7 PREVALENCE OF CHLAMYDIA TRACHOMATIS (CT) IN ADOLESCENT FEMALES. John J. Fraser, Philip J. Rettig, David W. Kaplan, Univ. of Okla. HSC, Okla. Child. Mem. Hosp., Dept. Peds., Okla. City. (Sponsored: M. I. Marks).

Little is known of the prevalence of CT in adolescents outside of sexually transmitted diseases clinic populations. We prospectively screened for cervical carriage of CT and Neisseria gonorrhoeae (GC) in 125 females (ages 14 to 20 years) presenting to a general adolescent clinic. CT cultures were done with a microtiter method using cycloheximide-treated McCoy cells.

Prevalence rates were: 8% for CT (10/125), 12% for GC (15/125), 2.4% for both CT & GC (3/125). There were no significant differences in mean age among CT+ (17±1.52 years), GC+ (18.4±1.68), and CT- GC- patients (17.7±1.54). Racial distribution of CT+ and CT- patients did not differ significantly. However, the prevalence of GC in blacks (8/61) was twice that of CT (4/61). Six of 10 CT+ patients used oral contraceptives compared to only 28/113 (25%) of CT- women (p=.028). CT+ patients were more likely than CT- or GC+ to have a negative history for genitourinary/gyneco logic (GU/GYN) symptoms (57.1%, 18.3%, 8.3% respectively). In addition, only 1/7 CT+ women, compared to 11/12 GC+, had a chief complaint referable to possible GU/GYN infection. Although tenderness on external abdominal exam did not correlate with either organism, uterine or adnexal tenderness on bimanual exam was more common in GC+ patients (7/12) than in those with CT (0/7) (p=.015) Overall, 17.6% of unselected patients undergoing pelvic exam had CT, GC, or both. The presence of CT was often not suggested by history or physical exam. Our data support cervical screening for both of these pathogens in sexually active adolescents.

8 LONGITUDINAL STUDY OF CATAMENIAL PRODUCT USE IN ADOLESCENTS: IMPACT OF TOXIC SHOCK SYNDROME(TSS). Charles E.Irwin and Susan G.Millstein (Spon.by Melvin M. Grumbach)Univ.of Cal., San Francisco, Dept.of Pediatrics.

To assess the impact of media coverage of TSS on adolescent catamenial product use, females from 2 high schools and 3 hospital based clinics were surveyed at 2 points in time. Survey 1 was distributed to 681 subjects in November 1980. Subjects were asked about their catamenial product use at menarche, summer of 1980 (prior to TSS publicity), the last menstrual period(after TSS publicity), and intentions for the next menstrual period.Survey 2 was given in August 1981. Of 681 subjects in Survey 1, 27%(n=183) agreed to participate in the follow up study; these subjects were more likely to be tampon users and to have decreased their tampon use following publicity. 62%(n=112) of the subjects returned the surveys:there were no differences between subjects who returned the survey and those who did not. Among subjects followed, 38% used tampons prior to publicity on TSS. After publicity there was a significant decrease in tampon use: 27% were using tampons (p<.005). At follow up, 32% were using tampons(ns). Subjects using tampons at follow up reported feeling significantly more susceptible to TSS than napkin users(t=2.88,p=.005). Although 59% of the tampon users believed their suceptibility to TSS would decrease if they used napkins, 87% said they would not change their product. Among napkin users, 75% believed their susceptibility to TSS would increase if they used tampons;75% would not change methods. Tampon use in adolescents has not returned to its pre-publicity levels. Although media coverage on TSS has decreased, the publicity may have had long term effects on catamenial product use in females.

9 ARRESTED PUBERTY IN MALES WITH HYPERPROLACTINEMIA. RESPONSE TO BROMOCRIPTINE (BR). Ronald I. Jacobson, Myron Genel and Bruce Bower, Dept. Ped. Yale U. Sch. Med. New Haven and Hartford Hosp., Dept. Med., Hartford, CT.

Prolactin (Pr) secreting pituitary ademonas are associated with infertility, impotence and ↓ testosterone(T) in adult males. Onset during adolescence would thus be expected to impair sexual development either via direct mass effect of a prolactinoma or from action of ↑ Pr per se. We have encountered arrested puberty in 2 males with ↑ Pr and observed hormonal and clinical improvement during therapy with the dopamine agonist Br.

At age 15 Case 1 remained Tanner II with declining height velocity of 3.5 cm/yr. Pr (normal <20 ng/ml) was 128-176 ng/ml and T 83 ng% (adult male >350 ng%). Tomograms showed small sellar erosion. After surgery was refused, Br (2.4 mg/day) reduced Pr to <10 ng/ml with rise in T to 640 ng%. Height velocity doubled to 8 cm/yr and maturation resumed. Case 2 presented at 17 with Pr 420 ng/ml, T 24 ng%, and a pituitary mass. After resection of a chromophobe adenoma plus radiation, ↑ Pr (500-1020 ng/ml) persisted with panhypopituitarism. Hypogonadism with ↓ T of 70 ng% and ↓ sperm count of 2.2 million/cc resolved with 5 mg/day Br which reduced Pr to <10 ng/ml while T rose to 683 ng% and sperm count to 18.5 million/cc. In both, withdrawal of Br led to ↑ Pr and ↓ T.

Puberty began normally at 12-13 yrs in both and cessation of maturation indicated underlying pathology, not physiologic delay. The dramatic response to Br therapy reflects the adverse role of hyperprolactinemia per se on male adolescent development.

● **10** THE EFFECT OF PEER COUNSELORS ON ADOLESCENT COMPLIANCE WITH ORAL CONTRACEPTIVES, Susan Jay, Robert H. DuRant, Tamsen H. Shoffitt, Charles W. Linder, Iris Litt. Medical College of Georgia and Stanford University, Department of Pediatrics, Augusta and Stanford.

Poor compliance with contraceptive regimens has been shown to be an important antecedent of adolescent pregnancy. The purpose of this study was to prospectively test the effect of a peer versus nurse counseling program on adolescent compliance with oral contraceptives. Fifty six females aged 14 to 19 from a lower socioeconomic background were predicted to be compliant or noncompliant based on a compliance index (Litt et al). The noncompliant subjects were then randomly assigned to a peer (n=25) or nurse (n=25) group. At the initial visit and at 1, 2, and 4 month follow-up visits all subjects received Ortho-Novum 1/35 combined with a tablet marker and were counseled by a nurse or peer. Compliance was measured using a Guttman scale consisting of: 1) avoidance of pregnancy 2) appointment adherence 3) pill count and 4) urinary fluorescence for riboflavin. At the first follow-up the adolescents counseled by a peer had a significantly ($p<0.02$) higher mean compliance level than the nurse group. At the remaining follow-up visits the peer group continued to have higher mean compliance levels although the differences were not statistically significant. Moreover, the subjects who were originally predicted to be compliant (n=6) and counseled by a nurse demonstrated lower ($p<0.02$) compliance and higher attrition ($p<0.05$) than the peer group. These results suggest that incorporating a peer counselor into the health care team may be an effective method of increasing adolescent compliance.

● **11** COUNTING ADOLESCENT MOTHER-INFANT INTERACTIVE BEHAVIORS RELIABLY. Ruth A. Lawrence, Elizabeth R. McAnarney, Marilyn J. Aten, Alfred Baldwin, Clara Baldwin and Howard P. Iker. Univ. of Rochester, Strong Memorial Hosp. Med. Ctr., Dept. of Pediatrics, Rochester, N.Y.

Evaluating adolescent mother-infant interactive behaviors from 10 min. videotapes necessitated the development of a counting method with particular emphasis on adolescent behaviors not yet described in studies of older mothers. Based on previous methods developed for counting adult mother-infant behaviors, our method consisted of 37 individual maternal items and 5 infant items. The maternal items were included under the 5 traditional categories of gentle touch, caretaking behaviors, proximity to mother, visual behavior, vocal/verbal behavior, and 2 additional categories: assertive touch and personal behavior, both thought to be unique to adolescents. Infant items were vocalization, general state, and activity, including eyes open or closed. Coders were trained, using a training videotape, to count the number of behaviors in 15-second sequences for the entire 10 minutes of the tape. Scores for each item were recorded on a score sheet and totaled. Coders practiced on 10 non-study tapes until they reached at least 80% agreement with an established coder. Pearson correlations confirmed intercoder reliability. Neither the intercoder agreement scores nor the Pearson correlations fell below .86 for any item on the scoring of 130 additional videotapes.

This method for measuring adolescent mother-infant interactive behaviors is, therefore, reliable.

12 PROFILE OF A HIGH SCHOOL POPULATION AT HIGH RISK FOR APLASTIC ANEMIA. Martha S. Linet, James M. Tielsch, Jan A. Markowitz, Lyle L. Sensenbrenner, Lee D. McCaffrey, Steven G. Warm, Sandra F. Vanderslice, W. Fred Morgan, James D. Bearden III, Moyses Szklo. (Spon. by Leon Gordis). The Johns Hopkins Univ. School of Hygiene & Public Health, Depts. of Epidemiology and Environmental Health Sciences; The Johns Hopkins Hospital, Johns Hopkins Oncology Center, Baltimore; and the Appalachia III Public Health District, Spartanburg, S.C.

Four teenagers in a South Carolina town (population 15-20,000; teenagers 1500-2000) were diagnosed as having aplastic anemia between 1974 and 1980. We estimated the annual average incidence rate in the age-specific population (14-17 years) to be 33 per 100,000 during this time period compared to 0.5 per 100,000 expected. All 4 teenagers attended one of 2 junior high schools in the town: 2 were brothers; 3 were males, 1 female; 3 were white, 1 black. In order to investigate the problem 2 approaches were used, a case-control study and a survey of all high school students in the town, comparing risk factors of students who had attended the "affected" junior high with those of students who had attended the unaffected junior high. The 4 cases were compared to matched normal controls, but no significant associations were found. In the survey we found no associations by junior high school with exposure to glue, paint or varnish, pesticides, history of hepatitis, mononucleosis, use of chloramphenicol or other suspected drugs. However, there appeared to be an association between the "affected" junior high school and employment in agriculture, specifically peach orchards. We are investigating this association in more detail.

13 DETERMINANTS OF CONDOM USE AMONG SEXUALLY ACTIVE ADOLESCENT MALES. Joan M. Lovett, Iris F. Litt, Catherine A. McDonald. Stanford University School of edicine, Department of Pediatrics, Stanford, California

Efforts to prevent unplanned teen pregnancy have focused ainly on educating sexually active adolescent females about the isks and prevention of unwanted pregnancy. Relatively little is nown about the teenage male partners' attitudes toward father- ood or his role in encouraging or preventing conception.

The purpose of this study is to describe the attitudes of eenage males toward contraception and fatherhood and to look at he determinants of condom use. The study population consists of 8 black, lower socioeconomic status, sexually active adolescent ales attending a teen clinic. The subjects completed a question- aire detailing their attitudes, knowledge, and behavior about amily planning. 51/68 subjects were 13 or younger when they irst had sexual intercourse. All except one subject wanted to ostpone fatherhood. Nevertheless, 19/68 subjects had unprotected ntercourse in the past 2 months. Of these, 14 think that condom se is a good idea or are undecided, but 7 of the 14 believe that omeone their age is not old enough to buy condoms. 18 subjects dentify a main problem with using condoms as "putting it on."

A randomized control trial is underway to determine whether an ducational intervention including free condoms is effective in romoting condom use. Subjects return for follow-up 2 months fter the intervention.

14 CIRCADIAN RHYTHMS OF BLOOD MINERALS IN ADOLESCENTS. Morri E. Markowitz, John F. Rosen, Mark Mizrachi. Dept. Peds., CRC, Computer Ctr., Albert Einstein ollege of Medicine, Montefiore Hosp., Bronx, N.Y.

We have previously described normal circadian rhythms of lood ionized calcium (Ca^{++}), serum total calcium (Ca_T) and hosphate (P_i) in healthy adult men (Science 213:672, 1981). To letermine if these mineral patterns vary in teen-agers, during eriods of rapid skeletal growth, we studied 6 normal males (Tanner 4-5) who were 13-17 years old. Blood was sampled every 0 min. for 24 hours via an indwelling venous catheter. Based pon analyses of data averaged across the 48 time points, 3 model urves were derived mathematically to describe all but minor luctuations in the raw data. These curves are described as ollows: a U shaped Ca^{++} curve with a peak at ∿11 AM and trough etween ∿4-6 PM; the P_i curve revealed 2 peaks: the smaller one ccurred at ∿6 PM and the larger peak at ∿4 AM; the Ca_T curve evealed 2 troughs: the larger trough occurred at ∿4 PM and the maller one at ∿7 AM. The diurnal ranges of variation were: Ca^{++} = 0.31 mg/dl, Ca_T = 0.43 mg/dl, P_i = 2.5 mg/dl. Intermodel orrelations were: Ca^{++}/Ca_T = .325*; Ca^{++}/P_i = .137; Ca_T/P_i = .-750** (* = p <.05, ** = p <.01). Comparison of these circa- lian rhythms to adult patterns revealed high correlation coeffi- ients; however, the diurnal variation in P_i was significantly reater (>2x). Conclusions: 1) Circadian rhythms in blood min- ral concentrations are present in adolescent males. 2) The wide iurnal range in P_i appears to be characteristic of teen-agers. 3) Deviations from these patterns may provide a sensitive diag- nostic basis for therapeutic intervention in disease states.

15 ADOLESCENT COITAL ACTIVITY AND INFANT PREMATURITY. Elizabeth R. McAnarney, Cynthia A. Bayer, Christine F. Kogut, Mary G. Silverman, Howard P. Iker. Univ. of Rochester, Strong Memorial Hosp., Dept. of Ped., Rochester, N.Y.

It is unclear whether there is a relationship between maternal 3rd trimester coital activity and infant prematurity. To learn about adolescents' 3rd trimester coital activity and the birth- weights and gestational ages of their infants, 75 young mothers consecutively enrolled in an adolescent maternity project were studied. Methods consisted of chart reviews and also semi-structured interviews conducted by the adolescents' primary nurses during the postpartum hospitalization. Mean maternal age at delivery was 17.3 yrs. (15.7-19 yrs.); 60% were black, 40% were non-black; the majority were of lower socioeconomic status. Thirteen(17%) reported no coitus during pregnancy. Sixty-two (83%) reported coitus during pregnancy; of these, 45(73%) reported 3rd trimester coitus. The mean birthweight of infants of mothers reporting 3rd trimester coitus was 2911 gms (850-4960 gms) and that of infants of mothers reporting no 3rd trimester coitus was 3412 gms (2430-4000 gms) ($p < .001$). Mean gestational ages (GAs) were 37.7 wks. (27-42) and 39.3 wks. (31-43) respectively. Eleven(14.7%) of the 75 infants weighed ≤2500 gms. Seven of these 11 had GAs ≤37 wks. Six of the 7 mothers of infants with both a birthweight ≤2500 gms and a GA ≤37 wks. reported 3rd trimester coitus. The influence of maternal age, race, parity, smoking, substance use, height and weight were also considered.

As a group, infants of mothers reporting 3rd trimester coitus had significantly lower birthweights than those whose mothers reported no 3rd trimester coitus.

16 ADOLESCENT SUICIDE GESTURES - A LONG TERM FOLLOW UP. Matilda S. McIntire, Thomas P. O'Brien, Carol R.Angle. University of Nebraska Medical Center, Department of Pediatrics, Omaha, NE 68105.

Self-poisoning with a low lethality of intent is estimated to occur at an annual rate of 30/1000 in the age group 10-24 years yet little is known concerning its long term significance. Pediatricians are frequently the primary medical contacts for the evaluation of both suicidal risk and overall perturbation of these adolescents, and their training is relevant to the observation of the effects of maturation on behavior. A nine year follow-up of 15 of 47 adolescents hospitalized at ages 12-18 years in a psychiatric facility because of severe perturbation associated with a suicidal behavior disclosed recurrent suicidal gestures in 47%. The overall incidence of 47 gestures by the 15 subjects peaked at ages 14-15. A sharp decline after age 18 supports the concept that suicidal behavior of low lethality is an age related response. Despite residual mild depressive symptoms in almost half, functional adaptation was good in the majority and was independent of the number of events or of the initial diagnostic category. All subjects considered themselves better adjusted, with greater life satisfaction and improved interpersonal relationships; 80% had completed high school and 93% were capable of stable employment. All subjects attributed benefits to multiple support systems, particularly a strong relationship with at least one emotionally mature person, a more favorable environment-usually accomplished by moving out of the house, achievement of education and employment skills, and economic independence.

17 THE EXPERIENCE OF HOSPITALIZATION BY ADOLESCENTS WITH CHRONIC DISEASES. Pierre-A. Michaud, Florence Pichot, Sonia Mandel, Maria Massi, Jean-Y. Frappier. Spon. by Claude C. Roy. University of Montreal. Sainte-Justine Hospital. Adolescent Medicine - Department of Pediatrics. Montreal - Quebec - Canada.

This study was designed to describe the way adolescents with a chronic disease experience their hospitalization. Seventy-seven subjects, aged 11 to 20 answered a self-administered questionnaire upon discharge from hospital. Their feelings were measured on a four-point scale. The distribution of feelings along this scale was wide, but tended more toward the positive than toward the negative pole. Those whose feelings were more negative had been hospitalized more frequently and were more preoccupied with disease-related problems; they more often described the atmosphere at home as bad and more often reported difficulties with their parents; finally, they said they were less involved in social activities on the ward. Preoccupations about disease-related problems were assessed using a four-point scale; most concerns were expressed toward their medical prognosis and professional future. Medical patients reported more preoccupations than surgical ones. The majority of the subjects reported that they would have liked greater opportunities to discuss their disease with doctors and nurses. With respect to social life, preferred activities were receiving visits and chatting with other patients and staff.

The results suggest that there is a considerable variation in the way adolescents with a chronic disease experience hospitalization. They underline the importance of social life on the ward and stress the educative and supportive role of the staff.

18 ALTERED EXERCISE RESPONSES IN PATIENTS WITH ANOREXIA NERVOSA. Dov B. Nudel, Norman Gootman, Michael P. Nussbaum and I. Ronald Shenker. SUNY at Stony Brook Long Island Jewish-Hillside Med. Ctr., Dept. of Pediatrics, New Hyde Park, N.Y. 11042.

12 patients with anorexia nervosa(AN) age 15±0.6 yrs had maximal exercise tests; results were compared to 14 age-matched (15.9±0.6 yrs.) controls(NC). Simple progressive exercise on a bicycle ergometer, with power increments every minute, were performed until exhaustion. Expired air was measured and integrated to minute ventilation. Fractional concentration of mixed expired gas was analyzed with a rapid responding O_2 analyzer. O_2 consumption(VO_2) was calculated from the minute ventilation (STPD) and mixed exhaled O_2. Anerobic threshold(AT) was determined as the point of alinear response of ventilation with a concomitant rise in end-tidal O_2. AT occurred at 67% of max. work(W) in AN and at 61% in NC. Blood norepinephrine(NE) was measured at peak exercise in 8 AN and 5 NC adolescents.

	Response to Exercise				
	HR	Syst.BP	W.Watt/kg	VO_2ml/kg/mn	NE pg/ml
AN	172±4.1	133±5.5	2.5±0.2	29.9±1.6	1646±424
NC	197±3.3	175±4.4	3.3±0.2	44.0±2.7	3710±818
p≤	0.001	0.001	0.025	0.001	0.05

ECG was normal in NC, however 25% of AN patients developed significant ST changes, yet remained asymptomatic. Most AN patients reached subnormal maximal HR, BP, power output, VO_2 and serum NE levels at peak exercise. These data suggest diminished sympathetic activity and an abnormal reflex response to the stimulus of exercise with AN; AN patients may also have a myocardial insult.

19 CROSS ETHNIC DIFFERENCES IN ADOLESCENT HEALTH CONCERNS Donald P. Orr and Renee Weinberg-Unterman (Spon. by Beverly C. Morgan). College of Medicine, University of California, Irvine, Department of Pediatrics, Irvine, Calif.

To identify if adolescent health concerns are related to ethnicity, 525, 7-12 grade students in a Southern California school district were surveyed; 62% were Anglo, 11% Hispanic, 8% Asian and 19% others. Hispanics considered themselves as healthy as others, however, they had 1½ times more unanswered health questions and problems ($p < .001$). While all ethnic groups had multiple health concerns, more Anglos were concerned about drugs, acne, alcohol use, obesity, contraception, and abuse. More Anglos felt that Adolescent Clinics should provide information and services about these areas ($p < .001$) compared to others. Suicide and saddness were concerns of equal numbers of Anglos and Hispanics. Perceived vulnerability to illness varried by ethnicity. More Hispanics felt susceptible to tuberculosis. However, they less frequently could identify its cause and considered it to be less serious ($p < .01$). While 14% of each group felt they would contract a STD, Hispanics would more often leave it untreated and could not identify its cause. While all groups utilized organized health services, Hispanics would more often suggest folk or home treatment for common illnesses (herbs, teas, curanderos, over the counter drugs) ($p < .01$). Expectations about services and treatments vary by ethnicity. Those providing health services to adolescents of varied ethnic groups must be aware of the subtle differences.

20 ADOLESCENT RISK-TAKING BEHAVIORS IN A RURAL UPSTATE NEW YORK COUNTY. Kathaleen C. Perkins, Andrew A. Sorenson, Elizabeth R. McAnarney, Univ. of Roch., Dept. of Ped. and Prev. Med., Rochester, N.Y.(Spon.-R. Hoekelman)

Public concern involving adolescent teen pregnancies is mounting while other social problems remain unchecked. These adolescent behaviors may be related. This study examines the correlations of various risk-taking behaviors among adolescents in a rural county in upstate N.Y. For 22 towns and 2 cities in this county, demographic information and data were gathered over a 3 yr. period for the following variables: drivers in motor vehicle accidents (MVA) by sex and age group; pregnancies by age group; arrests for felonies by age group; youth leaving school before completing 12th grade by sex; and placement on probation by age and sex. All of these risk-taking behaviors among adolescents living in the entire county are positively correlated. For those <17 yrs. of age the rate of pregnancies is significantly related to the rate of male drivers ≤20 yrs. in MVA's ($p < .03$), rate of males ≤20 yrs. arrested for felonies ($p < .001$) and the rate of males placed on probation ($p < .0001$) and the rate of 16 and 17 yr. old females who drop out of school ($p < .05$). It is interesting to note that the larger of the two cities (with 9000 teens) has consistently lower rates of adolescent risk taking behaviors than does the smaller city (3000 teens), except for male school drop-outs. Perhaps the most surprising finding is that the rate of teen pregnancies is negatively correlated with the proportion of adult females who have no high school education. This study points out the desirability of replacing the categorical approach to adolescent problems with an holistic one.

21 RENIN PROFILING-A CLINICAL APPROACH TO EVALUATING ADOLESCENT HYPERTENSION. James Prebis,Alan Gruskin,Jorge Baluarte, Martin Polinsky, Sharon Perlman and Bruce Morgenstern. St.Christopher's Hosp.for Children, Phila., PA.

Criteria by which adolescents can be categorized as having hypertension(HBP) associated with suppressed, normal, high or hyperresponsive plasma renin activity(PRA) have been established in a clinical research center setting. Confidence bands(95%) for the four-hour upright PRA 4.5±2.1(S.D.) ng/mg/hr in relation to the 24 hour urinary sodium excretion(renin-sodium index)were established in 30 normotensive adolescents. An oral Lasix(1 ml/kg) stimulation test to induce acute volume depletion was used to establish criteria for suppressed(increase<40%)and hyperresponsive (increase>150%)PRA. On the basis of the renin sodium index a high PRA was documented in 16% of 43 children with essential and 84% of 25 children with renal related HBP. Following Lasix stimulation PRA was suppressed in 11% and hyperresponsive in 14% of the children with essential HBP. Although the fractional increase in PRA in children with high PRA associated with either essential or renal related HBP was similar, it was less than ($p<0.05$) that observed in either normotensives or in those with normoreninemic essential HBP.

These two tests permit PRA to be critically defined in hypertensive adolescents. The availability of such data has permitted us to make rational decisions concerning the nature of additional studies, as well as enabling cardiovascular risk factors to be identified and followed. Also, such studies can be easily performed in an outpatient milieu.

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22 REDUCTION OF COMPLICATIONS IN HIGH RISK ADOLESCENTS AND THEIR INFANTS RECEIVING CARE IN A COMPREHENSIVE PREGNANCY PROGRAM. E. Quijano, M. Joseph. (Spon. by M.I. Cohen). Albert Einstein Coll.Med.,Dept. Peds.,North Central Bronx Hosp., Bx., N. Y.

One million adolescents become pregnant each year. Several authors have noted that pregnant teenagers are at high risk of illness and emotional disruption both pre and postpartum. A comprehensive pregnancy program was established to determine if such complications to adolescents and their babies could be reduced by providing multidisciplinary care for teenagers through pregnancy and with their infants for 12 mos. subsequent to delivery. The program was based at a municipal hospital within a medically underserved and economically depressed urban environment. Prenatal, obstetrical, postpartum and infant care were delivered by a team of a nurse coordinator, obstetrician, pediatrician, social worker, visiting nurse and psychiatrist. There were 306 adolescents (ages 12-16) and 229 infants cared for over a period of 2 yrs. Maternal complications included preeclampsia 2.9%, anemia 13.7%, Cesarean section 5.5%, premature birth 5.8%, postpartum endometritis 2.6%, and postpartum depression 1.3% of the 229 infants followed for 12 mos., 4 had congenital anomalies, 3 were abused; and 17 required hospitalization for various illnesses. 133 (58%) completed their immunizations. There were two neonatal deaths. These results demonstrate a far lower incidence of complications in these adolescents and their infants than has been previously reported. It would appear that a comprehensive multidisciplinary pregnancy program can contribute markedly to the reduction of morbidity and mortality in the high risk adolescent and her infant.

● **23** FACTORS PREDICTING FOLLOW-UP APPOINTMENT COMPLIANCE IN A FREE ADOLESCENT CLINIC. George C. Rodgers, Jr., George H.W. Christie, Vernon R. Hink, (Spon. by Billy F. Andrews), Univ. of Lou. Sch. of Med., Lou., KY, and the Onondaga Cty. Dept. of Hlth., Fam. Plan. Service, Syracuse, NY.

The computerized records of 950 consecutive new patients seen in a free adolescent clinic over a 3 year period were reviewed for compliance with initially scheduled follow-up visits. Follow-up visits were scheduled in the clinic for 248 new patients. Patients returning within two weeks of their scheduled date were considered to have complied. Using these criteria 134 (54%) appointments were kept. The following factors were analyzed as predictors of compliance: age, sex, race, school and employment status, living arrangements, location of residence, number of parents at home, whether sexually active, taking any medication, use of cigarettes, alcohol or marijuana, and contraception usage. In addition the number of patient identified presenting problems and the nature of patient and physician identified problems were analyzed. None of the demographic data showed a significant correlation with compliance. A significant association ($p < .01$) was shown between compliance and the number of problems initially identified by the patient. Patients presenting for routine examinations without identified problems had significantly poorer compliance (34%) than those with one (50%) or two or more (64%) problems. One patient identified problem, possible pregnancy, was found to be a significant ($p < .05$) negative predictor of compliance. These data identify specific adolescent patient groups where poor compliance can be expected. Additional reinforcement in these groups may be useful.

● **24** YIELDS ON COMMONLY DONE LABORATORY TESTS IN AN ADOLESCENT CLINIC POPULATION. George C. Rodgers, Jr., George H.W. Christie, Vernon R. Hink (Spon. by Billy F. Andrews), Univ. of Lou. Sch. of Med., Dept. of Ped., Lou., KY, and the Onondaga Cty. Dept. of Hlth., Fam. Plan., Syracuse, NY.

The computerized records from 950 first visits to a free health department sponsored adolescent clinic were reviewed. The records covered a three year period. Patient ages were 12-21 yrs (mean 16.5 yrs). There were 608 females and 342 males. The population was predominantly white lower middle class with 26% being racial minorities. A routine hemoglobin was obtained on 724 patients. Based on age and sex related normals 7.2% of patients (7.7% females and 6.4% of males) were anemic. A routine dipstick urinalysis was done on 696 patients and showed one or more abnormalities in 21%. Proteinuria was found in 15.7% of patients (16.8% of females and 14.1% of males). Glucosuria was detected in 2% of patients and hemoglobinuria in 1.4% of patients. More than one urine abnormality was found in 1.7% of patients. Routine PAP tests done on 106 patients yielded 12.3% abnormals (twelve Class 2 and one Class 3). N. gonorrhea cultures done on 132 patients yielded only two positives, both in suspected cases. Throat cultures for group A beta hemolytic streptococci were positive in 12 of 68 cultures submitted, while only 2 of 40 urine cultures were considered positive. Monospot tests were done in 31 patients with 2 positives. A routine VDRL was done in 715 patients with only one positive test. These data confirm that routine blood counts and urinalyses in adolescent patients identify significant numbers of abnormalities. The use of a routine VDRL does not seem justified.

25 RELATIONSHIP OF ENDOCERVICAL CHLAMYDIA INFECTION, ABNORMAL PAP SMEARS, AND CONTRACEPTIVE USE IN ADOLESCENT FEMALES. Mary-Ann B.Shafer, Janet C.Shalwitz, Julius Schachter and Richard L.Sweet (Spon. by Melvin M. Grumbach) Univ. of Cal., San Francisco, Dept. of Pediatrics, San Francisco.

Chlamydia infections are becoming recognized as important sexually transmitted diseases in adolescent females and are associated with abnormal Pap smears. 75 sexually active subjects ($\bar{x}$=15.8 yrs.,r=13-20 yrs) and 9 never sexually active subjects ($\bar{x}$=16.5 yrs,r=13-20 yrs), undergoing pelvic exams in a general youth clinic of an ambulatory pediatric setting, had Chlamydia trachomatis cultures and endocervical Pap smears done. All pregnant girls and girls with menses were excluded. Contraceptive use in the sexually active group included: 35% oral contraception; 24% barriers; 41% no method; 1 subject used an IUD. All 9 never sexually active subjects had normal Pap smears and negative chlamydia cultures. In contrast, 44%(15) of sexually active subjects had abnormal Pap smears. Of these 34%(11) used oral contraception; 19%(6) used barriers; 47%(15) used no method; (1 used an IUD). A large proportion of sexually active subjects had positive chlamydia cultures: 17%(13). More chlamydia positive subjects had abnormal Pap smears: 54%(7). Contraceptive use in chlamydia positive subjects included: 64%(7) oral contraception; 18%(2) barriers; 36%(4) no method. Chlamydia appears to be a common sexually transmitted disease in adolescent females and should be routinely cultured. The large number of abnormal Pap smears indicates the necessity of routine Pap smears in this population.

26 ARE ABNORMAL CT SCANS IN ANOREXIA NERVOSA ASSOCIATED WITH COGNITIVE, MEMORY, PERCEPTUAL-MOTOR OR PERSONALITY ABERRATIONS? I.R. Shenker, M. Nussbaum, M. Sonnenblick, (Spon. by P. Lanzkowsky). Sch. of Med., Health Sciences Ctr., State Univ. of N.Y. at Stony Brook and Long Island Jewish-Hillside Med. Ctr., Dept. of Ped., New Hyde Park, N.Y.

We have demonstrated that over 50% of anorexic patients have cerebral atrophy on CT Scans. In order to assess the psychological and cognitive implications of these changes evaluation was performed on 11 anorexic patients (9 females, 2 males, ages 12 to 20 years, mean age 15.9 years) to ascertain cognitive, memory, perceptual-motor and personality status. Average to superior scores were obtained by nine patients (82%) on the cognitive, memory and perceptual-motor measures:Wechsler Intelligence Scales, WISC-R or WAIS, Ravens Progressive Matrices, Trails A & B,Benton Test of Visual Retention, Berry-Buktenica Test of Visual Motor Integration, and Wide Range Achievement Test. Seven of these nine high functioning patients had moderate to severe cerebral atrophy on CT Scans (78%). Two additional patients with markedly abnormal CT Scans scored in very impaired ranges, but both had learning problems and school failure antedating the onset of anorexia by years. On tests of personality status 8 patients (73%) tested as mildly to severely depressed on the Beck Depression Inventory (Scores 11 to 43, Mean=23.8). Six of 10 patients showed markedly elevated MMPI scores consistent with personality pathology including depression. Five exhibited peak elevation (T-Scores 74-103, Mean=88) on the schizophrenia scale. Overall most patients remained cognitively intact, but the majority had significant depression and personality aberrations.

27 PREGNANCY OUTCOME IN THE VERY YOUNG ADOLESCENT Milton Westphal, Abner H. Levkoff, M. Clinton Miller, and Yvonne Michel. Medical University of South Carolina, Departments of Pediatrics and Biometry, Charleston, South Carolina.

Because of pediatricians' concern for pregnant adolescents, a group of 497 very young mothers age 13-15 years were compared to mothers 16 to 19 and 20 to 40 years by analyzing 22 factors for neonatal outcome, parturitional performance, obstetrical risk and physical characteristics. The data were derived from 6282 primiparous births over the past four years. Among factors studied were birthweight, gestational age, Apgar score, morbidity, mortality, presentation, length of labor, instrumentation, C-section, preeclampsia, cephalopelvic disproportion, premature rupture of membranes, maternal height, prepregnancy weight and weight gain during pregnancy. Analysis of variance tests showed no differences by age in maternal height and weight gain. Mean prepregnancy weight was higher in the 20 to 40 year age group. X^2 analyses were used to test the significance of associations among the remaining variables and maternal age. For the very young mothers, the observed values were not significantly different from the expected values for any of these 19 variables.

Pregnant adolescents and their offspring are not, according to these data, at a biological disadvantage. Literature suggesting that adolescent gravidae are at high risk may be based on data uncontrolled for parity.

28 FETAL OUTCOME - IS ADOLESCENT PREGNANCY A RISK FACTOR? Barry Zuckerman, Joel J. Alpert, Elizabeth Dooling, Edgar Oppenheimer, Ralph Hingson, Suzette Morelock, and Herb Kayne (spon. by Jeffrey B. Gould). Boston Univ. Sch. Med., Boston City Hosp., Depts. of Ped., Soc. Med. Sci.Boston Ma.

A study of maternal health and fetal development in a low SES population at Boston City Hospital provided an opportunity to explore whether(1)infants born to primiparous adolescents exhibit poorer outcome at birth than infants born to primiparous non-adolescents; and(2)if the outcome is poorer, whether the cause is adolescent status or other health habits or life situations. Four study pediatricians performed all physical and Dubowitz examinations without knowledge of the mothers' age. The birth weight, length, head circumference, length of gestation, Apgar scores and birth trauma of 275 infants of adolescent mothers (3-18 yrs) were compared at birth to 423 infants of nonadolescent mothers (19-30 yrs). The only difference noted was that infants of adolescents weighed 94 grams less ($p \leq .03$) than the infants of non-adolescents. Since the adolescents and nonadolescents differed on many characteristics which might affect fetal outcome, 23 factors were entered into a multiple regression analysis as independant variables. Health factors such as prepregnancy weight and weight gain, use of x-rays during pregnancy and marijuana use were independently and significantly ($p \leq .01$) associated with birthweight. Adolescent status was not independently associated with birthweight or any other growth or clinical risk parameter. Some of the health factors are amenable to clinical intervention and represent a greater risk to pregnancy outcomes than whether or not the mother is adolescent.

BEHAVIORIAL SCIENCES HEALTH SERVICES RESEARCH

29 A COMPARISON OF NON-FATAL MOTOR VEHICLE OCCUPANT INJURIES IN CRASH VERSUS NON-CRASH EVENTS. Phyllis F. Agran, Debora E. Dunkle (Spon. by Beverly C. Morgan), Coll. of Med., Dept. of Peds. and Public Policy Research Organization, Univ. of Calif., Irvine, Irvine, CA.

This study documents the incidence of non-fatal crash and non-crash events during a 16 mth data collection effort in 9 hospital emergency rooms located in one California county. Data were obtained from a standardized protocol and medical records (n=621). The Abbreviated Injury Scale (AIS) was used to grade injuries and the Injury Severity Score (ISS) was calculated. Comparisons of the mechanisms and severity of injuries between crash and non-crash events are described. Subsequent analysis indicates that approximately 12% of the children presenting to emergency rooms with motor vehicle related injuries were involved in non-crash events. Age-related differences between crash and non-crash children were significant in that younger children were primarily involved in the non-crash event. The mechanism producing the injury also differed between crash and non-crash children: while interior impact was the primary injury producing mechanism in both events, a much higher percentage of ejections occurred in the non-crash event (41% vs. 5%). ISS did not differ significantly between non-fatal crash and non-crash children, [X^2 (p) = 0.11]. Severe injuries are incurred in both crash and non-crash events, especially when a child is ejected from the vehicle. This severe mechanism of injury could be avoided by use of child restraint systems and/or by improved door lock mechanisms. Mandatory child restraint use legislation, if enforced, would be an effective preventive measure.

30 OBSTETRIC SURGICAL COMPLICATIONS OF ADOLESCENT PREGNANCIES. Betty L. Arnold, M. Douglas Cunningham, Diane M. Gagel, Department of Pediatrics, College of Medicine, University of Kentucky, Lexington.

Poor social and medical consequences of teenage pregnancies are generally known, but specific intrapartum and postpartum complications are less well documented. Medical records of early adolescent pregnancies ($\leq$ 14 yrs; n=109) were compared to primagravidas in late adolescence (15-19 yrs; n=111), and mature primagravidas (20-24 yrs; n=110). Infants of the youngest mothers were not significantly different for Apgar scores, gestational age, or birthweight. Both adolescent groups of mothers experienced 1 stillbirth. Three infants died in the youngest group; 2 infants died in each of the older groups. Youngest mothers had an increased rate of pre-eclampsia and were more likely to have third trimester bleeding. Of the mature group, 15.5% underwent cesarean section compared to 10.8% of the late adolescent group, and only 4.6% of the early adolescents (p=0.05). Forceps rotations were performed only for the early adolescent group (6.4%). Episiotomy was performed for 90.8% of the early adolescent group compared to 82.9% and 75.5% for the late adolescent and mature mothers. Fourth degree extension of episiotomies occurred in 17.4% of the youngest mothers compared to 7.2% and 6.4% for the older adolescents and mature mothers (p=0.01). Postpartum fever occurred in 12.8% of the under 14 group compared to 29.7% and 24.6% in the older groups (p<0.01). These data indicate a disinclination on the part of obstetricians to perform cesarean section for delivery of early adolescents, and a greater reliance upon episiotomy and forceps rotation.

31 PARENT-DOCTOR COMMUNICATION IN NEWBORN ETHICAL DILEMMAS. C.L. Berseth, Dept. of Pediatrics, Baylor College of Medicine, Houston, Texas (Spon. by Z. Friedman)

Since physicians (MD's) often counsel parents in decisions concerning newborn ethical dilemmas, MD's should be aware if parental attitudes differ from MD's attitudes. While 23 parents of 6wk old high risk newborns believe almost all babies can be saved, 44 pediatric residents are much more pessimistic ($p<.001$). Parents are more likely than MD's to favor resuscitation of infants born extremely prematurely or with brain damage ($p<.001$) and are less likely to favor active or passive infant euthanasia ($p<.001$) or abortion for the presence of a birth defect ($p<.001$). Parents believe babies with fatal anomalies not requiring ICU care should be sent home to die; MD's favor institutionalization or continued hospitalization ($p<.001$). While parents express a desire to know every detail about the care of their child, MD's believe giving less information provides adequate information. While 39 ICU nurses believe this pattern of MD communication imparts too little information, parents believe MD's tell them enough or too much about their babies ($p<.001$). Of 57% of parents with praises for ICU care, 3/4 spontaneously specify good communication with MD's as the major compliment. Parents are more optimistic than MD's that: 1) MD's always know how to save a sick baby, and 2) MD's can be trusted in the care of infants ($p<.001$), while they disagree that MD's are careless about caring for babies ($p<.001$). These data indicate that 1) parents have significantly different attitudes than MD's concerning ethical dilemmas, but 2) despite attitude differences, parents perceive that they maintain good communication with MD's and trust MD's have given ICU babies good care.

● **32** NONORGANIC FAILURE TO THRIVE (FTT): DEVELOPMENTAL & FAMILIAL CHARACTERISTICS. W.G. Bithoney and the Family Development Study, Children's Hospital, Boston.

41 Boston children hospitalized with nonorganic FTT were matched with 41 control subjects on age, SES, and race. A precoded maternal interview focused on family stress, isolation, infant health, and on the temperament and social maturity of the child. The data from the study were analyzed in several steps. A regression analysis was performed on all variables which significantly discriminated between cases and controls. 10 variables explained 81% of the between group variance on F-tests.

The most significant distinctions were poor child health ($p<.001$), high reactivity to visual and auditory stimuli ($p<.001$), and disordered feeding interaction ($p<.005$). Other significant case-control differences were: social isolation, few maternal opportunities to escape caregiving, the presence of a male adult in the family, fewer available extended family, fewer violent disagreements between parents, greater number of maternal unmarried years, and increased advocacy needs.

Children with FTT appear to have innate developmental idiosyncrasies. These conspire with social and familial factors to yield the current profile of nonorganic FTT. This study questions whether such findings are the cause of FTT or are better understood as its result.

33 ANOTHER MYTH: HOSPITAL VISITING PATTERNS OF INNER CITY MOTHERS. Eleanor C. Blitzer, Barry S. Zuckerman Janet T. Pozen (sponsored by Jeffrey B. Gould). Boston University School of Medicine, Dept. of Soc. Med. Sci., and Boston City Hospital, Dept. of Ped., Boston, Ma. 02118

Poor hospital visiting patterns of inner city mothers have been described as a problem in the adjustment of children to hospitalization. Our survey of staff (MD and RN) perceptions (N=62) of maternal visiting on our inner city pediatric unit confirms the prevalence of this formulation. Our study of actual visiting patterns and attitudes of mothers of 74 children consecutively admitted under the age of 5 does not support this view. While pediatric staff believed that only 20% of mothers visited 4 or more hours a day, visiting records show that 70% of mothers visited at least that and 30% of mothers roomed-in for at least one day. Also contrary to staff predictions, mothers age, employment, number of other children, and payment status were unrelated to the amount of time she visited. These mothers recognized the significance of visiting to the child regardless of the severity of their medical problem and stayed longer if they felt this helped their child cope with hospitalization ($p<.05$). Mothers who reported problem behavior prior to hospitalization in their children visited less ($p<.01$) and should be identified for appropriate intervention.

34 IMPACT OF CYSTIC FIBROSIS ON FAMILY LIFE WE Bohannon, SA Phillips, WF Gayton, and SB Friedman, University of Maryland School of Medicine, University of Maryland Hospital, Department of Pediatrics, Baltimore

A comprehensive assessment of the impact of cystic fibrosis (CF) was conducted with 43 CF families. A semistructured interview with parents (43 mothers and 29 fathers) focused upon family functioning, parent-child interactions, sibling and peer relationships, and medical issues related to CF. Parents' responses were coded by two independent raters to identify "major problems," "minor problems," or "no problems." Out of the 62 questions assessing areas of potential problems, only 8 were viewed by parents as posing "major problems" for themselves and/or their children. Areas thus identified will be presented in detail to indicate the nature of the problems. The impact of hospitalization was the most prevalent concern: 60% of mothers and 58% of fathers identified this as a "major problem." Issues included uncertainty regarding the outcome (34%), separation from the child (25%), and other pressing family responsibilities (16%). Communication between the parents was considered a "major problem" by 28% of mothers, but only 3% of fathers. Ten to 15% of parents described problems regarding their marital relationship, accepting the illness, feeling they should do more for their CF child, feeling their other children had been deprived or complained about inattention, or their relationship with the ill child's grandparents. These data indicate that most CF families are generally coping successfully with the impact of a serious chronic illness, but that health-care professionals should be alert to areas of potential problems.

35 RELATIONSHIP BETWEEN NEONATAL NUTRITION AND SUBSEQUENT DEVELOPMENT IN THE VERY LOW BIRTHWEIGHT PREMATURE INFANT. Frances Borian, Judy Bernbaum, Gilberto R. Pereira. (Spon. by W.W. Fox). Univ. of Pa. Sch. of Med., and Dept. of Peds., Children's Hosp. of Phila., Phila., PA.

The relationship between inadequate nutrition in early infancy and subsequent brain growth and development has been reported. To determine the extent of this relationship, we studied 19 high risk, very low birthweight, premature infants (mean $\pm$ SD birth wt. .97 $\pm$ .19 kg, gest. age 29 $\pm$ 2 wks) requiring intensive care management during the neonatal period and followed them up to 12 mos. adjusted age (AA). Nutritional status during the neonatal period was correlated with subsequent growth and development at 12 mos. AA using standard growth parameters and the Bayley Scales of Infant Development. Follow-up measurements were: wt. = 8.3 $\pm$ 1.2 kg; length = 72.3 $\pm$ 2.7 cm; head circumference = 45.3 $\pm$ 1.6 cm; Mental Developmental Index (MDI) = 71.3 $\pm$ 18.7; Psychomotor Index (PDI) = 78.4 $\pm$ 18.1. There was an inverse correlation between the number of weeks in the neonatal period in which the caloric intake was lower than 80 cal/kg/day ($r=.61$, $p<.01$) and protein intake was less than 2 gm/kg/day ($r=.52$, $p<.05$) with the PDI scores. Neonatal nutrition was only weakly related to growth parameters and MDI at 12 mos. AA. The low correlation with MDI may be due to the fact that abnormalities in motor development can be identified earlier than those in mental development and therefore this correlation should be retested at older ages. This study indicates that early inadequate protein and caloric intake is associated with lower PDI scores in premature infants at 12 mos. AA and emphasizes the need for close nutritional monitoring during the critical neonatal period.

36 CHILDREN'S PERCEPTIONS OF OWN AND MOTHER'S VULNERABILITIES AND MEDICINE USE EXPECTANCIES. Patricia J. Bush, Frances R. Davidson, Frances A. McCrackin, Ronald J. Iannotti (Sponsored by Joseph A. Bellanti, M.D.). Georgetown University School of Medicine Department of Community and Family Medicine, Washington, D.C.

Following a pilot study of 60 children in 1980-81, 420 children, grades K-6, were interviewed about their orientations toward medicines and abusable substances. Among specific areas were children's perceptions of vulnerability to common health problems (colds/upset stomach/fever/nervousness/trouble sleeping) and how they related to medicine use expectancies and perceptions of mothers' vulnerabilities and medicine use expectancies.

Results indicated children in all grades, SES level, and both sexes believed themselves to be more vulnerable than their mothers. On average, children were more likely than their mothers to take something special for colds, fever, upset stomach and less likely for nervousness and trouble sleeping. Expectancy scores were higher for children specifying medicines (rather than changes in their routine or diet) and lower SES children. These results suggest that expectancies of medicine use are formed early. Children distinguish between themselves and other family members relative to illness categories and might benefit if medicine use information was provided them directly by their physicians.

37 THE MOTOR EFFICIENCY RATING: A SYSTEM FOR DETECTING MINOR NEUROLOGICAL DYSFUNCTION. Betsy Busch, Melvin D. Levine and Lynn Meltzer. Children's Hospital Medical Center and New England Medical Center, Boston, MA.

The Motor Efficiency Rating (MER) was developed to provide a composite scoring system quantifying one type of minor neurological sign in the school-age child. 246 7-9 year-old children were studied. The sample included clinic patients referred because of learning problems and randomly selected second graders from the community, all of whom received physical examinations and educational testing. The community sample also received intelligence testing (WISC-R). All children had extensive neurodevelopmental assessments, within which were the component tasks of the MER System. The MER is comprised of 25 observations for the presence and severity of various associated movements; scores could range from 0 to 50. The mean MER for clinic children was 27.96 ± 10.37 while the mean MER for the community sample was 36.24 ± 8.81 ($p<.0001$). Strong correlations existed between low MER and other minor neurological signs ($p<.001$), temporal-sequential disorganization ($p<.001$), visual-spatial disorientation ($p<.001$), fine and gross motor difficulties ($p<.001$) and major attentional problems ($p<.001$). No significant relationship existed between MER and IQ scores or language function on the neurodevelopmental assessment. When single items were studied, much higher false positive and negative rates were found than for the composite rating system.

Minor neurological signs, such as associated movements, can be valid indicators of certain developmental dysfunctions, especially when quantified as aggregate findings.

38 THE PRIMITIVE REFLEX PROFILE: A NEW INSTRUMENT TO ASSESS INFANT MOTOR DEVELOPMENT. Arnold J. Capute, Frederick B. Palmer, Bruce K. Shapiro, Renee C. Wachtel, Alan Ross, and Pasquale J. Accardo. (Spon. by Mark Batshaw). The Johns Hopkins U. Med. Inst., The JFK Inst., Dept. of Peds., Baltimore.

The utility of primitive reflex assessment in the motor-impaired child has been hindered by lack of a quantitative description of normal reflex maturation. The Primitive Reflex Profile is a quantitative examination technique used to evaluate primitive reflexes. Standardization data was obtained on a cohort of 381 normal infants examined serially at each well baby visit between birth and two years of age. Reflex activity generally decreased with increasing age, although distinctive patterns of maturation were noted for individual reflexes. The Asymmetric Tonic Neck Reflex was present in the majority of subjects at birth, peaked at two months, then declined steadily throughout the first year. The Tonic Labyrinthine reflex in Prone was most pronounced at four-to-six months and declined more slowly. The Symmetric Tonic Neck Reflex was seen only in a minority of subjects between four and six months. The Moro Reflex was uniformly present at birth and was suppressed by six months. Nonsegmental Rolling ("log rolling"), both head-on-body and body-on-body, was replaced by segmental rolling after six months. Obligatory responses, seen frequently in cerebral palsy children, were not seen in any reflex at any age in this normal population. This standardized examination technique allows primitive reflexes to be objectively assessed.

39 PARENTAL EXPECTATIONS FOR INDEPENDENT FUNCTIONING OF CHILDREN WITH PKU AND CHILDREN WITHOUT PKU, THOMAS J. CASEY, M.D. DEBORAH M. PITALNIK, PH.D. (ST. CHRISTOPHER'S HOSPITAL FOR CHILDREN, TEMPLE UNIVERSITY SCHOOL OF MEDICINE. This study used a child training practices scale to examine independence training in children with phenylketonuria (PKU). 14 children whose families constituted the experimental group were from 2 to 5 years old, had been on the dietary regimen since prior to two months of age, were of normal intelligence, and had no siblings with PKU. Control group parents were matched for social class, child age, birth order, and number of children in family; none had children with handicaps. Parents of PKU children were significantly more restrictive of their children's independent functioning than were the parents of the NON-PKU children. Fathers and mothers of PKU children differed in the types of restrictions they expressed. More restrictions differentiated the PKU fathers from the NON-PKU control group fathers than differentiated the PKU mothers from the NON-PKU mothers. Social class, child age, and birth order were found to be significant intervening variables. Strong, internalized controls related to food restrictions were noted in the PKU children in the study, seemingly developed as a result of parental training strategies. Parents relied on these child controls to enhance dietary compliance in a manner that permitted the child more social independence.

40 THE EFFECTS OF WEANING ON INFANT BEHAVIOR IN THE FIRST YEAR Steven K. Clarke and Robert J. Harmon (Spon. by David A. Wenger), University of Colorado School of Medicine, Departments of Pediatrics and Psychiatry, Denver.

In the first phase of a multi-dimensional study of the effects of weaning from the breast on infant behavior, a maternal interview and questionnaire were developed and administered to 100 middle-class American mothers who weaned their infants during the first year of life. The major objectives of the interview and questionnaire were to provide detailed descriptive data about the human weaning process and to identify and assess the behavioral responses of infants to weaning in the first year.

Preliminary results indicate that some infants exhibit increased fussiness and/or a change in sleep patterns immediately following the onset of weaning, and that these effects are more likely to occur with infants whose mothers initiate weaning during the second half of the first year. One explanation for this apparent age-related differentiated response may be that breast-feeding becomes an increasingly important means of emotional assuagement for infants as they reach higher levels of cognitive and emotional development.

The mean and median age for the initiation of weaning was six months. The mean and median age for the completion of weaning was seven months. Many infants were reported to have weaned themselves, but most were receiving significant nutritional supplementation during this period of self-weaning. The most common reason given by mothers for weaning was that their milk alone was not adequately assuaging their infants' hunger.

41 LANGUAGE MILESTONES FROM 0-3 YEARS AS AN INDEX OF DEVELOPMENTAL STATUS. James Coplan, John R. Gleason, and Margaret L. Williams. SUNY-Upstate Medical Center, Dept. of Pediatrics, and Syracuse University, Syracuse, N.Y.

The need exists for a well-validated language screening instrument covering the first 3 years of life, since this is when most language skills emerge. To examine the relationship between language milestones and development during the first 3yr. of life, and to devise a brief language screening test suitable for physician use, an early language milestone scale (ELM Scale) was written, normed and validated. Fortyone items written by one of us (JC) were normed on 191 children age 0-36 months compromising a chronologic, racial, and socioeconomic cross section of the general population. Percentile values for the emergence age of each item were obtained; pass/fail criteria for the ELM Scale as a whole were developed based upon these values. The ELM Scale was then given to 119 children referred to us for evaluation of possible developmental disability. Each child was also formally tested by a psychologist and speech pathologist who were unaware of the child's performance on the ELM Scale, with the following results:

ELM Scale		Formal Testing: Abn	Formal Testing: Norm
	Abn	63	4
	Norm	2	50

Sensitivity = $\frac{63}{63+2}$ = .97

Specificity = $\frac{50}{50+4}$ = .93

We conclude that language milestones from 0-3 yr correlate closely with developmental status. The sensitivity and specificity of the ELM Scale justify its use as a screening instrument among children at risk for developmental disability.

42 NEONATAL AUDITORY BRAIN STEM RESPONSES-LACK OF PROGNOSTIC VALIDITY. C.Cox, M.Hack, D.Metz, RB&C Hosp. Dept. Ped., CWRU and CSU. Cleve.OH. (Spons.A.Fanaroff).

Although auditory brain stem responses (ABR) are widely recommended for assessment of neonatal auditory function, infants so tested have had little long term follow up. To assess the prognostic validity of neonatal ABR, we tested 50 VLBW(<1.5Kg) infants prior to discharge and then at 4 and 20 months corrected age.

Total (n=50)	Abnormal ABR n (%)	Comments
Neonatal	9(18%)	-
4 Months	3(6%)	All cochlear/central
20 Months	9(18%)	3 cochlear/central, 6 middle ear disease

Initially 9 neonates(18%)were abnormal (Wave V latency or C.T. >2 SD of normal). At 4 months only 1 of these infants and 2 others were abnormal. Thus of the 9 infants initially classified as abnormal only 1(11%) had abnormal responses at all 3 tests with permanent hearing loss at 20 months whereas of 41 infants initially classified as normal, 6(12%)were subsequently abnormal (4 with middle ear [M.E.] disease and 2 central defects). Abnormalities which disappeared after the neonatal period correlated best with birth wt., RDS, Neonatal risk score($p<.05$)and gentamycin therapy ($p<.001$). At 20 months 9(18%) infants were abn. only 3 of whom had been abn. as neonates(1 permanently impaired and 2 who had become normal at 4 months but now had conductive loss due to M.E.).

Thus, since neonatal ABR testing is a poor predictor of subsequent hearing loss and since M.E. contributes significantly to later hearing loss during infancy and early childhood, follow up hearing testing is imperative.

43 CHILD ABUSE BY THERMAL INJURY - Bernard J. Cullen, Pamela S. Brewster, Angela Best, MCO, Department of Pediatrics, Spon. by Margaret Robinson

A retrospective analysis of the records of children admitted to a burn unit of an urban hospital over a 5-year period was undertaken to determine the prevalence and characteristics of thermal injuries in these patients. Of the 110 pediatric admissions during this period, 14 (12%) were found to have inflicted thermal injuries that constituted child abuse. This group was mostly comprised of white males with a range in age of 8 months to 11 years (average age was 6.1 years.) Half of the abused children came from female-headed households, and were either the youngest or middle child and had three or fewer siblings. The burn characteristics revealed that 36% of the abused group were burned over 20% or more of TBSA, and over 70% of these were second degree scald burns.

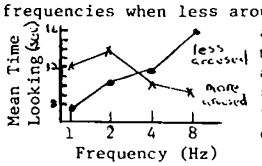
The distribution, depth and extent of the burns for children with inflicted thermal injuries demonstrated a variable pattern of thermal abuse for school age children involving the upper extremities (34%), trunk (17%), head and neck (11%), and buttocks and perineum (7%). While other studies have demonstrated the incidence of abuse at a younger age, this study suggests that the risk of child abuse by thermal injury does not decrease with age. Instead, although there is a prevalence of upper extremity burns, the occurrence of nonspecific burn patterns suggests that the distribution of thermal injuries may become more variable with the advancing age of the child, thus making the detection of abuse more difficult.

44 DEVELOPMENTAL OUTCOME OF ≤1250 GM. NEONATES BORN IN 1980: >90% RETRIEVAL IN A PROGRAM FOR AN INDIGENT POPULATION. MB Escobedo, JL Hilliard, J Schlansker, MA Hunter, C McLerran, Dept. of Pediatrics, Univer of Texas Health Science Center, San Antonio (Spon. by Y Brans)

The efficacy of neonatal intensive care for the very low birthweight (VLBW) infant has been difficult to evaluate in low income groups because of poor compliance and incomplete patient retrieval All VLBW infants (≤1250 gm) born at the Bexar County Hospital in 1980 have been followed in a program which provides continuity of contact with medical professionals from birth through 2 yr, comprehensive medical care, and periodic developmental evaluation. Of 5674 infants born in 1980, 47 (0.8%) weighed 500-1250 gm. Twenty-eight (60%) survived and 26 of 28 (93%) have been successfully followed for at least 1 yr. Mean birthweight and gestational age were 1026 gm. (range 709-1233) and 29 weeks (26-37). Sixteen (62%) were males and 16 (62%) firstborn. Four (15%) were SGA; the remainder AGA. Eight (31%) had Apgars at 1' or 5' ≤ 3; 21 (81%) required oxygen and 18 (69%) respirators. Eight (31%) had 17 hospitalizations in the first yr primarily for lower respiratory disease. Parents were primarily Spanish-surnamed (71%), married (71%) and indigent. Over half had annual incomes ≤$3,840. Sixteen mothers (61%) were ≤20 yrs old. Bayley exams at 12-18 mos. showed a mean MDI (mental) score of 95 (<50-115) with 2 (8%) >2SD and 4 (15%) >1SD below the mean. The mean PDI (motor) score was 90 (<50-111) with 1 (4%) >2SD and 6 (23%) >1SD below the mean. This inborn poor, Mexican-American, medically complicated, VLBW group was retrieved with an appropriate program design at a very high rate and was demonstrated to have a favorable developmental outcome.

45 ATTENTION IN NEONATES IS A FUNCTION OF AROUSAL STATE. Judith M. Gardner and Bernard Z. Karmel (Spon. by E. Brown) Albert Einstein Coll. of Med., Dept. of Psych., Bronx, NY and Mt. Sinai Med. Ctr., Dept. of Neurosurg.,NY

Deficits of attention in newborns have been implicated as predictors of neurobehavioral dysfunction. We devised a method based on the Fantz preference technique which produces a systematic pattern of attention describing the relationship between arousal states and visual preferences in neonates. Healthy full-term infants (n=12; mean postnatal age=51 hrs; mean birthweight= 3295 gms) were tested in two different states of arousal; a more aroused state (unswaddled prior to feeding) and a less aroused state (swaddled after feeding). Infants viewed simultaneous presentations of two 15 cm^2 homogeneous light fields, each of which was independently turned on and off by a square-wave generator set at one of four frequencies (1, 2, 4, or 8 Hz). In each condition, all combinations of two different frequencies were presented for 30 sec each. The mean amount of time infants looked at each of the four frequencies was calculated and plotted. The resultant curves for the two arousal conditions were compared and demonstrated that infants systematically look longer at faster frequencies when less aroused and at slower frequencies when more aroused ($p < .001$). Our method permits measurement of response patterns in two arousal conditions that together quantitatively describes neonatal visual attention. We believe that infants who deviate from this pattern should be followed for potential dysfunction.



46 HEAD CIRCUMFERENCE (HC) GROWTH AND DEVELOPMENTAL OUTCOME AT TWO YEARS IN VERY LOW BIRTHWEIGHT (VLBW) INFANTS. Steven J. Gross and Carol O. Eckerman (Spon. by Samuel L. Katz). Duke Univ. Med. Ctr., Dept. of Ped., Durham.

The predictive role of early HC growth for subsequent development was evaluated in all 85 survivors with birthweight <1500 gm. born from 1/1/78 to 3/31/79. Infants were divided into 4 groups based on HC at birth (<10% or ≥10%) and HC growth at six weeks (<3.5 cm or ≥3.5 cm). The VLBW infants and 95 full-term infants matched in social background were evaluated at 6, 15 and 24 months with neuromotor (NM) examinations and the Bayley Scales of Infant Development. The percent of POOR OUTCOME (major NM defect and/or DI <80) was significantly related to HC growth.

HC AT BIRTH:	<10%		≥10%		FULL-TERM
Δ HC AT 6 WKS:	< 3.5 cm (n=9)	≥3.5 cm (n=12)	<3.5 cm (n=32)	≥3.5 cm (n=32)	INFANTS (n=95)
6 MONTHS	100	42	43	7	2
15 MONTHS	100	8	44	3	3
24 MONTHS	100	25	55	19	16

The incidence of poor outcome for infants with HC at birth ≥10% and HC growth ≥3.5 cm was low and similar at each age to that for full-term infants. At 6 months, the other 3 groups of VLBW infants had poorer outcome. At 15 and 24 months, the two groups with less postnatal HC growth continued to show poorer outcome; however, the group with HC at birth <10% but greater postnatal HC growth demonstrated catch-up, such that outcome was now similar to that for full-term infants. The group with poorer HC growth at both periods showed uniformly poor outcome at all ages.

● **47** CRITICAL PERIOD FOR CATCH-UP GROWTH IN VERY LOW BIRTHWEIGHT (VLBW) INFANTS. M.Hack, I.Merkatz, S.McGrath, A.Fanaroff. Dept. Ped., RB&C Hosp., CWRU, Cleve. OH.

We have documented the important relationship between growth and developmental outcome of VLBW infants. To determine the potential and correlates of catch-up growth, we prospectively followed 182 VLBW (<1.5Kg) born in 1977-78 until 33 months corrected age. 147 were AGA (mean G.A., 29 wks; BW 1.2Kg; HC 26.5 cm; HT 38.8 cm) and 35 were SGA, <3% (mean G.A. 32 wks; BW 1.14 Kgs: HC 27.0 cm; HT 37.9 cm). They were defined as small if <3% and growing appropriately if >3% at 40 wks, 8, 21, and 33 months corrected age.

INTRAUTERINE GROWTH	WEIGHT <3 PERCENTILE AT 40 Wks n (%)	8 Months n (%)	21 Months n (%)	33 Months n (%)
AGA (n=147)	67(46%)	40(27%)	28(19%)	25(17%)
SGA (n=35)	32(91%)	17(49%)	17(49%)	16(46%)

Thus potential for catch up in SGA VLBW infants is limited to infancy and the failure to catch up in 46% may relate to the timing and severity of the growth deficit in utero. In contrast AGA infants may grow poorly during the neonatal period yet catch up as late as the 2nd year. Significant correlates of impaired growth at 21 months were head circ. <3% at 40 wks ($p<.0001$), social class ($p<.001$), marital status ($p<.003$), BW ($p<.005$), neonatal risk score ($p<.05$), low developmental quotient ($p<.05$) and neurological abnormality or chronic disease ($p<.04$). 7/15(47%) of infants with neurologic abnormality were small, whereas32/157(20%) of the neurologically intact infants were undergrown at 21 months.

Thus there appears to be a critical period for catch up growth in VLBW infants when intervention may be possible.

● **48** UTILIZATION OF PHYSICIAN ASSISTANTS ON A LARGE NEWBORN SERVICE. Joan E. Hodgman, Nancy Edwards, George A. Halterman, Division of Neonatology, Dept. of Pediatrics, USC School of Medicine and Womens Hospital, LAC/USC Med. Ctr., Los Angeles, Ca., USA.

On July 1, 1981 we began the initial year of a one year postgraduate training program for physician assistants (PAs) in the specialty of Neonatology. The program was established, 1)to provide primary care to high-risk newborns in a highly technological environment; 2)to provide PAs an opportunity for postgraduate training in a specialty area. Three PAs were selected on the basis of academic performance, completion of an accredited PA Program, national board scores, interviews, and prior experience. They were assigned to specific teams composed of a Fellow, a pediatric resident, and an intern. The PA follows the team schedule, including night call, and is responsible for admission work-ups in rotation with the intern, and for performing a variety of diagnostic and therapeutic procedures. The PA also has primary responsibility for follow-up management of the baby, always under appropriate physician supervision. PA "residents" are utilized in all areas of the service, i.e. the Normal Nursery, NICU, Special and Intermediate Care Nurseries, Delivery Room Resuscitation Team, and the High Risk Preemie Follow-up Clinic. Evaluations by supervising physicians reveal that the PAs are demonstrating a high level of clinical performance, and have been well received across the entire Newborn Service. We believe that utilization of PAs may be a viable solution to the problem of decreasing involvement of both practicing pediatricians and pediatricians in training, in providing primary care in newborn nurseries.

49 SOLEMNITY IN THE IRON DEFICIENT INFANT. Alice S. Honig and Frank A. Oski. College of Human Development, Syracuse University, and Dept. of Pediatrics, SUNY, Upstate Medical Center, Syracuse, New York.

In an effort to better characterize the behavioral changes that accompany iron deficiency in infancy a "Solemnity Score" (SS) was developed and utilized in conjunction with the Bayley Mental Development Index (MDI). Both tests were administered prior to, and one week after, treatment with IM iron. Infants, ages 9 to 12 months, were stratified into 4 groups based on laboratory tests:

	Hb	Ferritin	RBC Porphyrin	MCV
a. Normal	>11	>12 ng/ml	<30 µg/dl	>72 fl
b. Iron depleted	>11	<12 ng/ml	<30 µg/dl	>72 fl
c. Iron deficient	>11	<12 ng/ml	>30 µg/dl	>72 fl
d. Iron deficient	>11	<12 ng/ml	>30 µg/dl	<72 fl

Solemnity was scored as follows: 0, wreathed in smiles, with sparkling eyes, laughter; 1, quite smiley; 2, occasional smile; 3, one or two smiles/hr.; 4, no smiles/hr. After iron therapy both scores on the Bayley MDI and the SS changed significantly in the iron deficient infants. In groups 3 and 4 the mean increase in the MDI was 21.9; for groups 1 and 2 it was 5.4 ($p < .01$). The SS score fell from 2.72 to 0.61 in the iron deficient infants; in groups 1 and 2 the SS score changed from 1.5 to 0.85. Ten of 18 infants in groups 3 and 4 became less solemn and 6 remained unsolemn. In contrast only 3 of 20 infants in groups 1 and 2 became less solemn; 14 remained unsolemn. These results suggest that even non-anemic, iron deficient infants have a characteristic demeanor that should alert physicians to the presence of this common nutritional deficiency.

50 A PSYCHOLOGICAL EVALUATION OF PRE-ADOLESCENTS WITH RECURRENT ABDOMINAL PAIN (RAP). Susan Jakob, Louis Najarian, Fred Daum, Harvey Aiges, Jim Markowitz, and Mervin Silverberg. Yeshiva University, Department of Psychology and Cornell University Medical College, North Shore Univ. Hosp., Departments of Psychiatry and Pediatrics, New York.

To determine the specific psychological characteristics of pre-adolescent girls with RAP, three variables (1) dependency needs, (2) conflict about sexual identity, and (3) pre-disposition to somatization were evaluated in 7 pre-adolescent girls ages 10-13 with RAP, 7 with inflammatory bowel disease, and 7 without illness. All were matched for age and IQ by the W.I.S.C.-R. Each individual was given a standard psychological battery consisting of the Draw-A-Person, Thematic Aperception Test (T.A.T.), and Rorschach tests. Additionally, their parents answered questions regarding medical, psycho-social, and behavioral issues. All tests were administered by a researcher "blind" to the specific diagnoses and were scored independently by 2 psychologists. Several items in the questionnaire reveal significant differences related to dependency needs and predisposition to somatization ($p<0.05$) between those girls with RAP and the 2 other study groups. These results are confirmed by items in the T.A.T. and the Rorschach tests which also demonstrate significant differences in dependency needs, conflict about sexual identity, and pre-disposition to somatization. In summary, the psychological evaluation of pre-adolescents with RAP by questionnaire, T.A.T. and the Rorschach test indicate that pre-adolescent girls may have specific psychological characteristics which predispose them to recurrent abdominal pain.

51 INFANTS OF DRUG DEPENDENT WOMEN: EVALUATIONS BY THE BAYLEY SCALE OF MENTAL DEVELOPMENT, Karole Kaltenbach, Betty Leifer, Loretta P. Finnegan, Thomas Jefferson University, Department of Pediatrics, Philadelphia, Pennsylvania.

A longitudinal investigation is being conducted to evaluate the developmental status of 50 infants born to drug dependent women enrolled in Family Center, a comprehensive treatment program providing psychosocial and medical services as well as methadone maintenance for opiate abusing women. Infants were assessed at 6 and 12 months of age with the Bayley Scale of Mental Development. At six months of age, the mean mental development index (MDI) was well within the normal range (mean MDI = 105). However, males had significantly higher scores than females, mean MDI's were 109 and 102 respectively. Twenty-four infants have reached 12 months of age and their average performance continued to be within the normal range of development (mean MDI = 103). The repeated assessments at 6 and 12 months of age revealed a significant decline in Bayley Scores for male infants (6 month mean MDI = 114; 12 month mean MDI = 103). There were no differences in scores between male and female infants at 12 months of age. The sex differences found at 6 months of age are inconsistent with the literature and suggest the need for further research to determine if drug dependent women are more responsive to male infants during the first few months of life. Overall, these data indicate that infants born to drug dependent women do not suffer any demonstrable developmental sequelae during the first year of life.

52 KNOWLEDGE OF CHILD DEVELOPMENT IN DRUG DEPENDENT MOTHERS, Karole Kaltenbach, Betty Leifer, Loretta P. Finnegan, Thomas Jefferson University, Department of Pediatrics, Philadelphia, Pennsylvania.

Outcome of children born to drug dependent women has been an area of concern for health professionals. Previous research has been directed primarily toward identifying the medical risk factors associated with prenatal exposure to narcotic agents. This has resulted in little information regarding environmental risk factors concomitant to this population. In order to investigate the specific characteristics of these drug dependent women that are related to child rearing practices, a Knowledge of Child Development questionnaire was administered. Subjects where opiate abusing women enrolled in a comprehensive treatment program providing psychosocial and medical services as well as methadone maintenance. All of the women (N = 30) tested had a history of at least 2 years of drug abuse, an average of 11 years of education and an average age of 28 years. Of 33 test items, 14 were answered incorrectly by over 1/3 of the mothers and 6 questions were answered incorrectly by more than half. The most frequently missed questions pertained to basic developmental milestones. Mothers consistently underestimated the age by which a child should be able to walk, talk, and have the physiological maturity for toilet training. As a practical application of this information, parenting classes, within comprehensive treatment programs, should stress basic infant development in order to avoid unrealistic and inappropriate expectations that may damage mother-infant interaction.

53 NEONATAL PERCEPTIONS OF DRUG DEPENDENT MOTHERS, Karole Kaltenbach, Betty Leifer, Loretta P. Finnegan, Thomas Jefferson University, Department of Pediatrics, Philadelphia, Pennsylvania

A mother's perception of her newborn has been found to be an important factor in the psychological and social development of her child. In order to more fully understand the risk factors for infants born to drug dependent women, this study investigated how these women perceive their infants. Sixty drug dependent women and 21 non-drug dependent women of comparable socioeconomic and medical backgrounds were administered the Broussard Neonatal Perception Inventory 24 hours post partum. Drug dependent mothers had significantly more negative perceptions of their newborns than non-drug dependent mothers ($\chi^2 = 4.17$, $p < .05$). In addition, differences in maternal perceptions within the drug dependent group were found to be a function of severity of withdrawal. Mothers of infants who subsequently required pharmacotherapy for abstinence had significantly more negative perceptions than mothers of infants who did not require therapy ($\chi^2 = 7.38$, $p < .01$). Although drug dependent mothers may have more negative perceptions because they expect their infants to undergo abstinence, studies with normal infants have found that mother's perceptions are often unrelated to the physical condition of the child. These findings suggest that infants born to drug dependent women may be at risk for maladaptive mother-infant relationships and that maternal characteristics specific to this population must be better understood.

54 DEPRESSIVE SYMPTOMATOLOGY, ANXIETY AND LIFE EVENTS IN CHILDHOOD CANCER PATIENTS. Stuart L. Kaplan, Pam Lenon, Chantal Weinhold, Carol Einhorn, Philip Lanzkowsky. Sch. of Med., Health Sciences Ctr., SUNY at Stony Brook and Long Island Jewish-Hillside Med. Ctr., Dept. of Pediatrics, New Hyde Park, N.Y. 11042.

In order to study the prevalence of psychiatric symptomatology in childhood cancer patients the Beck Depression Inventory (BDI), Children's Depression Inventory (CDI), the State-Trait Anxiety Inventory (STAI), the State-Trait Anxiety Inventory for Children and a Life Events Inventory developed for this population were administered to 34 children with cancer between the ages of 8-18 years. Illness variables such as length of time since diagnosis and number of remissions were considered in the data analysis. Eight of the 17 adolescents studied obtained a cut-off score on the BDI indicative of mild depression and of the 17 children studied, five achieved a cut-off score on the CDI indicative of mild depression. In both children and adolescents there were significant differences between the depressed and non-depressed children on the other instruments administered. There were less positive life events ($p< .01$), more negative life events ($p< .05$) and more trait anxiety ($p< .01$) in the depressed than the nondepressed groups. Illness variables were not significantly related to life events and the other measures of psychiatric symptomatology. Thus, half of the adolescents studied and one third of the children studied demonstrated evidence of psychologic disturbance on all of the instruments administered.

55 INTRAVENTRICULAR HEMORRHAGE (IVH) VENTRICULAR DILATATION AND OUTCOME. Anne Koons, Shyan Sun, Richard Koenigsberger, Mathias Hagovsky, Carol Bechtold. (Spon. F. Behrle) New Jersey Med. School, Div. Neonatology, Newark, N.J.

From Sept. 1980 thru Sept. 1981, 21 infants with IVH were followed. Papile's classification with a modification in Stage III was used to categorize these neonates. Stage IIIa was used for posterior horn dilatation alone and/or minimal dilatation of the lateral ventricles, IIIb for moderate dilatation of entire ventricular system. Outcome was assessed quarterly by Bayley testing and neurologic exam. 4 of 7 patients with Grade IIIb IVH failed to demonstrate complete resolution of ventricular dilatation. Three infants (12, 9 & 5 months) had normal developmental assessment and neurologic exam, although head circumferences followed the 90th percentiles. A fourth infant with early reduction of ventricular size later developed progressive dilatation requiring shunting at 13 months.

IVH	Stage I	II	IIIa	IIIb	IV	
Bayley MDI >85	5	3	4	4	1	
84-75			1	1		
74-50				2(1 RLF)		6/21 Abn.
↑muscle tone		1		2		
Hemiparesis					1	

The finding of normal developmental outcome in all classes of IVH implies that other determinants besides the bleed may be more important prognosticators of CNS performance. Ventricular size does not necessarily correlate with any specific sign of CNS dysfunction. Extended evaluation is important to clarify ultimate outcome.

56 MATERNAL PSYCHOLOGICAL DETERMINANTS OF INFANT OBESITY: DEVELOPMENT AND TESTING OF TWO NEW INSTRUMENTS. Michael S. Kramer, Ronald G. Barr, Denis G. Leduc, Christiane Boisjoly, and Ivan B. Pless. McGill U. Faculty of Med., Depts. of Pediatrics and Epidemiology and Health, Montreal.

Since maternal psychological factors may affect infant feeding and thus "confound" the relationship between feeding and subsequent obesity, we have developed and tested two instruments to measure such factors. The Maternal Preconceptions of Ideal Infant Body Habitus (IBH) consists of 4 drawings of 9-month-olds exhibiting a range of body habiti from quite lean to very chubby; new mothers are asked to rank the 4 in order of preference for their new baby. The Maternal Feeding Attitudes (MFA) is a 10-item questionnaire addressing the new mother's food "pushiness". After extensive piloting, the final versions of both measures were tested (and retested) prospectively in a sample of 50 consecutive women giving birth to normal full-term healthy newborns.

Both the IBH and the MFA produced high test-retest intraclass correlation coefficients (R_I's): .92 and .95, respectively. Significant inverse correlations were found between the IBH and both maternal age ($r=-.38$; $P=.004$) and the Green SES index ($r=-.28$; $P=.025$), indicating that older, higher-SES mothers prefer leaner infants. Breast-feeding mothers had significantly lower mean IBH scores than did formula-feeding mothers ($P=.029$). The MFA, by contrast, was not associated with any of these variables. We conclude that maternal adiposity preference and feeding attitudes can be reliably measured. Owing to their possible associations with infant obesity and its determinants, we urge that these factors be included in future studies in this domain.

57 TREATMENT OF ANOREXIA NERVOSA (AN) IN A CLINICAL RESEARCH CENTER (CRC). Richard E. Kreipe, Barbara Lipinski, Christopher Hodgman, Dept. of Peds. & Psychiatry, Univ. of Rochester, Strong Mem. Hosp. Med. Ctr., Rochester, N.Y. (Sponsored by Gilbert B. Forbes)

Bruch has called behavior modification to induce weight gain in AN "perilous". We report key findings of a successful behavioral regimen that combined treatment and metabolic studies for 8 patients with AN (none with vomiting) in a CRC. All patients adjusted satisfactorily to the protocol and met the discharge weight goal in 26 to 64 days. The research-care team consisted of a pediatrician, a psychiatrist and the CRC staff, each with clearly defined roles. Each patient received a prescribed, constant diet for 6-day periods, during which metabolic balance studies were performed. Intake was increased by 300 Cal/day at the end of each period if weight gain was not at least 0.2 kg/day. The bathroom door was locked; complete bed rest was enforced for 24 hrs. if any day's food was not eaten; and staff accompanied the patient to other areas of the hospital. We were encouraged to find that: 1) patients perceived the controlled, consistent research protocol as supportive; 2) patients were minimally "manipulative", due to the finely regulated environment of the CRC, which contrasted beneficially with their adverse home environments; 3) the on-site metabolic kitchen added flexibility and palatability to the diet, 4) the dietitian's professional advice aided in the acceptance of the diet; and 5) a nurturant research team could initiate therapeutic changes in the patients and families while conducting clinical studies. These findings suggest important treatment principles for patients with AN in other settings.

58 A CONTROLLED STUDY OF PRE-SURGERY PREPARATION FOR CHILDREN. I. Franklin Kuhn, Jr., Samuel LeBaron, and Lonnie Zeltzer. (spon. by Charles Grose). The Univ. of Tex. Hlth. Sci. Ctr., Dept. of Pediatrics, San Antonio, Texas.

Standard preparation programs to reduce anxiety of children about to undergo surgery are assumed to benefit children and parents. To test that assumption, 60 children (3-11 years), admitted to a county hospital for nonemergency surgery, were randomly assigned to 1 of 4 experimental groups: (1) child preparation, (2) parent preparation, (3) both child and parent preparation, and (4) no preparation. Preparation techniques included videotapes, coloring books, structured parent interviews, and written guidelines for parents. Dependent measures of children included: (1) self-reports of anxiety ("fear thermometer" rating fear of 15 aspects of hospitalization and surgery), (2) behavioral observations made by 2 independent raters on children's anxiety and cooperation during hospitalization (88% perfect agreement between the 2 raters), (3) physiological measures of anxiety (including pulse, respiratory rate, blood pressure, nausea, vomiting, medication needs), (4) length of hospital stay, and (5) problem behaviors pre-, during, and post-hospitalization (rated by parents). Parents also rated their own anxiety during their child's hospitalization and their satisfaction following discharge. Analysis of variance and covariance indicated no differences between the 4 groups for any of the dependent measures. The data indicate that standard pre-surgery preparation does not necessarily reduce either children's or parents' anxieties or increase parental satisfaction. We conclude that such preparation should be individualized rather than standardized.

59 DECREASING MORTALITY AND MORBIDITY OF INBORN VERY LOW BIRTH WEIGHT (VLBW) INFANTS ≤ 800G. Savitri P. Kumar, Endla K. Anday, Linda M. Sacks and Maria Delivoria-Papadopoulos. Univ. of PA., Dept. of Pediatrics, Phila., PA.

Paucity of data exists on the mortality and morbidity of infant ≤800g. The present study reports on the in hospital course of 15 of 34 inborn infant survivors delivered at the Hosp. of the Univ. of PA. between Jan.1980-Sept.1981. Mean ±SEM birth weight and gestational age were 705 ± 24g (range 500-800g) and 27 ± .4wks (range 25-31wks), respectively. Ten infants were small for gestational age (SGA) with a male:female ratio of 1:4. Maternal complications were present in all cases; 6 (40%) were delivered by C-section. The mean Apgar scores at 1 and 5 min were 4.5 and 6.4 respectively with a mean admission pH of 7.28. Three infants died in the neonatal period. Major complications included necrotizing enterocolitis (6/15), with 2 infants dying at 6wks of age, patent ductus arteriosus (6/15), with 2 requiring ligation, culture positive sepsis (6/15) and intraventricular hemorrhage documented by EMI scan (5/15). Mean duration of mechanical ventilation was 51 days and was principally for apnea. No infant developed severe brochopulmonary dysplasia. Birth weight was regained in a mean of 12 days. Only 1 infant had >Gr 2 retrolental fibroplasia. Mean duration of hospitalization was 118 days. Currently, follow up in 8 of 10 infants who are between 9 and 17 months of corrected age shows that except for 1 infant with microcephaly and delayed development, the remainder of the infants appear to be free of major disabilities. Although it is too early to prognosticate it seems that the outcome for the extremely low birth weight infant may be no different than that of their heavier counterparts.

60 LONG-TERM FOLLOW-UP OF NEONATES REQUIRING A PACEMAKER FOR CONGENITAL HEART BLOCK. R.A. Lazarte, E. Goldson, M. Kemper, and J. Hernandez Dept. of Perinatology, The Children's Hospital, Denver, Colorado

Between 1970 and 1979 four infants with complete congenital heart block were admitted to The Children's Hospital in Denver, Colorado. In all of the cases the diagnosis was suspected prenatally because of fetal bradycardia or difficulty in detecting fetal heart tones. The infants had birthweights between 2800 and 3380 grams. Three of the patients were full term and one had a gestational age of 33 weeks. The premature had hydrops fetalis and a maternal history of systemic lupus erythematosus. One of the term infants was later found to have an atrial sental defect of the ostium secundum type which was repaired at nine years of age. Three of the infants had transvenous pacemakers placed within the first eight days of life. All of the children ultimately required permanent pacemakers which were placed between 29 days and three years of life. All of the children have survived to date and have had no restrictions in their physical activity because of the pacemaker. One child has required four revisions of the pacemaker in the 11 years since her birth. The children were seen for developmental follow-up between ages 18 months and 11 years. The assessment tools used included the Bayley Scales of Infant Development and the Stanford-Binet Intelligence Scale. All of the children are functioning in the normal range.

The purpose of this communication is to point out that with early aggressive management children survive complete heart block and can grow up functioning as normal individuals.

61 REASSESSMENT OF RELATIONSHIP OF PERINATAL RISK FACTORS AND CHILD ABUSE. John M. Leventhal and Susan A. Egerter (Spon. by Paul L. McCarthy). Yale University School of Medicine, Yale-New Haven Hospital, Department of Pediatrics & Child Study Center, New Haven, Connecticut.

The purpose of this study was to determine whether prematurity and/or young maternal age are important risk factors for child abuse. Previous studies, most of which have used a case-control design, have provided contradictory evidence about the relationship of these factors to abuse because of the failure to use comparable controls, to clearly define abuse, and to take account of differences in clinicians' likelihood of detecting abuse.

To investigate these risk factors, a case-control design was used. Cases were 106 children who: (1) had been reported to the YNHH child abuse registry from 1/75 to 12/79, (2) had evidence of definite or probable physical abuse based on an independent review of the incident, and (3) had been born at the same hospital. For each case, a control who had no evidence of abuse was chosen from a log of births and matched according to birthdate, sex, race, method of payment for the hospitalization, and provider of health care (to minimize detection bias). Perinatal data were abstracted from the hospital charts. Analysis showed that the rates of prematurity (gestational age <37 weeks) were no different in cases and controls: odds ratio (ω)=1.43, X^2=0.53, p>.5. The rate of teenage mothers (age <20) at the birth of the abused child was higher in the cases than the controls (ω=1.86, X^2=3.60, p=.058). Thus, prematurity is not a risk factor and young maternal age at birth is likely a risk factor for abuse. These results emphasize the need for careful research design in such studies.

62 THE MATCHING FACES ATTENTION TASK, Craig B. Liden, (Spon. by Thomas K. Oliver), School of Medicine, Univ. of Pittsburgh, Dept. of Ped., Children's Hos. of Pgh.

The Matching Faces Attention Task (MFAT) provides a structured means to obtain quantitative and qualitative data regarding selective attention in school age children. MFAT requires children to selectively attend and problem solve in performing a distinctive feature analysis on each of 24 test items. Response time and correctness of match is recorded for each test item. Total correct (TC) and total response time (TRT) scores are broken down to information regarding cognitive tempo, vigilance, distractibility and problem solving efficiency. The task takes 5-10 min to complete and requires test booklet-Form A or B, and a stopwatch.

Selective attention as measured by TC improved with age in a normative population (N=350). TRT decreased with age. TC strongly correlates with measures of other developmental functions: fine motor (.305), auditory sequential memory (.410), visual sequential memory (.391), receptive comprehension (.491), syntax comprehension (.349), and expressive vocabulary (.491). MFAT successfully discriminated between groups (N=135) of high, moderate and low achievers (p<.01) and correlated with reading (.466), math (.546), and total achievement (.533).

In clinical trials (N>500) the MFAT has been documented to be useful in: discriminating types of inattention; contributing to selection of candidates for drug therapy; generating cognitive intervention strategies; and longitudinally monitoring attentional status. On the basis of initial studies, MFAT would appear to be a cost effective and efficient clinical and research tool for describing selective attention in school age children.

63 SOMATIC GROWTH PATTERNS IN CHILDREN OF MOTHERS USING HEROIN AND METHADONE: BIRTH TO 3 YEARS. Marta H. Lifschitz, Geraldine S. Wilson, Murdina M. Desmond. Department of Pediatrics, Baylor College of Medicine, Houston.

An association of fetal growth retardation with maternal heroin use is well known. Studies of growth patterns of infants born to methadone mothers yield inconsistent information. This study reports longitudinal growth in infants born to 3 groups of women: 22 heroin users (H), 21 methadone-maintained (M), and 28 controls (C) matched for maternal age, race, marital status and prenatal care, in a community hospital serving a low S.E. population. Additional psychoactive drug usage was prevalent among both drug groups. Birthweight, length, and head circumference (adjusted for gest. age) of drug groups (H,M) were significantly smaller than controls (p<0.001). M-group remained significantly smaller (p<0.05) than C at 6 wks(wt,ht,FOC) & 3 mo.(ht,FOC) while H babies differed from C only in ht. Analysis of data from 6 mo.-3 yr. revealed similar group means and a high incidence of short stature and small FOC in controls as well as H and M.

		H (n=22)	M (n=21)	C (n=28)
FREQUENCY (AND %) OF	Wt <10%	2(9)	3(14)	4(14)
MEASUREMENTS BELOW	Ht <10%	5(23)	8(38)	10(36)
NORMS AT 3 YEARS	FOC<<5%	3(14)	5(24)	3(11)

Regression analyses indicated that maternal drug use affected birth measurements to a greater extent than did race, prenatal care, or SES. At 3 years, growth parameters were unaffected by these factors, including maternal drug use. We conclude that intrauterine growth is impaired by drug use, but subsequent growth, while below norms, is comparable to that of low SES controls.

64 COMPARISON OF PSYCHOMETRIC TEST AT ONE AND SIX YEARS NEWBORNS ≤2500 GMS. AT BIRTH. Philip Lipsitz, Marsha Sonnenblick, SUNY at Stony Brook, Health Sciences Center, Dept. of Pediatrics, LIJ-HMC, New Hyde Park, N.Y.

Annual psychometric tests were followed from the 1st to the 6th birthday in 35 children with no gross neurologic defects, 16 males, 19 females, birthweight ≤2500 gms. Ten were ≤1500 gms. (VLBW), mean 1293 ± 106 gms. mean gest. age 29.9 ± 1.9 wks.; 25 (LBW) mean 1795 ± 252 gms., gest. age 34.6 ± 2.4 wks. The tests used were: 1 yr. Bayley Scale of Infant Development(BSID), Mental Developmental Index(MDI), Psychomotor Developmental Index (PDI): 2-5 yrs. Stanford-Binet Intelligence Scale(SB): 6 yrs. Wechsler Intelligence Scale for Children-Revised(WISC-R), Verbal, Performance and Full Scale IQ's, and Visual Motor Integration Test(VMI). Results were:

Test	VLBW	LBW	p
BSID MDI	83.2 ± 21.8(50-112)	100.2 ± 18.5(50-142)	≤ .05
PDI	79.5 ± 16.0(58-111)	98.7 ± 18.7(58-147)	≤ .01

The SB, WISC-R and VMI scores were not significantly different. The LBW group were functioning in the normal range at 1 yr., but not the VLBW group. 9 of 10 VLBW increased their IQ scores by a mean of 38.7 pts. at 6 yrs. Conclusions: 1) VLBW developmentally score lower than LBW at 1 yr. of age, but catch up by 2 yrs. of age. 2) Developmental testing of newborns ≤2500 gms. at 1 yr. is not predictive of scoring at 6 yrs. 3) There is a moderate correlation (r=0.54) of SB at 2 yrs. and WISC-Verbal IQ at 6 yrs. 4) There is no sex difference in BSID and WISC-R. 5) Sex and birthweight do not interact as factors in development.

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65 CO-SLEEPING IN CLEVELAND. B. Lozoff, A. Wolf (Spon. by M. Klaus), Case Western Reserve U. School of Med., Depts.of Pediatrics and Psychiatry, Cleveland, Ohio.

This study describes the prevalence and correlates of sleeping in the parental bed among healthy children between 6 months and 4 years of age. A sample of 99 children was enrolled in an interview study on the basis of well-child care appointments in representative pediatric facilities. 45% of children had slept with parents in the month preceding the interview. The prevalence of co-sleeping patterns was: never (47%);an isolated or extraordinary occurrence (8%); occasionally (>1x/month,<2x/week)(8%); part night at least twice a week (18%); all night at least twice a week (19%). Children who slept with parents only in an extraordinary circumstance were not considered co-sleepers. Recent co-sleeping occurred in 73% of black and 33% of white families. Regardless of race, a co-sleeping child was significantly more likely to be over two years old, not living with the father, and tended to have a less-educated mother. Co-sleeping seemed to reflect a parental approach to sleep management of adult presence and body contact, i.e.,co-sleeping children were significantly more likely to have their bed in the parent's room, to have adult company when falling asleep, to be given body contact other than co-sleeping in response to night waking, and less likely to be put in their own sleeping place to fall asleep or to be given a bottle to hold. Night waking was more common in children who slept with parents (p=0.03), regardless of co-sleeping pattern. Few families had discussed their practices with their pediatricians. These results demonstrate that co-sleeping is common, though generally against pediatric recommendations and without pediatrician awareness.

66 THUMBSUCKING, TRANSITIONAL OBJECT ATTACHMENT, AND PEDIATRIC SLEEP ADVICE. B. Lozoff, A. Wolf (Spon. by M. Klaus), Depts. of Peds.& Psychiatry, CWRU, Cleveland.

Thumbsucking and transitional object attachment have been considered normal and important aspects of young children's developing independence. To test an alternate hypothesis, that they are a function of falling asleep without adult company, a representative sample of 99 mothers of healthy children between 6 months and 4 years of age were interviewed. 50% of the children fell asleep with adult company, almost always the mother's. The prevalence of falling asleep without an adult present increased only slightly over this age range, from 43% to 56%. Regardless of age, these children were significantly more likely to suck their thumbs (p=0.04) and to use a transitional object (p=0.001). Other common behaviors when falling asleep, such as drinking a bottle or sucking a pacifier, and uncommon ones, such as crying, self-rocking, or grinding teeth, did not differ in the two groups. Children who fell asleep with parental company were more likely to be rocked (p=0.02) but less likely to require any special object or behavior (p=0.04). There was no difference in the prevalence of bedtime struggles or night waking. The association between falling asleep while breastfeeding and thumbsucking or transitional object use could not be determined, because only 5 children were still being nursed to sleep. The results indicate that thumbsucking and transitional object attachment are not simply normal aspects of a child's increasing independence. Rather, they may be the product of pediatric recommendations that young children fall asleep alone, advice which deviates from the practice in most human societies and our own past.

67 **AN ELEVEN YEAR LONGITUDINAL STUDY OF PRETERM INFANTS.** L.C. Mayes, N.P. Haywood, V. Kirk, D.C. Buchanan, G. Hedvall, M.T. Stahlman. Vanderbilt Univ. School of Medicine, Dept. of Ped. & Psych., Nashville.

Because preterm infants show compensatory catch-up in growth and development, test scores from the first 3-5 years may not reflect later outcome. We have followed to age 11 years 169 preterm infants with neonatal respiratory distress born 1961-70. An additional 68 were seen to age 7. Yearly exams included psychological testing and growth measurements. The mean gestation and birthweight were 34.8 weeks and 2200g (964-4100). Twenty-seven infants were <1500g. The distribution of weight (wt) and height (ht) for those >1500g approximated the standard growth curve for term infants by age 3-5 years. However, those < 1500g remained small: 85% of this group were < 50%, and of these, 25% were < 5% at age 5 for both ht and wt. Though means of yearly DQ's obscure the wide distribution of scores, the values become comparable to those of the general population:

Mean DQ at Age (years):	1	2	3	5	6	11
<1500g	**84**	**89**	**80**	**90**	**94**	**95**
n(number)	12	17	22	23	18	14
>1500g	**93**	**91**	**92**	**101**	**104**	**101**
n	104	124	127	139	117	109

When considered individually, infants usually had a >10 point increase in DQ between 3 and 6 yrs. The test instrument changed from the Stanford Binet at age 3 to the Wechsler at age 6. Parental age and education, mode of delivery, and severity of respiratory distress did not correlate with outcome. We conclude that, because changing test scores in the first 5 years reflect both different instruments and compensatory catch-up in preterm infants, DQ's do not predict outcome until age 5-6.

68 NEONATAL ASSESSMENTS IN VERY LOW BIRTH WEIGHT INFANTS: CAN THEY PREDICT NEUROBEHAVIORAL OUTCOME? Cecelia McCarton, Allan Danziger, Diane Kurtzberg, Holly Ruff and Herbert G. Vaughan, Jr. (Spon. by Michael Cohen) Albert Einstein College of Medicine, Depts. of Pediatrics, Neuroscience and Radiology, Bronx, New York

The extent to which the developmental outcome of very low birthweight (VLBW) infants can be predicted from neonatal assessments has been an unresolved question. In our study, 61 consecutive infants weighing less than 1500 gms at birth were examined at 40 weeks post-conceptional age (PCA) with CT scans and the Einstein Neonatal Neurobehavioral Assessment Scale (ENNAS). Subsequent neurobehavioral development was assessed at 7,12 and 18 months using the MDI and PDI scores of the Bayley Scales.CT scans were called abnormal if they showed diffuse periventricular low densities and/or other specific lesions (e.g., intracranial hemorrhage or ventricular enlargement). The ENNAS is a 22 item exam; the sum of abnormal items gave a score for each infant. A multiple linear regression was performed comparing the CT data and ENNAS scores at 40 weeks PCA with later assessments of neurobehavioral development (Bayley scores). Both the CT scan findings and the ENNAS scores were significantly related to MDI and PDI scores at 7, 12 and 18 months. In summary, either CT scan data or ENNAS scores at 40 weeks PCA are statistically reliable predictors of neurobehavioral development in VLBW infants over the first 18 months of life. Therefore, the availability of these two clinical assessments, both with predictive reliability, offers an important opportunity to determine which VLBW infants may need early intervention.

69 THE EFFECTS OF MATERNAL SOCIAL SUPPORT AND STRESS ON THE PROSPECTIVE MORBIDITY OF ASTHMATIC CHILDREN Fernando S. Mendoza, John A. Martin, Ruth T. Gross, Iris F. Litt, Norman J. Lewiston, Joann Blessing-Moore, Stanford University School of Medicine, Department of Pediatrics, Stanford

Social support and stress are modifiers of a person's health status. In a chronic disease such as asthma, they have been implicated in the disease outcome. We examined prospectively the effect of a mother's social support and stress on her child's morbidity from asthma.

Over a 9 month period mothers of asthmatic children, ages 3-11 years, were evaluated 3 times by means of a mailed self-administered questionnaire designed to assess their social support and stressful life events. Concurrently, their children's morbidity from asthma was assessed monthly by monitoring the days of disability from the asthma, the number of unscheduled physician visits for the asthma and hospitalization resulting from the asthma. An initial group of 39 mothers completed and returned the first questionnaire, while 28 and 22 completed and returned the second and third questionnaires at 4 and 9 months respectively.

The data showed that the social support of responding mothers was fairly stable over the study period, as was the number of stressful life events. However, there was no correlation between the mothers' social support and stress and their children's morbidity from asthma. These results contrast with our previous retrospective study and suggest that a mother's social support and stress may have more of an effect on her perception of severity of the asthma than the actual morbidity.

● **70** ECOLOGIC REFORMULATION OF PEDIATRIC SOCIAL ILLNESS: Eli H. Newberger, Thomas J. Marx and the Family Development Study. Children's Hospital, Boston.

48 children under 4 years hospitalized for child abuse,97 for accidents, 41 for failure to thrive, and 23 for ingestions were matched individually with controls suffering from comparably acute medical conditions on age, social class, and race. A structured maternal and paternal interview yielded 63 significant single-variable comparisons in these domains: child health and development, past and present family disruption and conflict, parental physical and emotional health, and environmental setting. Discriminant function analysis suggested interrelationships among the case groups and an additive mode of pathogenesis, with more severe stresses associated with more severe childhood symptoms.

Cluster analysis on a random half-sample identified three cohesive groups, characterized as ecologic equilibrium, adversity, and crisis. This reformulation subsumed respectively increasing proportions of severe symptoms and replicated successfully on the other half-sample. Its elaboration gives a convenient matrix for organizing data from practice and a value free alternative to the present manifestational classification system, which adds insult to injury.

71 A FIVE YEAR PROSPECTIVE STUDY OF INFANTILE FUNCTIONAL PATTERNS: Judith S. Palfrey, Melvin D. Levine, Cary Aufseeser, and William Kent, The Children's Hospital Medical Center, Boston, Massachusetts.

Parent questionnaires eliciting data on sleeping-feeding-crying patterns in 75 3 and 6 month old babies were scored for "intrinsic traits", "level of parental conern", and "family adustment". There were significant associations with subsequent ratings by teachers on a kindergarten performance profile. These were strongest for the 3 month old "intrinsic traits": "Trouble getting to sleep" at 3 months correlated negatively with teachers' assessments of "leadership" (.37), "peer interaction" (.41), "class participation" (.41), "communication" (.42), and "overall social" (.47). "Excessive crying" and "poor consolability" had the next most negative association (.30-.41). Feeding problems correlated at .23-.36. The infant sleeping-feeding-crying measures did not relate to kindergarten teachers' assessments of "mastery" (e.g., "persistence", and "use of time", "conformity of routine", and "following directions"). Parental overconcern during infancy and poor family adjustment to the new baby were not nearly as predictive of kindergarten social dysfunction as were "intrinsic traits".

Follow-up of the 17 subjects with the greatest number of problems in infancy showed a consistently high proportion with social-emotional concerns at 30-42 months and kindergarten entry.

The data suggest that for a subgroup of children infantile functional disorders may be antecedents of poor social transition to school but are not predictive of difficulty with classroom competence and task mastery in kindergarten.

72 VIDEOPHONE (VP) USE IMPROVES MATERNAL INTEREST IN TRANSPORTED INFANTS. Robert E. Piecuch, Robert S. Roth, Ronald I. Clyman, Susan H. Sniderman, Philip A. Riedel, Roberta A. Ballard. Mt. Zion Hospital and Medical Center, Department of Pediatrics, San Francisco, California.

Lack of maternal involvement in the early neonatal period is thought to be associated with later problems in the maternal-infant relationship. In order to increase a mother's interest in her transported sick newborn we developed a VP system between our ICN and one of our referring hospitals. We used a digital slow scan VP to show hospitalized mothers their infants during their phone calls. To determine how effective this device was in increasing a mother's interest in her infant, we monitored the frequency of phone calls made from the mother to the hospital staff. We compared the frequency of phone calls between mothers who were offered VP (N=7) and those who had regular telephone service (N=7). All mothers delivered at the same referring hospital and were similar in maternal age and parity, cultural and socioeconomic background, marital status, and length of hospital stay after delivery. Their infants were similar in gestational age, birthweight, sex, admitting diagnosis and length of stay in hospital. We found that the mean number of phone calls made per day by the study mothers (1.0 ± 0.3 calls/day/mother, $\pm$ SE) was significantly greater than the number made by the control mothers (0.2 ± 0.1, $p<.025$). In addition, after the mothers left the hospital, the study mothers continued to call more frequently about their infants (0.91 ± 0.17 vs 0.35 ± 0.15 calls/day/mother, $p<0.05$). Use of VP during separation immediately after delivery increases the mother's interest in her sick infant.

73 TRENDS IN COST OF LIVING FOR INFANTS WEIGHING 1000 GRAMS OR LESS AT BIRTH. Jeffrey J. Pomerance and Sharyn Brown. UCLA School of Medicine, Cedars-Sinai edical Center (CSMC), Department of Pediatrics, Los Angeles.

In the 1980 fiscal year at CSMC (4/1/80 - 3/31/81), 29 infants weighing 100 grams or less at birth received neonatal intensive care. The '76/1980 average cost comparisons, based on collections, are as follows ›unded to the nearest thousand):

RTHWEIGHT < 1000 gms	1976	1980 PREDICTED (86% INFLATION)	1980 OBSERVED
›st/Survivor	$40,000	$75,000	$87,000
›st/Non-Survivor	$14,000	$26,000	$35,000
Survival	40	-	62
›st/Infant Admitted	$25,000	$46,000	$67,000
›st to Produce 1 Survivor	$62,000	$115,000	$108,000

The cost increases over and above inflation can be attributed to new chnology which in turn is reflected in improved neonatal outcome. The ›proved survival "efficiency" can best be appreciated when one com- res the 1976/1980 approximate costs of producing one survivor: $62,000 d $108,000 respectively, an increase of "only" 74% despite an increase average hospital charges of 86%. However, the average cost per ≤1000 am infant admitted, rose from $25,000 in 1976 to $67,000 in 1980.

Can society afford the high cost of survivors? The 1980 group of fants cost society over $1.9 million. Inflation tends to blur the true :rease in cost, however, evidence suggests that additional infants are rviving at costs less than predicted by the rate of inflation. The rate of flation, on the other hand, may drive our society to the untenable sition of allowing salvagable infants to die.

74 COST OF CARING FOR INFANTS WEIGHING < 1000 GRAMS AT BIRTH: A NATIONWIDE COMPARISON. Jeffrey J. Pomerance, Jeanne W. Ruderman, and Sharyn own, UCLA School of Medicine, Cedars-Sinai Medical Center (CSMC), ›partment of Pediatrics, Los Angeles.

Inter-hospital cost comparisons may be inaccurate as services provi- d, and patient course and outcome differ between hospitals. To ercome this difficulty, all billed hospital goods and services provided to ›roup of infants cared for at CSMC were itemized and tallied. By then ›lying hospital-specific charges for every item on the bill of each ›ant, inter-hospital charge comparisons could be made.

In the 1980 fiscal year at CSMC (4/1/80-3/31/81), 29 infants (62% ›vival) weighing ≤ 1000 grams at birth were admitted to our Neonatal ensive Care Unit (NICU). To date, hospital charges of 15 of 29 infants survivors, 9 deaths) have been compared with the charges that would ve been generated at 7 other tertiary NICUs across the nation. Inter- ›spital comparisons appear in the following table. (CSMC = 100%).

	Mean %	% Range		Mean %	% Range
om charges	69	57-81	Central Supply	47	0-144
spiratory Rx	34	8.8-58	Radiology	86	56-122
armacy	19	13-35	Miscellaneous	34	20-50
boratory	76	50-129	TOTAL	49	30-72

Percentage breakdown of the total charges at CSMC is as follows: ›m charges-31%; respiratory therapy (ventilators, oxygen, transcutane- › monitoring, blood gases)-38%; pharmacy-11%; laboratory-10%; central ›ply-5.7%; radiology-2.2%; miscellaneous-2.0%.

Likely, the wide variation in charges reflects regional differences in ›spital costs of supplying goods and services, patient population, percen- ›e of charges recovered, as well as hospital billing practices.

75 NEWBORN BEHAVIOR: PREDICTIVE PATTERNS FROM 3 DAYS TO 1 MONTH. Vasuki Ramakrishnan, Geraldine S. Wilson, W. Daniel Williamson, Murdina M. Desmond, Department Pediatrics, Baylor College of Medicine, Houston.

While it is expected that maturation and stabilization of be- vior occurs rapidly during the first month of life, it is stulated that some patterns of an infant's later behavior may predicted from early postnatal behavior.

To investigate this issue, 211 normal full-term infants were ›essed with the Neonatal Behavioral Assessment Scale (NBAS) 3 days and again at 1 month. The relationship between the ›res of individual NBAS items (27 behavioral items and 17 ›cited responses) was analyzed using the Pearson Coefficient Correlation. Significant correlation ($p \leq 0.05$) was found on ›ehavioral items (alertness, motor maturity, pull-to-sit, ›idliness, activity, tremulousness, and hand-to-mouth) and 3 ›cited responses (incurvation, tonic deviation of head and ›s, and tonic neck reflex). The highest correlation was ›tained for hand-to-mouth ($p=0.001$), incurvation ($p=0.008$), and ›nic neck reflex ($p=0.002$).

These data indicate that some patterns of behavior, particu- ›rly items in motoric performance, are consistent between the › age periods while others related to such important behaviors orientation and state control are not predictive.

76 A SURVEY OF STUDENT SELF-REPORTING OF DYSFUNCTION: Leonard Rappaport and Melvin D. Levine, The Children's Hospital Medical Center, Boston, Massachusetts.

A self-administered student profile with 60 quotations from children with learning problems was given to 420 4th and 6th graders (71% of population) along with teacher ratings. Matched hospital learning clinic patients (110) also were studied.

Community students reported their greatest number of concerns in fine motor control, attention, and efficiency and least in the visual-spatial area. Sixth graders reported fewer concerns than 4th in all areas ($p<.05$) and were significantly less likely to agree with teacher ratings. Boys reported more problems in attention ($p<.001$) and memory ($p<.05$), girls in gross motor output ($p=.0001$). There were no sex differences on total profile scores.

Teachers rated boys with more problems than girls in behavior ($p=.0001$), homework completion ($p<.01$), spelling ($p<.05$), writing ($p=.0001$), concentration ($p<.05$), and in reading ($p=.051$), but not in mathematics or peer relations.

Of students who rated themselves ≥ 2 S.D.'s below the total mean, 94% had at least one problem area by teacher rating; 69% had 3 or more. Of those above the mean on the total profile, only 11% had ≥ 3 teacher-identified problems.

Differences were found between the community and clinic samples on the total profile ($p<.05$) and in most individual areas.

There are wide variations and developmental changes in tendencies to acknowledge areas of dysfunction. By comparing teacher evaluations and self-assessment, useful diagnostic clues and counseling strategies can evolve.

77 GENERATIONS AT RISK: VIOLENCE IN THE LIVES OF PREGNANT DRUG ABUSING WOMEN, Dianne O. Regan, Betty Leifer, Loretta P. Finnegan, Thomas Jefferson University, Department of Pediatrics, Philadelphia, Pa.

Among the critical factors associated with child abuse are: 1) parental drug and/or alcohol abuse; 2) extreme poverty; 3)chaotic life style; 4) parents abused as children; 5) violent episodes between parents. The pregnant drug abusing population treated by the Family Center Program (FCP) is already at risk according to the first 3 factors. To ascertain levels of violence (factors 4 and 5) in the lives of our patients, we developed a questionnaire which is completed on admission. A sample of 78 methadone maintained pregnant women was compared with 43 pregnant non-psychoactive drug using women of similar socioeconomic status. The results indicate that FCP women have had, and continue to have, considerably more violence in their lives than the comparison group. More FCP women report having been beaten as children (29% vs. 18%, $p<.05$), the majority identifying their mothers as the perpetrator. Even more significant is the difference in the percent having been beaten as adults, usually by husband or partner (71% vs. 18%, $p<.001$). Sexual abuse is also frequently reported with 26% having been molested or raped as children (mean age = 11.5 years) in contrast to 9% of the comparison group ($p<.001$). The disruptive environment, past and present, of a population of women who are already at high risk for dysfunctional parenting illuminates the critical need to intervene in the cycle of intergenerational transmission of violence.

78 THE DECISION TO BREASTFEED AMONG POOR MOTHERS Joan Richardson, Phil Nader, Dave Rassin, Tom Baranowski, University of Texas Medical Branch, Department of Pediatrics, Galveston, Texas

While many professional organizations have strongly encouraged the breastfeeding of infants, less than half the population of delivering mothers have chosen to do so. What factors influence mothers to breastfeed, or not? A survey was conducted of all mothers (358) delivering live births in July 1981 at UTMB without intensive care required of the mother or the infant. The survey instrument included basic demographic data, reproductive history, sources of prenatal care and prenatal education, knowledge of recommended infant feeding practices, perceived modeling of breastfeeding, self-efficacy of breastfeeding, sources of social influence for breastfeeding or not, expectations and expectancies of breastfeeding, and social support for breastfeeding. Data was collected from hospital records on parity, gravity, apgar scores, gestational age, rooming-in practice and infant feeding practice in the hospital. The sample consisted of 40.8% Anglo, 36.3% Black, 17.3% Mexican and 5.6% other American mothers. Twenty-five of the mothers knew that the American Academy of Pediatrics advocated breastfeeding, only 40% personally believed that breastfeeding was best form of infant feeding. Data will be presented on the relationship of each of the variables to actual breastfeeding, and the relative importance among these variables in predicting the decision to breastfeed. This is the first survey of lower income minority group mothers concerning the decision to breastfeed.

79 THE IMPACT OF MOTOR DISABILITY ON PEER INTERACTION. Nancy B. Rieder, Leila Beckwith, (Spon. by A. Hayek), Univ. of New Mexico School of Medicine and Univ. of California, Depts. of Pediatrics, Albuquerque, NM and Los Angeles, CA.

This is a study of peer interaction between handicapped children (motor and/or mental disabilities) and normal children integrated into an intervention nursery program. Motor and cognitive/Adaptive scores were obtained using the Gesell Developmental Assessment. Eight categories of peer interaction were time sampled for 30 second intervals. Normal peers made a contribution greater than expected. That is, they interacted 35% and children with disabilities interacted 17% of the intervals (X^2=7.3, p<.01). The normal children did not interact only with each other but with the children with disabilities as well. Peer interaction was independent of cognitive/Adaptive scores. Children with an Adaptive score $\geq$ 30 months did not interact more than children with an Adaptive score < 30 months (X^2=0.65, p n.s.). Children with less severe motor disabilities (defined as a motor score $\geq$ 18 months) interacted more with peers than those with more severe motor disabilities (X^2=11.47, p<.01). Yet those with the more severe motor disabilities had higher cognitive/Adaptive scores (average Adaptive score 33 months) than peers with less severe motor disabilities (average Adaptive score 26 months). Thus, for children in the sensorimotor period, a motor disability has a much greater impact on peer interaction than cognitive/Adaptive ability. This has important implications for the structure of intervention programs for the preschool child.

80 A PROTEIN SPARING MODIFIED FAST (PSMF) DIET, EXERCISE, AND BEHAVIOR MODIFICATION IN MANAGING OVERWEIGHT CHILDREN. Michael S. Rosenbaum, Arthur W. Faris, John F. Shriner, Valerie H. Blankenship, and Robert M. Suskind. Univ. of South Alabama, Coll. of Med., Dept. of Peds., Mobile, Alabama.

A PSMF diet (1.5 gm protein/kg of ideal body wt, supplemented with a multiple vitamin with iron, calcium, and potassium) combined with group and individual exercise and behavior modification was initiated in 20 overweight children ranging in age from 7-17 (wt/ht M = 165%). Children and their parents attended weekly sessions over a 7-wk period and were then followed monthly. Results at the end of the 7-wk program showed a wt loss of 7.6 $\pm$ 0.7 kg*. Results for 12 of these children at the 1-mo follow-up showed a wt loss of 8.9 $\pm$ 1.1 kg and for 10 of these children at the 2-mo follow-up a wt loss of 9.8 $\pm$ 1.8 kg. For 6 children whose hts were measured at baseline and at the 2-mo follow-up, the mean ht velocity was 73.3 $\pm$ 26.3%. Biochemical assessment of the children demonstrated: (a) decreased serum cholesterol (baseline M = 170.1 $\pm$ 3.8 mg/dl; 5-wk M = 143.4 $\pm$ 4.7 mg/dl); (b) increased uric acid followed by a return to baseline levels (baseline M = 6.5 $\pm$ 0.4 mg/dl; 1-wk M = 9.8 $\pm$ 0.6 mg/dl; 5-wk M = 6.4 $\pm$ 0.3 mg/dl); and (c) unchanged serum Glu, BUN, Creat, Na, K, Cl, HCO_3, Ca, Phos, T.Bili, D.Bili, Prot, Alb, Alk Phos, SGOT, γ-GT, and LDH. These preliminary results demonstrate the efficacy of the PSMF diet, exercise, and behavior modification in the outpatient management of childhood obesity. Additional studies are being undertaken to evaluate weight maintenance strategies.

*M $\pm$ SEM

81 MATERNAL-INFANT BONDING IN WOMEN UNDERGOING REPEAT ELECTIVE CAESAREAN SECTION. Diane Ross-Harrison and Jeffrey J. Pomerance, USC School of Education, UCLA School of Medicine, Cedars-Sinai Medical Center, Department of Pediatrics, Los Angeles, California.

Caesarean section (CS) has been associated with poor maternal-infant attachment. As the immediate postpartum period has been identified as a critical time for establishing a maternal-infant bond, the objective of this study was to determine if extra visual and tactile contact at birth between mothers and infants delivered by CS made any difference in their attachment three months after birth. Accordingly, 40 middle-class women scheduled for repeat CS with epidural anesthesia were divided into two groups: Control group: routine hospital care during delivery (infant removed from delivery room 3-10 minutes after birth); Experimental group: 45-75 minutes additional visual and tactile contact during and following surgery.

Three months later, the behavior of 33 of the 40 mothers were recorded by a blinded observer during a 10 minute mother-infant play period. In addition, a questionnaire was administered to each mother concerning the effect that a CS delivery had on her personal life and on her attitude toward her infant. From a preliminary analysis of the data collected, it appears that extra contact under the given circumstances, does not influence maternal-infant attachment. It should be emphasized, however, that no untoward effects of extended maternal-infant contact were observed, and all mothers enjoyed the experience. This, in itself, may justify extended contact when it is medically safe.

Further studies need to be conducted with women from different socio-economic backgrounds and with women undergoing unscheduled primary CS.

82 METHYLPHENIDATE TREATMENT OF HYPERACTIVE CHILDREN: EFFECTS ON THE HYPOTHALAMIC-PITUITARY-SOMATOMEDIN AXIS F. Schultz, J. Hayford, M. Wolraich, R. Hintz, R. Thompson. College of Medicine;University of Iowa Hospitals; Dept. of Pediatrics; Iowa City and Stanford University Medical Center; Dept. of Pediatrics. To further define the influence of methylphenidate on the growth hormone-somatomedin axis and prolactin secretion, serum growth hormone and prolactin concentrations were measured in samples collected by continuous withdrawal and in response to provocative stimuli. Somatomedin C levels were measured in fasting samples only. The nine hyperactive subjects were all studied during methylphenidate therapy(on)and after drug discontinuation(off). Serum growth hormone concentration showed the expected pattern of variability from hour to hour in subjects both on and off drug. The usual sleep associated peak in growth hormone concentration was observed in both groups. Comparison of mean 24 hour growth hormone concentrations on =3.82±0.39(SEM) and off =4.38±0.35 ng/ml methylphenidate revealed no significant difference(p>.1). Subjects on methylphenidate responded to arginine stimulation with significantly greater hormone concentrations than subjects off methylphenidate at 45 minutes (p=.05)and 60 minutes (p<.05)after initiation of the arginine infusion. Mean prolactin concentrations on =13.7±1.8 and off 13.0±1.7 mg/ml were not significantly different (p>.1). Mean fasting somatomedin concentration on methylphenidate =0.76±.03 U/ml and off =0.88±.03 U/ml were not significantly different (p>.1) and were within the range of normal for children. Growth deficits in hyperactive children treated with methylphenidate do not appear to be related to dysfunction of the hypothalamic-pituitary-somatomedin axis.

83 PSYCHOLOGICAL STABILITY IN PKU DIET TERMINATION AT AGE THREE. Edward Schwartz, Debra Hufstetler, Richard J. Allen, Univ. Mich. Hosp., Dept. of Ped., Ann Arbor MI.

156 demographically unselected Michigan hyperphenylalaninemic infants were diagnosed between 1965-77. Of these 94 were divided into 3 groups based on dietary phenylalanine tolerances measured between the age of 6-18mos. Severe PKU were those with dietary phenylalanine restricted to 190-450mg/24hrs to maintain blood phenylalanine levels of 5-10mg%. A diet of 451-1000mg/24hrs was defined as mild while "hyperphe" were those on an unrestricted diet. Sixty-one diagnosed before 6mos had phenylalanine blood levels above 20mg% while 33 had lower levels. Ten infants had pretreatment levels above 20mg% but dietary phenylalanine tolerances of 451-1000mg/24hrs. Psychological testing at age 3 revealed the mean IQ of the severe group to be 92.5 (N=51) the mild group 93.6 (N=18) and "hyperphe" group 96.5 (N=25). Longterm outcome of repeated psychological tests following diet termination (with written informed consent) at 3 years shows no statistically significant change in IQ in the severe group over time and up to age 13 (see table).

TERMINATION OF DIET / FOLLOWUP AGE	AGE 3 / 5 YR	AGE 3 / 7 YR	AGE 3 / 9 YR	AGE 3 / 11 YR	AGE 3 / 13 YR
N	46	30	20	10	7
MEAN IQ AT AGE 3 AND FOLLOWUP	93.5 / 93.1	91.4 / 95.2	91.1 / 92.0	94.9 / 90.3	91.6 / 98.3

Comparable IQ stability is found in the mild and "hyperphe" groups. Early initiated control for severe PKU, terminated at age three, is effective in maintaining a normal IQ.

84 NEURODEVELOPMENTAL OUTCOME OF 3 YEAR OLD INFANTS WEIGHING <1000g AT BIRTH. Elsa Sell (Spon. by Otakar Koldovský). University of Arizona, Department of Pediatrics, Tucson, Arizona.

This study describes the outcome of infants born from 1976 to 1981 in southern Arizona. Mortality of those <751g was 85%; survivors had mean birth weight of 596g, gestation of 27 wks and hospitalization of 150 days. Mortality of those 751-1000g was 42%; survivors had mean wt of 889g, gestation of 28.3 wks, and hospitalization of 97 days. Of 80 survivors, 54 were followed from 8 mos. to 3 yrs. Physical examination and developmental assessment (DDST <1 yr; Bayley Scales 12-30 mo; McCarthy Scales at 3 yrs) were scheduled at 12, 18, 24 and 36 mos. after birth. Handicap was defined as mild (suspect neuro., corrected develop. < 1 SD, or mild visual problem), moderate (abnormal neuro., or corr. develop. < 1 SD, or blind), or severe (abnormal neuro. & develop. < 1 SD, + blind).

	<751g (n=9)			751-1000g (n=45)	
No handicap	2	22.2%		19	42.2%
Mild handicap	1	11.1%		15	33.3%
Moderate handicap	3	33.3%	33.3%	7	15.6%
Severe handicap	3	33.3%		4	8.9%
			p<.01		12.3%

Five of 7 with severe handicaps were functionally impaired. Nine were blind with RLF (55.6% in <751g group and 8.9% in 751 - 1000g group - p<.01).

Outcome of 751-1000g infants was thus similar to others' data but that of infants <751g differs from a recent study reporting no RLF and 12% cerebral palsy. Comparison of results from different centers will enable definition of factors responsible for the observed discrepancies and thus, improve parental counseling.

85 FACTORS AFFECTING GROSS MOTOR DEVELOPMENT IN A NORMAL POPULATION. Bruce K. Shapiro, Renee C. Wachtel, Frederick B. Palmer, Pasquale J. Accardo, Alan Ross, Arnold J. Capute (Spon. by Mark Batshaw). The Johns Hopkins J. Med. Inst., The JFK Inst., Dept. of Peds. Baltimore.

The ages of attainment of 12 gross motor milestones (rolling prone to supine, rolling supine to prone, sitting [supported], sitting [unsupported], coming to sit, creeping, crawling, pulling to stand, cruising, walking, walking backwards, running) were obtained prospectively during well baby visits in the first two years of life. Three hundred eighty one children who were born at term and subsequently judged to be "normal" at one year (Bayley Scales of Infant Development PDI and MDI>68) comprised the study population. Analysis of the data, using ANOVA techniques, reveal the following: (1) Race is a significant factor ($p.<05$) in age of milestone attainment for 11/12 milestones. (2) Sex is a significant factor ($p.<05$) only for cruising and walking. (3) A sex/race interaction is noted wherein motor achievement was earliest in nonwhite females, followed by nonwhite males, white males, and white females. (4) Socioeconomic status (SES) does not appear to be a factor in milestone attainment among whites and only exerts a modest effect among nonwhites. (5) The variance across SES is largely accounted for by race. "Normal" motor development encompasses several distinctive subgroups. Recognition of the existence of these subgroups and establishment of appropriate norms may enable clinicians to identify motor delayed children at an earlier age. Further research is needed to define the etiology of the observed differences.

86 YALE NEUROMATURATIONAL ASSESSMENT SCALES (YNMAS) - A NEWLY DEVELOPED INSTRUMENT IN THE ASSESSMENT OF LEARNING DISABILITY. Sally E. Shaywitz, Bennett A. Shaywitz and Susan L. Groll, Yale Univ. Sch. of Med., Depts. Peds. and Neurol., New Haven, Connecticut, 06510.

The notion that in children with disorders of learning and behavior, examination for "soft" neurologic signs(SS) offers a window on CNS function assumes particular relevance to pediatricians who are increasingly participating in screening for learning disability(LD). We evaluated 105 boys classified as LD, normal(N) or gifted(G) with a series of parent, physician and school-related forms. This report focuses on the YNMAS which include fine and gross motor, memory, language and laterality scales. In all gross motor tasks there were no differences between LD and N/G. In other scales, LD generally performed more poorly than either N or G, these differences, however, disappeared when IQ was covaried. Overall Total score differences separating LD from N and G remained($p<.01$). Unexpectedly, both LD and G exhibited more mirror (associated) movements than N. Frequencies of L handedness($p>.25$) and mixed dominance($p>.75$) did not differ over groups nor correlate with measures of activity, attention or academic achievement. Superior(lower) Total scales were noted in older N and G children, while Total scores did not differ between younger and older LD's. Our results indicate that overall Total SS scores may have utility in discriminating LD from N/G children. Caution is urged in interpretation of individual SS, particularly related to IQ. Caveats are offered regarding mirror movements, which not only characterized LD but high achieving G as well and in utilizing gross motor performance in screening for learning disabilities.

87 GIFTED AND LEARNING DISABLED: SHARED BEHAVIORAL CHARACTERISTICS OF GIFTED AND LEARNING DISABLED CHILDREN. Sally E. Shaywitz and Kate McGraw (Spon. by Bennett A. Shaywitz), Yale Univ. Sch. of Med., Department of Pediatrics, New Haven, Connecticut, 06510.

We studied 105 normal (N), gifted (G) and learning disabled (LD) boys, ages 9-11 assessing intelligence, learning and behavior. LD were significantly more impaired than either N or G in behavioral scales assessing activity and attention independent of IQ and SES. Separation of G into high (IQ $\geq$ 139) and low IQ (IQ < 139) groups indicated no differences in motor and language scales but significant differences in early state, activity, attention, impulsivity and organization, each favoring the low IQ G. There was no difference between the two G groups in achievement tests except that the high IQ G was superior in mathematics. Comparison of high IQ G to LD indicated no significant differences in behavior, although G continued to score better on intelligence and achievement tests. Our data suggests that highly G children may exhibit behavioral qualities that not only differ from the normal but may resemble behaviors usually associated with children at risk for learning disabilities and that the G represent a heterogeneous population - the lower IQ reflecting a continuum of the normal population, the higher IQ G representing a distinct group with superior academic and achievement functioning but behavior more representative of that usually associated with LD children. Pediatricians should recognize that disorders of attention and activity may not only be associated with LD and suggest that a diagnosis of highly G be added to the differential diagnosis of activity and attention difficulties.

88 PLASMA METHYLPHENIDATE LEVELS PREDICT ATTENTION AND ACTIVITY: RESULTS IN A DOUBLE-BLIND PLACEBO STUDY. Sally E. Shaywitz, Marc M. Sebrects, Peter Jatlow, George M. Anderson, J. Gerald Young, Donald J. Cohen and Bennett A. Shaywitz, Yale Univ. Sch. of Med., Depts. Ped., Lab. Med., Neurol., and the Yale Child Study Ctr., New Haven, CT 06510.

While large numbers of children are treated with methylphenidate (MPH) for attention deficit disorder (ADD), its pharmacokinetics and mode of action have not been clarified. We conducted a double-blind drug-placebo study in which each subject served as his own control. Subjects were 13 boys (7.1 to 12.8 years, mean 10.6) satisfying rigorous criteria for ADD; 9 had hyperactivity (H) and 4 did not (no H). Each of 3 doses of MPH (0.3 mg/kg O.D., 0.3 mg/kg B.I.D., and 0.6 mg/kg O.D.) or placebo (B.I.D.) was administered for 3 weeks. MPH terminal half life averaged 2.5 hours, and MPH levels in a child given the same 0.3 mg/kg dose on two occasions were highly replicable, averaging 10.3 vs 10.0 ng/ml (2 hours), 8.2 vs 8.2 ng/ml (3 hours) and 12.2 vs 13.4 ng/ml (peak). Hyperactivity and attention improved on all doses better than placebo with the 0.3 mg/kg B.I.D. and 0.6 mg/kg daily doses producing the best response. Plasma concentrations of MPH were significantly related to clinical response, and children with ADD (H) responded better than those with ADD (no H). Plasma concentrations of MPH may be useful in assessing clinical response. Higher doses (0.3 B.I.D., or 0.6 mg/kg) are superior to lower for behavior and blood levels may be useful in explaining apparent non-response or individual differences.

89 THE IMPACT OF NEONATAL LOSS. R. Siegel, A. Glicken, S. Henneberry, C. Cleveland, L.J. Butterfield, and R. Harmon. The Children's Hospital, Denver, Colorado.

This paper will describe a research study which was designed to evaluate the impact of neonatal loss on families. An interview questionnaire was developed which allowed for assessment of how families were coping with the loss of their infant, and inquired about events surrounding their infant's death. This permitted the study of maternal grieving, as well as the effects of staff interventions on this process. A total of 38 married women were interviewed at 3 and 9 months following the loss of their infant.

The findings supported the observations of other researchers who describe a heightened potential for long-term ill effects on families suffering a neonatal loss. Findings showed that most families did describe their neonatal loss as having had a major impact on their functioning. It was also shown that although neonatal loss has significant effects on family functioning and maternal grieving, in general these effects are greatest immediatly after loss and at 3 months and begin to lessen at 9 months following the loss. 89% of mothers reported sadness or depression at 3 months; the data showed similar differences at 3 and 9 months, respectively with 80% vs. 74% reporting their life was significantly different as a result of the loss, 29% vs. 10% reported severe marital difficulties, 47% vs. 48% financial problems, 58% vs. 28% difficulty sleeping, and 49% vs. 26% eating problems. Many mothers described the period from 2-4 months as most difficult since often family and friends became less emotionally available and expected them to be "back to normal".

Withdrawn Prior to Publication

91 THE BURDEN ON THE SYSTEM OF HEALTH-CARE FROM MIDDLE EAR DISEASE DURING THE FIRST THREE YEARS OF LIFE. David W. Teele, Jerome O. Klein, Bernard Rosner, and the Greater Boston Collaborative Otitis Media Study Group. Boston Univ. School of Med., Harvard Med. School, Boston City Hospital, Depts. of Pediatrics and Preventive Medicine, Boston.

To determine the proportion of visits during the first 3 years of life which were accounted for by either acute otitis media (AOM) or middle ear effusion (MEE), we studied 2568 children prospectively from birth. AOM was defined as middle ear fluid in an ill child and MEE as asymptomatic middle ear fluid.

Prevalence of AOM or MEE by reason for visit and by year of life

Reason for visit	Year 1		Year 2		Year 3	
	AOM	MEE	AOM	MEE	AOM	MEE
Illness	32.0%	2.9%	31.9%	3.2%	27.5%	4.2%
F/U ear disease	17.2%	16.9%	15.2%	18.1%	15.5%	17.7%
F/U other illness	13.8%	7.2%	12.4%	7.1%	7.5%	6.1%
Well baby visit	4.1%	1.8%	4.8%	2.6%	2.6%	4.8%

AOM or MEE was diagnosed at 17.5%, 24.0%, and 24.1% of all visits during years 1,2, and 3 of life respectively. After excluding well-baby visits, AOM or MEE was diagnosed at 32.3%, 32.1%, and 30.3% of visits during years 1,2, and 3. Of all visits made to follow-up any prior illness, visits to follow-up AOM or MEE accounted for 64.3%, 71.0, and 70.0% respectively.

Prevention and better management of AOM and MEE could produce significant reductions in demand on the health-care system.

92 4-7 YEAR EVALUATION IN TWO GROUPS OF SGA INFANTS Nergesh Tejani, Eve Winer, Vijaya Atluru, Raymond DiGiuseppe, Leatrice Borofsky. Spon. by Platon J. Collipp. Nassau County Medical Center, Health Science Center, SUNY at Stony Brook, Dept. of Ob/Gyn, East Meadow, NY.

A brain sparing type of head growth pattern has been described in small-for-gestational-age (SGA) neonates born of hypertensive mothers (Group A), as opposed to a low profile head growth pattern in SGA neonates born of normotensive mothers (Group B). Based on this finding, 20 SGA children in Group A were compared with 35 SGA children in Group B at the age of 4-7 years. Children were compared for growth, neurological function, and intellectual development.

Results: 1. No differences were found in growth characteristics of Groups A&B. 2. Group A showed better scores on intellectual testing, especially verbal IQ ($P < .05$). 3. Group A showed a larger number of major neurological deficits. 4. In verbal and full scale IQ scores, Group A showed a negative correlation with gestational age and birth weight ($P < .05$), while Group B showed a positive correlation ($P < .01$).

Conclusion: 1. SGA neonates in Group A score better on intellectual testing than those in Group B, possibly due to a brain sparing effect. 2. Neurological injuries seen more commonly in Group A reflect intrapartum hypoxia and indicate careful intrapartum fetal monitoring. 3. In Group A, delivery should be effected as soon as lung maturity is established, as prolongation of pregnancy after this is detrimental. In Group B, provided fetal function tests are adequate, mothers may be allowed to go into spontaneous labor.

93 PREMATURE BIRTH: THE EFFECT ON BREASTFEEDING, M.A. Trause, J. Hilliard, V. Malek, L. KRAMER, The Fairfax Hospital, Falls Church, Va., Sponsored by P. A. Jose

To examine the breastfeeding experiences of mothers of preterms (PT), questionnaires were sent to all mothers of PT infants hospitalized at Fairfax Hospital from April 1980-April 1981 (n=260) and to 480 mothers of full term (FT) delivering vaginally during the same period. Data were obtained from 112 PT (mean GA=31wks.) and 202 FT mothers. Of those intending to breastfeed, fewer PT then FT mothers were nursing at 2 (65% vs 85%, $p<.005$) and 6 months (38% vs 56%, $p<.05$).

Nonetheless, most PT mothers intending to breastfeed were doing so at 2 months. These mothers were compared to PT mothers intending to nurse who were not successful. Infant hospitalization was shorter in the successful group ($p<.006$) despite no differences in GA or BW. Among the most interesting findings, infants of successful mothers generally sucked or slept during first nursing attempts whereas infants of unsuccessful pairs often cried ($p<.005$). Success or failure in nursing PT infants was influenced by support from fathers and friends ($p<.005$) but not by hospital physicians, nurses or private OBs and Peds.

Establishing lactation with hospitalized premies is difficult. Yet mothers who find proper support can be successful. Nursery policies and attitudes should be reviewed to determine how to support their efforts.

94 MULTIPLE MINOR ANOMALIES AND DEVELOPMENT-Donna Van-Overloop, Richard R.Schnell, Lewis B.Holmes Children's Hospital Medical Center & Mass. Gen. Hosp.Boston, MA.

The presence of multiple minor anomalies at birth has been correlated with subsequent hyperactive behavior (Science 199:563,1978) and mental deficiency (J Pediatr 65:189,1964). We examined 7,157 newborn infants for 101 minor physical features. 10% had 3 or more minor anomalies (MA), defined as having no medical/surgical importance and occurring in less than 4% of infants of the same race.

98 children with 3 or more MA were reevaluated at ages 4 to 6 years with the following: WPPSI or WISC-R, VMI, the Auditory Association and Grammatic Closure subtests from the ITPA, the Draw-a-person and a hearing screening test. The parent accompanying the child was administered the Vineland Social Maturity Scale. Each child also was observed through a one-way mirror for a five minute play period. The room was divided into four quadrants, each of which had a toy in it. The number of quadrants entered, the number of quadrants changed and the longest number of seconds spent on an activity were recorded. A 5-pt. clinical rating of activity level was assigned to each child based on times out of seat, general distractibility and overall attention span. Three point ratings of emotional stability were assigned each child based on his responses and verbalized concerns during the administration of the Wechesler scale and the Draw-a-person.

There were no significant differences on any of the above measurements between infants subdivided by the number of minor anomalies. None of the infants was mentally retarded. Thus, an increase in minor anomalies was not felt to have a strong relationship to learning disabilities or increased activity level.

95 DEVELOPMENTAL "CATCH UP" PHENOMENON IN PRETERM (PT) SMALL FOR GESTATIONAL AGE (SGA) INFANTS. Betty R. Vohr, William Oh. Brown Univ., Women & Infants Hosp. Dept. of Ped., Providence, RI

The growth pattern, neurological & developmental performance of 21 PT SGA & 20 PT appropriate for gestational age (AGA) infants matched for birth weight, socio-economic status and date of birth were prospectively studied. 19/21 SGA (90%) & 15/20 AGA (75%) of infants born in 1975 and '76 were followed yearly for 5 yrs. SGA mean b.wt. (M±SD) was 1220±195g and AGA 1195±190g. At 5 yrs. of age, mean wt. and length of SGA infants remained at the 3rd-10th% compared to 25th-50th % for AGA. Mean head circumferences, however, were comparable for both groups and were at the 25th-50th %. Neurological assessments showed 2 SGA cases with mild spastic diplegia(10%) and 1 AGA infant with spastic diplegia. The table below shows the developmental data of study infants.

	BAYLEY MDI		STANFORD BINET		
	12 mo.	24 mo.	3 yr.	4 yr.	5 yr.
SGA	77±16	89±21	87±10	99±12	96±13
AGA	95±20	116±19	101±12	107±13	106±13
p	<.02	<.02	<.006	ns	ns

SGA infants have significantly lower DQ scores than AGA controls at 1-3 yr.; however, both SGA and AGA infants gradually make developmental gains. Developmental "catch up" for AGA infants occurs by 12 mo. in contrast to 4-5 yrs. for SGA. Overall neurodevelopmental outcome was good despite the fact that these data reveal early developmental delay of PT SGA infants with late "catch up" by 4-5 yrs., stressing the importance of long term follow up to accurately assess outcome.

96 ETHICAL VALUES AND PEDIATRIC CARE: A COMPARISON OF PEDIATRIC AND NON-PEDIATRIC RESIDENTS AND FACULTY. Paul R. Williams and Caroline L. Kaufman (Spon. by Allen W. Root), Departments of Pediatrics and Sociology, College of Medicine and College of Social and Behavioral Sciences, University of South Florida, Tampa, Florida.

Physicians' social and moral values are important to the extent they influence decisions in patient care. This study compares pediatricians' and non-pediatricians' attitudes and behavior in medical practice. A sample of 178 USF School of Medicine physicians (13 pediatric: 45 non-pediatric residents; 20 pediatric: 100 non-pediatric faculty) were surveyed concerning patients' rights to free choice, patients' rights to refuse treatment, national health care, equity in allocating medical care, abortion, and treatment of handicapped children. Significant differences ($p<.05$) were found between pediatricians' and non-pediatricians' attitudes toward suicide, abortion, belief in an afterlife, and equity in allocating medical resources. Pediatric residents and faculty did not support patients' rights to choose suicide or abortion. Pediatric residents would perform life-saving surgery on a Down's syndrome infant, while non-pediatric residents would not. Pediatric residents and faculty were more likely to encourage continuance of an unwanted pregnancy than were non-pediatricians. Pediatricians showed a greater tendency to employ religious values in making decisions than non-pediatricians. These findings suggest that for this sample pediatricians differ from other specialists in their ethical beliefs and that their decisions involving patient care reflect these differences.

97 PARENTAL RESPONSE TO THE DEATH OF A TWIN Ann L. Wilson, Lawrence J. Fenton, Dennis C. Stevens, and Douglas J. Soule. Univ. of S. Dakota, School of Med., Sioux Valley Hospital, Dept. of Pediatrics and Dept. of Psychiatry, Sioux Falls, S. Dakota.

To examine the emotional impact of the death of a twin on mothers and fathers, a study was conducted comparing the responses of eight sets of parents who lost a twin with eight sets of parents who lost a singleton newborn. In each group the babies had a mean gestational age of 31 weeks and the mean length of time between the death and survey completion was 15 months. The mean age at death was 2.8 days for the twins and 10.5 days for the singletons. The parents completed a questionnaire which covered their emotional reactions and social interactions during the first six weeks following the loss and their present response. Analyses of variance indicated that although mothers experienced more depressive symptoms than fathers ($p = .001$) and that symptoms diminished over time ($p = .032$), there was no significant difference between the responses of parents who lost a twin and those who lost a singleton. All of the mothers and 80% of the fathers of twins report being told by others to feel fortunate for having a living twin, yet 60% of these parents report experiencing a physical longing to be with their baby following his/her death and continue to frequently think of their dead twin. No parent of a surviving twin reported prefering not to discuss their baby's death. These findings indicate that the existence of a living twin does not lessen parental grief and those who care for these families should be aware of this fact as they counsel parents in their bereavement.

98 NEWBORN BEHAVIOR AND NEUROLOGIC STATUS AT 1 MONTH IN INFANTS OF WOMEN WHO SMOKE DURING PREGNANCY. Geraldine S. Wilson, W. Daniel Williamson, Jane Stitt, Judy Kautz. Dept. of Pedi., Baylor College of Medicine, Houston.

The purpose of this study was to determine whether cigarette smoking during pregnancy affected neurobehavioral function of newborn infants. Subjects were healthy, full-term infants, 173 born to mothers who smoked 10 or more cigarettes daily (S) and 173 to non-smoking mothers (NS). They were assessed at 3 days on the Neonatal Behavior Assessment Scale (NBAS). 96 S and 115 NS returned at 1 month to be examined neurologically and on the NBAS. On the initial NBAS, S showed decreased orienting behavior on 3 items (Table) and differed on 2 items related to state control (more rapid onset of irritability and increased utilization of hand-to-mouth activity). On the 1 month exam, these behavioral differences had resolved but NS were found to smile more frequently. Also, a significantly greater number of S (25) than NS (10) had abnormal or suspicious neurologic findings ($p<.05$). Combinations of increased muscle tone, hyperreflexia and excessive irritability (insulated crying state) were the most common findings. These data suggest the need for further follow-up to determine the implications these early differences have for ultimate neurodevelopmental and behavioral outcome.

Age	NBAS Item	Mean Scores → (S)	(NS)	(p)
3 days	Alertness	3.67	4.10	<.05
	Orientation, inanimate visual	4.14	4.78	<.05
	Orientation, animate visual	2.51	2.97	<.05
	Rapidity of build-up	4.10	3.54	<.05
	Hand-to-mouth facility	4.44	3.87	<.05
1 mo.	Smiles	.72	1.37	<.05

99 FATHER INTERACTION WITH PRETERM AND FULLTERM INFANTS. Michael W. Yogman, Harvard Med. Sch., Dept. of Ped., Children's Hosp. Med. Ctr., Boston. (sponsored by T. Berry Brazelton) This study describes the interaction of fathers with preterm infants, and compares it to mothers' interactions with preterm infants and the interactions of both parents with fullterm infants. Parent-child interactions at 5 months are related to perinatal complications and to developmental outcome at 18 months. Ten preterm and ten fullterm infants were recruited as newborns with their parents, and followed longitudinally until they were 18 months post-term conceptual age. At 5 months post term, all infants were videotaped during 3-minute en-face interactions with each parent. Episodes of play defined as "games" were subsequently coded. While mothers and fathers did not differ significantly in overall number of games played with fullterm infants, with preterm infants fathers played significantly fewer games than did mothers ($P<0.02$). In particular, fathers played significantly fewer non-arousing (verbal/visual vs. tactile/limb-movement) games ($p<0.05$). The data suggest that fathers adapted to the stress of the preterm infant by decreasing the number of games they play. Cross-time correlations showed different patterns of relationships for preterm infants' interaction with mothers and fathers. Healthier premature infants played fewer arousing games with mothers ($r=.75$), but not with fathers. Although fathers generally played a more indirect role, nevertheless the number of nonarousing games both parents played was more highly correlated with 18-month Bayley psychomotor scores ($r=.67$) than that of either parent alone. The study demonstrates fathers' adaptations in facilitating the preterm infant's development.

CARDIOLOGY

100 LONGITUDINAL EXERCISE DATA IN SICKLE CELL ANEMIA. Bruce S. Alpert, E. Victoria Dover, Wesley Covitz, William B. Strong, (Spon. by A.F. Robertson) Department of Pediatrics, Medical College of Georgia, Augusta

Cross-section exericse studies in our laboratory have shown impairments in maximum values of blood pressure (BP), heart rate (HR), and working capacity (KgM/min/kg) (WC) in children with sickle cell anemia (SS). Also, ischemia (I) was noted on the exercise ECGs: definite (D) I (15%), equivocal (E) I (34%), non (N) I (51%). Radionuclide angiography during exercise has confirmed decreased ejection fraction in the patients showing DI on exercise ECG. We sought to determine whether progression in the course of SS patients' cardiac dysfunction could be observed from short-term (1-3 yr) or long-term (4-7 yr) follow-up (F/U) longitudinal data. We performed 76 paired tests, 36 short-term and 40 long-term. The percentages of DI, EI, and NI ECGs for the F/U periods in relation to the initial ECG interpretation were:

	SHORT-TERM F/U			LONG-TERM F/U		
Initial ECG	DI	EI	NI	DI	EI	NI
DI	62	0	38	50	0	50
EI	0	25	75	13	25	62
NI	5	5	90	4	7	89

The hemoglobin and WC were lower in the cases developing DI than the other groups. The BP, HR, and WC values changed over time as would be expected by the period of growth and aging. No uniform change in myocardial oxygen supply/demand occurred over time. Further studies of the mechanisms of both improvement and deterioration are needed.

101 AUTOMATED BLOOD PRESSURE MEASUREMENT DURING ERGOMETER EXERCISE. Bruce S. Alpert, Nadine L. Flood, Ian C. Balfour, William B. Strong (Spon. by A.F. Robertson), Department of Pediatrics, Medical College of Georgia, Augusta.

Terminal digit preference and intra-observer variablity would reduce the accuracy of multi-institutional determinations of blood pressure (BP) response to exercise in healthy children or patients with congenital heart disease. Because patient motion and environmental noise increase the difficulty of manually obtaining Korotkoff sounds during exercise, we evaluated an automated system of BP measurement (Critikon 1165) in 121 children undergoing maximal cycle ergometer stress testing. The system uses acustic transduction with ECG gating and microprocessor signal filtering. A blinded observer measured BP simultaneously from the same arm (K1 and K4) as the system cuff. Correlation coefficients (r) between the manual and automated values were:

		Exercise Stages				Recovery (min)		
	Rest	1	2	3	Max	1	3	5
SYST	.92	.91	.96	.97	.96	.95	.92	.92
DIAS	.90	.85	.92	.86	.85	.77	.82	.85

These r values were higher in a subset of 79 subjects in whom a stethophone adapter was used instead of a stethoscope; The automated system eliminates all observer bias and would allow the pooling of data from multiple centers for BP determinations during exercise.

102 RESPONSES TO EXERCISE IN CHILDREN WITH SICKLE TRAIT. Bruce S. Alpert, Nadine L. Flood, William B. Strong (Spon. by A.F. Robertson), Department of Pediatrics, Medical College of Georgia, Augusta.

Sickle trait (AS) is usually considered a benign condition, although renal, hematologic, and muscular complications related to sickling are well-reported in periods of hypoxia and/or acidosis. Studies in our laboratory have shown impairments in the maximum exercise variables heart rate (HR), blood pressure (BP), and workload (W) in patients with sickle cell anemia (SS). The SS patients had a high incidence of ischemia on the exercise ECG. We sought to determine whether AS subjects had similar reductions in exercise variables as the SS patients. We performed maximal cycle ergometer stress testing on 48 children, ages 4-21, with AS. While no child developed definite ischemia, 4 (8.3%) had equivocal ischemia. The incidence of equivocal ischemia in healthy black children is 2.6%. Because maximum exercise values of HR, BP and W are age and size-dependent, Z score analysis was performed. The Z scores for female and male AS subjects, compared to data from healthy black children, are shown below (PWC = peak working capacity index, * = $p < 0.005$):

	HR	BP	Max W	PWC
Female	-1.16 (*)	-.26	-.68 (*)	-.65 (*)
Male	-1.13 (*)	+.33	-.99 (*)	-1.23 (*)

Since no ischemia was observed during exercise, we recommend unrestricted activities for AS children. The BP responses to exercise in AS subjects was normal, but further work is needed to define the mechanism of the HR and W impairments observed.

● 103 HEMODYNAMICS AND ORGAN BLOOD (BF) FLOW BEFORE AND AFTER DUCTUS ARTERIOSUS (PDA) OCCLUSION IN SURFACTANT TREATED PRETERM LAMBS. Barry G. Baylen, Hiroshi Ogata, Machiko Ikegami, Harris L. Jacobs, Alan H. Jobe, and George C. Emmanouilides, UCLA School of Medicine, Harbor-UCLA Medical Center, Dept. of Pediatrics, Torrance, CA

The hemodynamic effects of PDA were studied by occluding the ductus arteriosus of 10 preterm lambs (120-124 d. G.A.) in the first 4 hrs of life. Animals were treated with surfactant at birth and mechanically ventilated. Organ BF and left ventricular (LV) function were measured using cineangiography, and labeled microsphere methods. The PDA was occluded by obstruction of its lumen with a catheter balloon. Regional BF (ml/gm) and the following hemodynamic measurements were obtained just before and up to 30 minutes after PDA occlusion: Pulmonary (QP) and systemic (QS) flows: "effective" Qs-ml/kg (Qs eff); mean pulmonary and aortic pressures (PA/AO); LV ejection fraction (EF%) and end diastolic pressure (LVEDP). Mean arterial blood gases before occlusion were PO_2 (68±11 SE, Torr), pCO_2 (32±2) and pH (7.38±.02).

(MEAN)	QP/QS	QS eff	PA/AO	EF%	LVEDP	HEART	CARCASS	GI
PRE	1.9	130	.73	74	5	1.1	.10	.2
POST	1.0†	228†	.57†	72(NS)	5(NS)	2.4†	.17†	.4†

Early surfactant therapy is associated with ductal constriction and moderate left-right shunt. Left ventricular function (EF%,LVEDP) is not impaired. However, "effective" systemic blood flow notably to the heart, carcass and GI tract is significantly decreased (†p<.01). Thus, left-right ductal shunting in prematures may have detrimental affects upon organ blood flow in spite of adequate LV performance.

104 NONINVASIVE CARDIAC OUTPUT (CO) MEASUREMENT DURING EXERCISE IN CHILDREN WITH CONGENITAL HEART DISEASE Robert H. Beekman, Charles Marks, Albert P. Rocchini, Victor L. Katch, (Spon. by Amnon Rosenthal) University Of Michigan Medical School, C.S. Mott Children's Hospital, Pediatric Cardiology Exercise Physiology Laboratory, Ann Arbor, MI

To validate the accuracy of the Indirect Fick (CO_2 rebreathing) technique in children Indirect Fick CO was compared to Direct Fick CO and the thermodilution (TD) CO in 9 children (age 7-19 years) with congenital heart disease. Diagnoses were aortic stenosis (n=5), postoperative coarctation (n=2), postoperative tetralogy of Fallot (n=1), and corrected transposition (n=1). CO was measured at rest and during supine bicycle exercise at 200 KgM/min (n=9), 400 KgM/min (n=6), and 600 KgM/min (n=3). VO_2 and VCO_2 were measured continuously by open-circuit spirometry and rapid response gas analyzers. TDCO was measured twice at rest and during the third minute of each exercise stage. Aortic (Ao) and pulmonary artery (PA) O_2 saturation and pCO_2 were then measured. Ao pCO_2 was then estimated from end-tidal pCO_2, and PA pCO_2 was estimated by Defares rebreathing technique. CO_2 content was determined from estimated and measured pCO_2 using Comroes CO_2 dissociation curve. Since estimated Ao-PA CO_2 content difference (CO_2 diff) related linearly to measured CO_2 content difference ($y=.29x + 2.54$, $r=0.64$, $p<.001$), CO_2 diff was adjusted by this equation. There was a linear correlation between Indirect Fick CO (VCO_2/CO_2 diff) and both Direct Fick CO ($y=.57x + 5.36$, $r=0.71$, $p<.001$) and TDCO ($y= .59x + 2.92$, $r=0.85$, $p<.001$). A poor correlation ($r= 0.45$) was found for resting CO alone. Thus the Indirect Fick CO technique, as described, provides a simple, accurate, noninvasive estimate of exercise CO in children with heart disease.

● 105 THE EFFECTS OF AFTERLOAD STRESS ON MYOCARDIAL FUNCTION IN NEWBORN AND ADULT SHEEP. William Berman, Jr., Deborah Christensen. University of New Mexico School of Medicine, UNM Affiliated Hospitals, Department of Pediatrics, Albuquerque, New Mexico.

The effects of increased preload and afterload were examined separately in 7 newborn and 6 adult sheep, instrumented chronically. Myocardial function was evaluated by peak dp/dt of the left ventricle (LV dp/dt) and the pre-ejection period to left ventricular ejection time ratio (PEP/LVET). Preload was increased by the rapid infusion of 30ml/kg of isotonic saline; afterload was increased by the infusion of 0.2mg/kg/min of methoxamine. Heart rate variations were minimized by pretreatment with atropine (0.02mg/kg). Preload elevation increased arterial and venous pressures, reduced the PEP/LVET ratio and increased LV dp/dt to a comparable extent in newborns and adults. Afterload stress increased arterial and venous pressures to a similar extent in newborns and adults, but myocardial contractile indices changed more in the newborns (PEP/LVET ratio +12%, LV dp/dt -21%) than in adults (PEP/LVET ratio +6%; LV dp/dt -8%). The neonatal myocardium, operating at a high baseline level of function, has limited reserve to respond to acute increases in circulatory afterload. This fact, in conjunction with the previously demonstrated limited preload and heart rate reserve of the neonatal myocardium, may explain the dire circulatory consequences of left sided obstructive lesions in the neonate.

● 106 DIGOXIN EFFECTS IN INFANTS WITH CONGESTIVE HEART FAILURE. William Berman, Jr., Colleen J. Niland, Steven M. Yabek, Terrence Dillon. University of New Mexico School of Medicine, UNM Affiliated Hospitals, Department of Pediatrics, Albuquerque, New Mexico.

Digoxin therapy was assessed in 18 infants (mean age 4 mos.) with congestive heart failure due to VSD (14), coarctation (2), aortic stenosis (1) and myopathy (1). Appropriate maintenance therapy was calculated by pharmacokinetic analysis performed after IV administration of 1/2 the loading dose. Drug effect was assessed by echocardiography, RBC Na-K ATPase determination and subjective evaluation before and 5 or more days after treatment was started. Steady state drug concentration averaged 1.4±0.5 ng/ml (predicted value 1.5 ng/ml). Drug $t_{1/2}\beta$ (21.9±8.0 hr) and volume of distribution (9.9±0.7 L/kg) varied moderately between patients. Mean values of echocardiographic variables are shown below:

	$F_cS(\%)$	LV_d(%nl)	V_{cf}(1/sec)	PEP/LVET
Pre-Rx	28	140	1.8	0.420
Post-Rx	34	148	1.9	0.423

Only 4 of 18 patients showed an inotropic response. RBC Na-K ATPase decreased in each patient, from 20.8±5.8 nmolP_i/mg/min before treatment to 12.0±2.0 nmolP_i/mg/min at therapeutic steady state. 9 of 18 patients, however, responded clinically, evidenced by reductions in heart rate, respiratory effort, sweating and liver size. Because biochemical, inotropic and clinical drug effects were not consonant in this series, we suggest mechanisms other than inotropic stimulation must be invoked to explain digoxin's beneficial effects in some patients.

● 107 MUSCULAR INTERVENTRICULAR SEPTUM FORMATION IN THE CHICK EMBRYO. G. Ben-Shachar, R. V. Lucas, R. A. Arcilla, F. J. Manasek; University of Minnesota, Division of Pediatric Cardiology, and Pritzker School of Medicine, The University of Chicago Hospitals and Clinics, Departments of Anatomy and Pediatrics, Chicago, Illinois

We have reexamined the traditional views that a) the 2 ventricles are developmentally separate and distinct entities, and b) the muscular interventricular septum (MIVS) is, from its beginning, a discrete structure separating the 2 primitive ventricles. Sixty dissected chick embryo hearts were studied at different stages of development with scanning electron microscopy. Ventricular trabeculations (TR) develop rapidly beginning at stage (ST) 17 (2½ days). These appear morphologically as superior plates and columnar trabeculations. At ST 21 (3½ days), the TR become denser in the ostium bulbi region where the superior plates begin to adhere to each other at ST 26 (5 days) to form the sinus septum. Fusion of adhering TR proceeds in a cranio-caudal direction producing the MIVS, and is complete by ST 30 (6½ days). Remnants of opposing TR endocardial surfaces were identified as intraseptal channels. We suggest that persistence of these channels may result in single or multiple muscular ventricular septal defects. The formation of the MIVS from preexisting TR suggests that the 2 ventricles are not necessarily separate developmental entities but arise by division of a single, primitive ventricular chamber. Our findings have implications to the concept of univentricular hearts: the ventricular chamber in single ventricle represents the persistent primitive chamber which should not be identified to be anatomically left ventricle or right ventricle.

● 108 ISOLATED AORTIC VALVE REPLACEMENT IN CHILDHOOD: NON-INVASIVE EVALUATION OF LEFT VENTRICULAR FUNCTION G. S. Bisset, III, S. S. Hirschfeld, R. A. Meyer, F.W. James, S. Kaplan, Depts. of Peds., Tulane Univ. Med Center, New Orleans and Univ. of Cinn. Coll. of Medicine, Cincinnati

M-mode echocardiography (MME), electrocardiography (ECG) and graded exercise testing (GXT) were utilized to assess left ventricular (LV) function in children with prosthetic aortic valves (AoV). Since 1964, there have been 15 survivors of isolated AoV replacement, aged 11-19.5 yrs (16.3 yrs). All but 2 are asymptomatic (1 has residual aortic insufficiency (AI) and 1 severe obstruction). Each patient (pt) had abnormal GXT's and MME's prior to AoV replacement. Resting ECG's, 2 months-2yrs post-operatively (PO), revealed that 10 (67%) had LV hypertrophy, 2 (13%) had signs of healed anterolateral myocardial infarction and 2 (13%) had residual ST-T wave changes. Nine pts had GXT's 2 months-12yrs (3.6 yrs) PO. Six (67%) had an abnormal blood pressure response with maximum exercise (ME), 7 (78%) had working capacities <70% of the expected normal value and 2 had abnormal ST segment changes (>2mm depression) with ME. MME in 12 of the 15 pts one month-13yrs PO demonstrated LV enlargement in 6 (50%), abnormal septal motion in 6 (50%) and LV free wall and/or septal thickness >2 SD above expected normals in 11 (92%). The LV systolic time intervals and percent shortening (%S) were abnormal in 7 pts. Children with predominant AI had the worst LV recovery rate. All 4 had persistently dilated, thick LV's on MME and abnormal %S. Persistent LV dysfunction is noted in the majority of the children after prosthetic AoV implantation. Early intervention, particularly in children with AI may improve the long-term outcome.

109 CHARACTERIZATION OF SINGLE VENTRICLE WITH COMBINED PULSED DOPPLER AND TWO-DIMENSIONAL ECHOCARDIOGRAPHY
George S. Bisset, III, Stephen S. Hirschfeld, Tulane Univ. Sch. of Med., Dept. of Ped., Tulane Med Center, New Orleans

Pulsed Doppler (PD) and 2-dimensional echocardiography (2-DE) were utilized to assess the anatomic and hemodynamic status of patients (pts) with single ventricle (SV). Of 13 children, 11 had SV of left ventricular type, 1 had SV of right ventricular type and 1 had SV of the undifferentiated variety. Evaluation of atrioventricular (AV) valve morphology revealed 5 pts with 2 AV valves (each had a small tricuspid valve (TV)), 4 with common AV valves, 1 with a single TV and 3 with single mitral valves. AV valve insufficiency was demonstrated by PD in 3 of the 4 pts with common AV valves and 1 additional pt with a small, straddling TV. The great vessel positions were identified as d-transposed in 4, l-transposed in 4 and normal in 5. PD examination with the Doppler sample volume (DSV) positioned in the main pulmonary artery revealed 2 pts with ductal-dependent pulmonary blood flow. Two pts had normal pulmonic valves (PV's) with typical PD continuous flow patterns indicating patent ductus arteriosus. Four others had turbulent systolic flow patterns consistent with antegrade flow through stenotic PV's. With the DSV positioned distal to the aortic valve no pt demonstrated disturbed flow, indicating an absence of aortic or sub-aortic obstruction. The atrial septum was intact in 2 pts and absent in 1. A patent foramen ovale versus secundum atrial septal defect was demonstrated in 5 pts. In conclusion, 2-DE-PD provides an accurate non-invasive assessment of SV morphology and hemodynamics. Catheterization may be obviated in many of these pts particularly when palliative surgery is comtemplated.

● **110** DEVELOPMENTAL DIFFERENCES OF THE MYOCARDIAL CONTRACTILE RESPONSE TO THE CALCIUM ANTAGONISTS. R.J.Boucek,Jr P.S.Mushlin,M.Shelton,V.Starnes,R.D.Olson,(Spon.by T.P Graham,Jr.);Vanderbilt Univ., Dept. of Ped., Nashville, TN.

Since developmental differences in the effect of Ca^{++} on myocardial contractility(MC)have been described, we hypothesized that the calcium antagonists, verapamil(V),nifedipine(N)and diltiazem (D)may also exhibit age-related differences on MC.Thus, we evaluated the dose-response relationship of V,N and D on indices of MC, developed pressure(DP)and maximal rate of pressure development(dP/dt)in the isolated blood-perfused immature(I;n=6)and adult(A;n=5) rabbit heart.The table below shows the values(x±SEM)for the concentration(μM)found to inhibit by 20% and 50% the DP and dP/dt at a constant pacing rate. (*p < 0.01, I vs A).

		-Concentration to inhibit DP-		-Concentration to inhibit dP/dt	
		20%	50%	20%	50%
V	I	9 ± 2*	52 ± 5.8*	9 ± 2.3*	54 ± 8*
	A	110 ± 10	510 ± 140	110 ± 30	470 ± 1.3
N	I	9 ± 1.7*	--	11 ± 3.5*	--
	A	140 ± 34	--	130 ± 28	--
D	I	130 ± 35	880 ± 90*	130 ± 28	990 ± 250*
	A	520 ± 250	3200 ± 700	550 ± 180	2800 ± 560

The results show that V and N are 10 times more potent in depressing MC in I than A hearts and that D exhibits significantly less age-related effects on MC than V or N.The data suggest age-related differences either in receptor affinity for the calcium antagonists or a greater dependence on extracellular Ca^{++} influx in the I heart.

111 DYSRHYTHMIAS AFTER ATRIAL SEPTAL DEFECT REPAIR
Tim Bricker, Paul C. Gillette, D.A. Cooley, and Dan G. McNamara. Lillie Frank Abercrombie Section of Pediatric Cardiology, Baylor College of Medicine and Texas Children's Hospital, Houston, Texas.

Postoperative electrocardiograms were reviewed in 292 patients with isolated secundum atrial septal defects. PR interval shortened by the seventh postoperative day ($P < .05$) in comparsion to the preoperative PR interval. 228/292 (78%) were only observed to be in sinus rhythm. 9/292 (3%) had a preoperative dysrhythmia. 64/292 (22%) had a postoperative dysrhythmia. 22 (8% of total) of these patients were symptomatic. 16/65 (5% of total) had a tachydysrhythmia. 6/292 (2%) currently have a pacemaker (5% of our pediatric patients with pacemakers). In 17/292 patients (6% of total and 26% of those with dysrhythmias) dysrhythmias were noted in the first three days postoperatively. 22/292 (7% of total, 34% of dysrhythmias) presented with dysrhythmias between the fourth and fourteenth day after surgery. 7/292 (2% of total, 11% of dysrhythmias) presented from two weeks to three months postoperatively. 4/292 (1.4% of total, 6% of dysrhythmias) presented from three months to one year postoperatively. 3/292 (1% of total, 5% of dysrhythmias) presented from one to three years postoperatively. 7/292 (2% of total and 10% of dysrhythmias) presented at from three to eight years postop. 4/292 (1.4% of total and 6% of dysrhythmias) presented at greater than eight years postoperatively. The latest presentation of symptomatic dysrhythmia was seventeen years after surgery. 5/292 (1.7%) had Holt-Oram syndrome. All five had postoperative dysrhythmias.

● **112** CORRELATION OF ENDOCARDIAL AND EPICARDIAL ACTIVATION IN PATIENTS WITH ENDOCARDIAL CUSHION DEFECT
Robert Campbell, Macdonald Dick, Douglas M. Behrendt Paul Hees, University of Michigan Medical School, C.S. Mott Children's Hospital,Section of Pediatric Cardiology,Ann Arbor, MI

Epicardial and left ventricular endocardial activation were analyzed in 5 patients (age 4 mos. to 9.5 years) with endocardial cushion defect (ECD, 4 partial, 1 complete) intraoperatively prior to surgical repair. Epicardial activation, recorded from up to 47 sites over the entire epicardium, demonstrated an abnormal activation sequence; earliest activation was recorded from the diaphragmatic left ventricular (LV) surface 11.2 msec (range 4-15 msec) after QRS onset. Depolarization then spread laterally and anteriorly over the LV. Latest LV activation occured at the basal anterolateral surface 43 msec (range 34-50 msec) after QRS onset. Latest epicardial activation overall was recorded along the RV inflow area 69.9 msec (range 52-92 msec) after QRS onset. LV endocardial activation, recorded from three sites occured earliest in the posterior paraseptal area 10.6 msec (range 0-18 msec) after QRS onset. Subsequent activity occured at the anterior paraseptal area 21.4 msec (range 12-39 msec) after QRS onset, and at the free wall 21.6 (range 11-35 msec) after QRS onset. These data document for the first time that in patients with ECD the previously reported early posterior epicardial activation not only corresponds to but also is preceded by early activation of the underlying posterior endocardium. This activation sequence explains the superior leftward frontal plane QRS axis, and is in accord with the observed posterior displacement of the cardiac conduction tissue in patients with ECD.

113 EFFECTS OF RIGHT AND LEFT ATRIAL STIMULATION ON ATRIAL REFRACTORY PERIODS AND A-V NODAL CONDUCTION
Alfonso Casta, Abimbola Talabi, David W. Sapire (Spon. by Randall M. Goldblum) University of Texas Medical Branch, Department of Pediatrics, Galveston, Texas

The effect of left atrial (LA) stimulation on refractory periods (RP) and A-V nodal conduction (A-H) have not been previously reported in children (C). Indirect measurements from coronary sinus stimulation have been obtained in adults with dysrhythmias (D). Ten C (8 preoperative and 2 postoperative) with congenital heart defects and with no evidence of D were evaluated electrophysiologically by atrial extrastimulation at the same cycle length (CL) (500 msec) from both the right atrium (RA) and LA. The LA was stimulated directly through an interatrial communication. Rapid RA pacing was also performed. The effective RP of the RA and LA ranged between 130-240 msec; and 100-250 msec respectively. The functional RP of the RA and LA ranged between 210-320 msec; and 140-280 msec respectively. There was no significant difference between the RP for RA and LA by the paired "t" test. Atrial refractoriness was reached first preventing evaluation of A-V nodal RP in 7 C. The A-H intervals measured from RA and LA stimulation at a CL of 500 msec ranged between 70-120 msec; and 55-105 msec respectively. The A-H interval was significantly shortened by LA stimulation ($p<0.05$). Our findings indicate that in C the site of atrial stimulation has no significant effect on atrial RP and A-V nodal conduction is significantly shortened when evaluated by LA stimulation. Shortened A-H intervals on LA stimulation can be explained by earlier entry into the lower A-V node from the LA with retrograde conduction to the low RA.

114 DIABETIC CARDIOPATHY IN POORLY CONTROLLED ADOLESCENT DIABETICS: NORMALIZED VALUES WITH IMPROVED DIABETIC CONTROL
S. Castells, R. Cooper, R. Stein, M. Noval, H. Copur, and K. Kwateng, SUNY, Downstate Med Ctr, Dept of Ped, Brooklyn, N.Y.

Nineteen insulin dependent diabetics, ages 15.3±0.5, (SEM) and 23 controls ages 14.8±0.5, had exercise stress testing and M-mode echocardiograms during a period of poor diabetic control while receiving once a day insulin. Cardiac function was reevaluated after 3 months of improved diabetic control achieved with bi-daily insulin injections. Two indices of diabetic control, M-value and serum Hb A_{1C} significantly improved on bi-daily therapy. M-value decreased from 108±20 to 37.5±4.2, $p<0.01$ and Hb A_{1C} from 12.7%± 0.6 to 8.9%±0.6, $p<0.01$. Systolic blood pressure and resting pulse rates were elevated during periods of poor control as compared to normals (P.B.: 121.5±2.5 and 105.5±1.6, $p<0.03$, and P.R.: 78.6±3.6 and 70.9±2.9, $p<0.05$) and decreased to normal values after 3 months of better diabetic control. M-mode echocardiography revealed right ventricular enlargement. Right ventricular internal dimension in diastole ($RVID-_d$) was 17.97±1.13 in poor diabetic controls and 14.32±0.95 in controls, $p<0.01$ and decreased to 16.54±0.13, after 3 months of good control with bi-daily injections, N.S. from controls. All other echocardiographic parameters including chamber dimensions and left ventricular functions were normal. Exercise stress testing revealed no evidence of ischemic changes suggestive of coronary artery disease. These findings suggest the presence of decreased right ventricular compliance without coronary artery disease in poorly controlled juvenile diabetics which improves with better glucose control.

115 VENTRICULAR ARRHYTHMIAS IN CHILDREN WITH MARFAN'S SYNDROME Su-chiung Chen, Leonard Fagan, Soraya Nouri, Mark Sivakoff, James Donahoe (Sponsored by Thomas Aceto, Jr.), St. Louis University School of Medicine, St. Louis, MO

Conduction disturbances are common in children with Marfan's syndrome, but the occurrence of serious ventricular arrhythmia has not been stressed. An 18 yr male with mild mitral regurgitation (MR) had cardiac arrest and was successfully resuscitated. He was found to have ventricular tachycardia (VT) and frequent premature ventricular contractions (PVCs). This prompted us to review our group of 24 children with Marfan's syndrome. They were first seen at the mean age of 7.4 yr (4 mo-16 yr) and were followed for a mean of 5.7 yr (1-22 yr). Six died and 6 were lost to follow-up. Four had no significant heart disease. E.K.G.s were available in 22 patients (pts) and 19 were abnormal. PVCs were noted in 8 pts: 2 had severe MR, 4 had mild MR, 1 had mild aortic dilatation (AO dil.), 1 had no mitral or AO abnormalities. Three pts were asymptomatic but the other 5 were symptomatic. The 2 with severe MR had congestive heart failure and underwent mitral valve (MV) replacement. Three had VT in addition to PVCs: 1 had syncope and arrest, 2 had chest pain with fatigability; 2 of these had MV prolapse and AO dil. with left ventricular enlargement, but 1 had no detectable MV or AO abnormality. Ventricular arrhythmia can occur in children with mild MR or no valvular disease, without clinical evidence of myocardial infarction or dysfunction. Holter monitor recordings or stress E.K.G.s are helpful for detection and treatment of ventricular arrhythmia in symptomatic pts.

● **116** **HEMODYNAMIC MEASUREMENTS IN THE EMBRYONIC CHICK CARDIOVASCULAR SYSTEM**

Edward B. Clark and Norman Hu, Division of Pediatric Cardiology, Department of Pediatrics and the Cardiovascular Center, University of Iowa Hospitals and Clinics, Iowa City, Iowa

Little information is available on the hemodynamic changes during morphogenesis of the heart. We measured heart rate, mean dorsal aortic blood flow ($\bar{Q}$) and mean arterial blood pressure ($\bar{P}$) in 160 white Leghorn chick embryos on day 3 (stage 18), day 3.5 (stage 21), day 4 (stage 24) and day 5 (stage 27) of incubation. Dorsal aortic blood velocity was measured with a 20 MHz pulsed-doppler flow meter using a 1 mm piezoelectric crystal positioned at a 45° angle to the dorsal aorta. Dorsal aortic diameter was measured with a micrometer eyepiece and blood flow was calculated. *In-vitro* correlation, the velocity meter was linear (y=.85x+1.19, r=.99) over a range of 1 to 20 mm/sec. Mean arterial blood pressure was measured with a servo-null pressure system from a 5 micrometer tip diameter cannula inserted in the right vitelline artery. *In-vitro* correlation of the pressure system was linear (y=1x-.24, r=.99) from 0 to 39 mmHg. Total vascular resistance was calculated as $\bar{P}/\bar{Q}$.

($\bar{x}$±1SEM)	Stage 18	Stage 21	Stage 24	Stage 27
Heart rate bpm	165±3	177±3	183±3	188±3
$\bar{Q}$ mm³/sec	.18±.01	.39±.02	.78±.03	1.52±.06
SV mm³	.06±.003	.13±.005	.26±.009	.49±.02
$\bar{P}$ mmHg	.68±.02	.86±.04	1.05±.03	1.22±.06
TVR	3.78	2.21	1.35	.80

These techniques will allow the study of the embryonic cardiovascular system during the critical period of cardiac morphogenesis.

● **117** PERICARDIAL EFFUSION(PE)IN RHESUS-SENSITIZED FETUSES--AN EARLY ULTRASOUND INDICATOR OF DEVELOPING FETAL HYDROPS.* Greggory R. DeVore, Lawrence D. Platt, and Bijan Siassi. The University of Southern California School of Medicine, Los Angeles County Women's Hospital, Depts. Obstetrics and Pediatrics, Los Angeles, Calif. 90033.

Rhesus hemolytic anemia, although observed less frequently since the introduction of Rhogam, still presents a diagnostic and therapeutic challenge to the clinician. In severely affected pregnancies, unless intrauterine transfusion (IUT) is initiated, fetal hydrops can develop with ensuing death. From an ongoing study of 250 high risk pregnancies, the pericardial space of 13 Rh-sensitized fetuses was imaged with two-dimensional-directed M-mode echocardiography (2D-MM)and evaluated for evidence of a PE. When present, the PE occurred as early as 20 weeks of gestation and its presence preceded the appearance of ascites, soft tissue edema, or pleural effusion as manifest by ultrasound. In three fetuses the PE resolved following IUT. One fetus, in which the PE was diagnosed 48 hours prior to birth, was noted to have the PE on neonatal echocardiographic examination following birth. In conclusion, the pericardial sac, due to its limited potential space, appears to (1) be the site of the earliest manifestation of fluid accumulation in fetuses destined to develop hydrops and (2) is a sensitive method of monitoring the effectiveness of IUT.

*Supported by a grant from THE THRASHER RESEARCH FUND

118 EFFECT OF MORPHINE, BENEDRYL AND CHLORALHYDRATE ON THE SINUS NODE IN THE EARLY POST-OP CARDIAC PATIENT. Macdonald Dick, Craig J. Byrum, Paul Hees, Douglas M. Behrendt. University of Michigan Medical School, C.S. Mott Children's Hospital, Department of Pediatrics, Ann Arbor.

Morphine (MS), benedryl (B), and chloral hydrate (CH) are widely used as sedatives in patients with cardiac disease; however, no data exist regarding the effect of these drugs on the sinus node early post-op. To examine the effect of these agents, as well as baseline day-to-day variation (V) and effect of supine (P) position, we measured the total sinoatrial conduction time (SACT) (n=33) and the maximal corrected sinus node recovery time (CSNRT) (n=46) using programmed stimulation. Thirty-three to 46 children, age 0.2 to 19.9 yrs; (mean 6 yrs) were studied in the upright position through bipolar transthoracic pacing wires at 1 to 9 days (mean 4 days) following surgery. Statistical analysis demonstrated no significant difference between the means of the paired observations or among the means between the 6 groups. We conclude that 1) MS, B, CH, and MS with B do not predictably alter the sinus node when employed in this clinical setting. 2) There is no significant variation in SACT or CSNRT related to day-to-day change or the supine position.

		N	BEFORE msec x_1±SD	AFTER msec x_2±SD	(x_1-x_2)±SD msec	P VALUE
TOTAL SACT	V	5	134±45	123±51	11±30	NS
	P	5	139±10	144±21	-5±18	NS
	MS	6	99±53	105±62	-6±13	NS
	B	3	93±26	85±29	8±15	NS
	MS+B	3	120±40	117±45	3±13	NS
	CH	4	138±22	135±15	3±9	NS
MAX CSNRT	V	10	189±104	178±84	11±91	NS
	P	6	140±44	176±87	-36±60	NS
	MS	9	149±101	180±133	-31±124	NS
	B	5	149±86	128±89	20±24	NS
	B+MS	3	187±185	133±86	54±108	NS
	CH	4	169±25	139±27	30±21	NS

119 VALUE OF ACUTE ELECTROPHYSIOLOGIC DRUG TESTING IN CHILDREN WITH ATRIOVENTRICULAR RE-ENTRANT TACHYCARDIA: PROCAINAMIDE, QUINIDINE, OUABAIN. Macdonald Dick, Robert M. Campbell, Craig J. Byrum, Paul Hees, University of Michigan Medical School, C.S. Mott Children's Hospital, Section of Pediatric Cardiology, Ann Arbor, MI

Patient	Atrium ERP			AVN ERP			AC Retrograde ERP			AVRT		
	P	Q	O	P	Q	O	P	Q	O	P	Q	O
1	↑	NA	→	→↑	NA	→↑	↑	NA	NA	A	NA*	→
2	↑	↑↑	↑	→↑	→↑↑	→	NA	NA	NA	A	A*	→
3	↑↑	NA	NA	→↑	NA	NA	→	NA	NA	A	NA*	NA
4	NA	↑	↑	NA	↑	→	NA	↑↑	→	NA	A*	→
5	↑	NA	NA	→↑	NA	NA	→	NA	NA	A	A*	NA

→ = No change ↑ = Increase ↓ = Decrease
NA = Not available A = Abolished acutely
* = Abolished with chronic PO med.

To determine the most effective drug for control of orthodromic atrioventricular re-entrant tachycardia (AVRT) refractory to Digoxin, Propranolol, or both, we performed acute electrophysiologic drug studies (EPDS) in 5 adolescents (age 12-19 years).Procainamide (P) (10 mg/kg IV; 4.9 mcg/ml serum level),Ouabain (O) (0.01 mg/kg IV not exceeding .5 mg), or Quinidine (Q) (20 mg/kg/day po X4d; 2.24 mcg/ml serum level) was administered and EPDS was repeated. Response to drugs was evaluated by inhibition of sustained AVRT and by measuring the effective refractory period (ERP) of the atrium, AV node and accessory connection (AC). Ouabain demonstrated variable effect on the atrial ERP and no effect on AVRT.P and Q prolonged the atrial ERP (4/4 tested) and AC retrograde ERP (2/4).AVRT was abolished in each patient tested acutely with P or Q, and also by chronic oral Q (follow-up 7.5 mos).We conclude that acute EPDS is a valuable technique to assess drug response in patients with refractory AVRT and that acute P response corresponds to chronic Q response.

120 REVERSIBLE HYDROCEPHALUS FOLLOWING REVISION OF SEVERE SUPERIOR VENA CAVAL (SVC) OBSTRUCTION COMPLICATING THE MUSTARD OPERATION. Terrence Dillon, William Berman, Jr., Steven M. Yabek, Robert Siegel, Bechara Akl. University of New Mexico School of Medicine, UNM Affiliated Hospitals, Department of Pediatrics, Albuquerque, New Mexico.

SVC obstruction is a well-recognized complication of the Mustard operation for transposition of the great vessels. We describe 3 patients who underwent Mustard repair at a mean age of 9 months and developed increasing head circumference (HC), facial edema, and cerebral edema or documented hydrocephalus postoperatively. Cardiac catheterization (CC) showed severe SVC obstruction with a mean SVC pressure of 27 mmHg and a mean pressure gradient of 19 mm Hg between the SVC and systemic venous atrium. The azygous vein was widely patent in all 3 patients. The first patient died at 27 months of age and was found to have diffuse cerebral congestion and mild right uncal herniation. Computerized axial tomographic (CAT) scans in the remaining 2 patients revealed cerebral ventricular dilatation with widening of the cortical sulci compatible with communicating hydrocephalus. The second patient underwent surgical revision of the SVC obstruction after which the HC and CAT scan reverted to normal and the mean SVC pressure at repeat postop CC fell to 11 mm Hg. The third patient underwent surgical revision only recently, but already has shown resolution of the facial edema and normalization of HC. In conclusion, severe SVC obstruction following the Mustard operation may result in chronic cerebral congestion and hydrocephalus despite azygous decompression. The CNS abnormalities are reversible with surgical relief of the SVC obstruction.

121 EVALUATION OF PULMONARY ARTERY BANDING WITH 2-DIMENSIONAL ECHOCARDIOGRAPHY. Terrence Dillon, William Berman, Jr., Steven M. Yabek, Bechara Akl, P. Sue Corlew. University of New Mexico School of Medicine, UNM Affiliated Hospitals, Department of Pediatrics, Albuquerque, NM.

Seven infants (mean age 2.5 months and mean weight 3.5 kg) with severe intractable congestive heart failure secondary to large left to right shunts and pulmonary hypertension underwent pulmonary artery (PA) banding. The series included 4 patients with single ventricle, 2 with complete AV canal without AV valve incompetence, and 1 with interrupted aortic arch (IA) and ventricular septal defect (VSD). The initial patient with IA and VSD underwent contrast injection in the inferior vena cava and had marked right to left shunting across the VSD, consistent with excessive banding. The remaining 6 patients underwent supraternal notch echocardiography--5 in the immediate postoperative period and 1 one year postoperatively. In these 6 patients the entire circumference of the PA band was visualized. The mean ($\pm S_2D.$) cross sectional area (CSA) at the band was 1.57(±0.40) cm^2/M^2 in contrast to the pre-operative mean CSA of the PA of 5.91(±1.60) cm^2/M^2. The mean CSA of the ascending aorta was 2.50(±0.77) cm^2/M^2. The patient evaluated 1 year postoperatively was also noted on echo to have encroachment by the band on the right PA and this was confirmed angiographically. Two of these 6 patients underwent postoperative cardiac catheterization and were found to have systolic pressure gradients of 70 and 100 mm Hg across the band. In conclusion, 2-Dimensional echocardiography allows immediate and long-term evaluation of the efficacy and complications of PA banding.

122 MODIFICATION OF CARDIOPULMONARY DOPAMINE (D) RESPONSE BY CONTINUOUS TOLAZOLINE (T) INFUSION IN UNANESTHETIZED NEWBORN LAMBS. Willa H. Drummond and Becky J. Williams, University of Florida College of Medicine, Shands Teaching Hospital, Department of Pediatrics, Gainesville.

Newborn lambs had catheters placed in the pulmonary artery (PAP), aorta (SAP), left atrium (LAP) and inferior vena cava; the ductus was tied and a flow transducer placed around the main PA. After recovery, lambs (n=4, age 5-15 days) were studied on two successive days. On one day D was infused at 2.7, 27, and 270 ug/kg/min. On the alternate day during continuous T infusion (5 mg/kg/hr),D was infused at the same doses. All pressures, pulmonary blood flow (QP), and heart rate (HR) were measured. Pulmonary (PVR) and systemic vascular resistance (SVR) and PVR/SVR were calculated. No changes occurred with T infusion alone, or low dose D infusion. Medium dose D + T showed almost significant difference (p=.06-.08) in SAP, LAP and SVR and higher heart rate (293±45 vs 171±20, P<.05; paired t) relative to D alone. With D alone, SAP, PAP, LAP and SVR rose over the dose range with no change in QP. A tendency for higher PVR/SVR occurred at both medium and high D doses plus T than with D alone (.38±.04 vs .29±.03 and .36±.07 vs .23±.02, p=.1) At high dose D, we observed (*p<.05):

	SAP	SVR	PAP	PVR	LAP	HR	QP
Base D	73.3±4	.42±.03	23.1±.8	.122±.01	2.1±.4	177±13	209±19
D+T	74.5±4	.42±.07	20.5±1	.103±.01	1.9±.5	187±20	205±26
270ug D	150±8	.66±.08	38.6±6	.15±.01	12.9±2	217±25	274±9
D+T	90±15*	.35±.09*	34.8±5	.105±.01*	5.3±3*	279±25*	295±50

These cardiopulmonary effects are very similar to those seen when D is infused during phentolamine α-blockade. (Williams:Drummond, 1981). Thus, tolazoline modified the cardiopulmonary dopamine response by permitting a greater increase in cardiac output, and by partially blocking dopamine's systemic and pulmonary α-adrenergic effect.

123 MYOCARDIAL INFARCTION AFTER PROSTACYCLIN (PGI_2) TREATMENT OF NEONATAL PULMONARY HYPERTENSION (PH). Willa H. Drummond, Becky J. Williams, William B. Blanchard, Curt J. Bucholz, Carole L. Bucholz, University of Florida College of Medicine, Shands Teaching Hospital, Dept. of Pediatrics, Gainesville.

PGI_2 is an endogenous vasodilator and platelet antiaggregatory agent currently being used to inhibit platelet function during cardiac bypass and after myocardial infarction in adults. It has also been used with variable success for dilating pulmonary arterioles in several infants with PH. We treated a 39 wk, 2540 gm infant with PH using PGI_2 under a blind protocol. Initial placebo infusion failed to change pulmonary (PAP) or systemic (SAP) arterial pressure, or PaO_2. Subsequently, PGI_2 at 25 ng/kg/min changed mean PAP from 46 to 34 mmHg, SAP from 52 to 45 mmHg, and PaO_2 from 19 to 80 torr. The baby's oxygenation stabilized for 3 hrs. Then, drug infusion was inadvertently terminated for 25 min. Systolic PAP rose to >100 mmHg, without SAP change, and oxygenation deteriorated. Fifteen minutes after PGI_2 was restarted at the previous dose, PAP fell from >100/15 to 40/10 and SAP from 60/44 to 56/18. At this point an idioventricular rate of 60 developed, and the infant could not be resuscitated. At autopsy, a 2.5x1.0 cm septal infarct was found using supravital staining techniques, and was timed to have occurred <6 hr. premortem. Thus, phenomena involving either endomyocardial perfusion changes, or perhaps rebound (Sinzinger, Prost.21:49, 1981) or dose related (Jorgenson, Thromb. Res. 19:877, 1980) platelet hyperaggregability, appear to be a risk when chronic PGI_2 infusions change acutely.

124 LONG-TERM FOLLOW-UP OF DYSRHYTHMIAS FOLLOWING THE MUSTARD PROCEDURE FOR TRANSPOSITION Mark C. Duster, Paul C. Gillette, Dan G. McNamara, Lillie Frank Abercrombie Section of Cardiology, Baylor College of Medicine and Texas Children's Hosp., Houston, TX

In 1974 we reported a high incidence of dysrhythmias (dys) after the classical Mustard operation (Group A), but a lower incidence in patients (pts) in whom the operation was modified to lessen the chance of damage to the sinus node (Group B). We report here 7 years (yrs) additional follow-up on these pts. Group A (37 pts) was followed from 6 weeks to 14 yrs (mean=8.9 yrs). Group B (44 pts) was followed from 6 weeks to 9 yrs (mean=4.7 yrs). All ECGs on these pts were reviewed. The dys were classified as sinus (SR), passive dys (sinus bradycardia), active dys (atrial flutter), or conduction disturbance. Results were expressed as the incidence per number of different rhythms during follow-up intervals. The incidence of SR in Group B (80%) was greater than Group A (27%) during the first 2 yrs. However, after 7 yrs, the incidence of SR in Group B had fallen to 58%. This was coupled with an increase in passive dys. The incidence of active dys (Group A 4-18%, Group B 4-9%), and conduction disturbance (Group A 4-20%, Group B 3-13%) remained relatively unchanged in both groups during the study. These data suggest that late occurring dys remain a problem after the Mustard procedure even if sinus node trauma at the time of surgery is minimized. Progressive scarring along baffle suture lines may be an explanation.

125 PROPRANOLOL INDUCED MYOCARDIAL PRESERVATION Stanley Einzig, Herbert B. Ward, Ting Wang, Richard Bianco, John E. Foker, (Spon. by Edward L. Kaplan), University of Minnesota Hospitals, Departments of Pediatrics & Surgery, Minneapolis.

The metabolic and hemodynamic effects of acute propranolol (P) administration (1 mg/kg IV) prior to ischemia were studied in dogs subjected to 20 min of normothermic global ischemia on cardiopulmonary bypass (CPB). Pre CPB ATP levels in P dogs were similar to levels in control (C) dogs (4.95±0.14 umoles/g wet wt). On CPB during reperfusion ATP levels were better preserved with P treatment (table). P treatment did not alter heart rate (HR), mean aortic pressure (AO, data not shown), myocardial oxygen consumption (MVO_2) or left ventricular blood flow (BF).

	HR (beats/min)	CI (ml/min/kg)	MVO_2 (ml O_2/min/g)	LVBF (ml/min/g)	ATP (umole/g)
On CPB					
C(n=16)	119±6	101±5	0.027±0.005	0.65±0.04	2.45±0.12
P(n=7)	114±7	108±6	0.018±0.003	0.51±0.07	3.58±0.33+
Post CPB					
C(n=16)	136±8	100±7	0.077±0.010	0.99±0.08	2.56±0.17
P(n=7)	103±6*	70±9*	0.049±0.007*	0.77±0.16	4.04±0.30+

(n=# of dogs, values are mean ± SE, *p<0.05, +p<0.01 P vs C by t-test)

Post CPB ATP levels in P dogs recovered better and reached 80% of pre-ischemic levels. AO pressure was similar in the two groups and P dogs came off CPB more smoothly with fewer arrhythmias. P treatment, however, decreased HR, CI and MVO_2. Therefore, P treatment was clearly beneficial for the myocardium subjected to ischemia as ATP levels were higher and MVO_2 was decreased. P use for myocardial protection may require catecholamine stimulation to augment CI following CPB.

126 NONINVASIVE ASSESSMENT OF LEFT VENTRICULAR FUNCTION USING PULSED DOPPLER ULTRASOUND. Marlowe W. Eldridge, Dale C. Alverson, William Berman, Jr. Lovelace Medical Center, and University of New Mexico School of Medicine, UNM Affiliated Hospitals, Department of Pediatrics, Albuquerque, New Mexico.

We testetd the ability of a pulsed Doppler velocity meter (PDVM) to quantitate myocardial performance noninvasively. Studies were performed in 7 adult dogs under general anesthesia by controlled ventilation. Peak ascending aortic blood flow velocity (V_{AO}, cm/sec) and its first derivative, blood flow acceleration (dV_{AO}/dt, cm/sec^2), were measured noninvasively and compared to mean aortic (A_O,mmHg) and left ventricular (LV,mmHg) pressures, the rate of LV pressure development (LV dp/dt,mmHg/sec) and the pre-ejection period (PEP) to left ventricular ejection time (LVET) ratio (PEP/LVET). Mean values prior to interventions were: V_{AO}=45.5, dV_{AO}/dt=1003, A_O=88, LV=115/8, LVdp/dt 2150 and PEP/LVET 0.320. After inotropic stimulation with dobutamine, LVdp/dt rose to 4400, PEP/LVET fell to 0.256, and both V_{AO} and dV_{AO}/dt increased to 62.4 and 1432 respectively. Propranolol administration (.2mg/kg, IV) and preload elevation (30ml/kg saline) caused parallel changes in noninvasive and invasive performance indices. Programmed pacing trains also caused similar changes in V_{AO}, dV_{AO}/dt and LVdp/dt. Afterload elevation by methoxamine infusion, however, affected LVdp/dt little (-6%), caused a small elevation in PEP/LVET (+11%), but depressed both V_{AO} and dV_{AO}/dt substantially (-47% and -43% respectively). The PDVM provides useful noninvasive information about LV function which in some, but not all circumstances, parallels changes in LVdp/dt.

127 EARLY TRICUSPID CLOSURE AS A PREDICTOR OF RIGHT VENTRICULAR HYPERTENSION IN VENTRICULAR SEPTAL DEFECT. P.L.Ferrer,M.Pinto,A.Pickoff,G.Enriquez,D.Tamer,O. Garcia,G.Wolff,and H. Gelband. Department of Pediatrics. University of Miami School of Medicine, Miami.

M-mode Echo and cardiac caths were performed in 44 children (7ds-12yrs,x̄2.5yrs). Pts. were divided into 4 groups:I) 14 pts. c̄ RV or PA systolic pressures (RVP,PAP)<50 mm Hg, and pulmonary vascular resistance (PVR)<3 U/M_2;II) 13 pts. c̄ RVP or PAP>50 mm Hg, PVR<3 U /M_2;III) 10 pts. c̄ RVP or PAP>50 mm Hg,PVR>3 U/M_2;IV) 6 pts. c̄ RVP>50 mm Hg and infundibular pulmonic stenosis (IPS). 27 Normal pts. (4mos-17yrs,x̄5yrs) had only Echo. The value between tricuspid and mitral closure (Tc-Mc) was utilized to assess early tricuspid closure.

	Normal	I	II	III	IV
Tc-Mc	22±8	17±4	-1±7	-4±5	2±6
Tc-Mc(early, <10 msecs.)	0/27*	0/14*	11/13*	10/10*	6/6*
"p" c̄ normal	-	NS	<.001	<.001	<.001
"p" c̄ GI	NS	-	<.001	<.001	<.001

Tc-Mc=msecs.±SD,*=pts.

Correlation coefficients (CC) of Tc-Mc in pts. s̄ IPS were:RVSP,r=-.763;PASP,r=-.742;CC c̄ RVSP in pts. c̄ IPS, r=.660.

Thus,early tricuspid closure (decreased Tc-Mc) is a sensitive (27/29 pts,93%) and specific (no false positive) parameter in detecting RV hypertension in pts. c̄ VSD.

128 HEMODYNAMIC SIGNIFICANCE OF PULMONIC VALVE MOTION IN VENTRICULAR SEPTAL DEFECT. P.L. Ferrer, M. Pinto, A. Pickoff, O. Garcia, V. Bennet, and H. Gelband. Department of Pediatrics, University of Miami, School of Medicine, Miami.

Pulmonic valve (PV) motion has been considered of no value in predicting pulmonary artery hypertension (PAH) in adults. PV motion was evaluated in children c̄ VSD c̄ PAH c̄ or s̄ increase in pulmonary vascular resistance (PVR) and compared c̄ 2 groups of controls. M-Mode Echos and cardiac cath. were performed in 38 children (7 days to 12 yrs.). Patients were divided into 3 groups: I) 14 pts. c̄ RV or PA systolic pressures (RVP,PAP)<50 mmHg and PVR <3 U/M_2; II) 14 pts. c̄ RVP or PAP > 50 mmHg, and PVR<3 U/M^2; III) 10 pts. c̄ RVP or PAP>50 mmHg; and PVR>3 U/M_2; Normal patients had only Echo.

	Normals	I	II	III
↓PVDSV*	0/27	0/14	1/14	8/9
Notching	0/27	0/11	10/14	7/10
↓"a" wave	0/27	4/14	7/14	6/10
Fluttering	4/27	7/14	**10/14	**7/10

*PVDSV=Pulmonic valve diastolic slope velocity (<15 mm/sec)
** coarse

In summary, decreased PVDSV (<15 mm/sec) is useful in predicting PAH and increased PVR in patients c̄ VSD; notching suggests PAH c̄ or s̄ increase in PVR; decrease in "a wave" and fluttering have low specifity and therefore are not useful. Thus, the Echo pattern of motion of PV may be useful in children with VSD. Specifically, decreased PVDSV appears promising in detecting VSD patients c̄ PAH associated to increased PVR.

129 MITOCHONDRIAL RESPIRATORY ACTIVITY AFTER ACUTE HYPOXIA IN ISOLATED PERFUSED RAT HEARTS: TIME RESPONSE. Ellen O. Fuller, Joseph W. Starnes, Dennis I. Goldberg, Linda M. Sacks and Maria Delivoria-Papadopoulos. Univ. of PA. School of Med., Depts. of Physiology and Pediatrics, Phila., PA.

Heart mitochondria of newborn and adult animals subjected in-vivo to hypoxia show increased state 3 respiratory activity. To determine whether an increase occurs in the absence of factors extrinsic to the tissue, studies in isolated perfused hearts were conducted. 31 excised rat hearts were perfused by retrograde, single-pass perfusion through the aorta with Krebs Henseleit buffer and 8 mM glucose at PO_2=631±14 mmHg (control) or PO_2=155±11 mmHg (hypoxia). 28 hearts were perfused for 20 min each; control hearts (N=8) with high PO_2 perfusate only, while the remainder were switched to low PO_2 perfusate for the last 2½ min (N=2), 5 min (N=8) or 10 min (N=9) of perfusion. Three more hearts were perfused for 25 min using high PO_2 perfusate for 10 min, then low PO_2 perfusate for 15 min. Mitochondria were then isolated and state 3, state 4 respiratory rate and ADP/O determined. Spontaneously beating, non-ejecting hearts responded to hypoxia by 27% decreased heart rate, 29% increased coronary flow after 10 min. Hypoxia did not alter state 4, ADP/O, or the yield of isolated mitochondrial protein. However, state 3 respiration (natoms O_2 min^{-1} mg^{-1} mitochondrial protein) increased from control values of 306±7 to 330±8 after 2½ min, 355±16 after 5 min, and 371±6 after 10 min of hypoxia respectively. Values after 15 min of hypoxia were also elevated. These data indicate that heart mitochondria adapt to brief periods of hypoxia in a time dependent pattern and that these responses need not be mediated by neural or hormonal changes.

130 AGE-RELATED ALTERATIONS IN CIRCULATORY FUNCTION DURING HYPOXIA. Norman Gootman, Phyllis M. Gootman, Barbara J. Buckley, Peter G. Griswold and Barbara J. Peterson. SUNY at Stony Brook, Long Island Jewish-Hillside Med. Ctr., Dept. of Pediatrics, New Hyde Park, N.Y. 11042.

The effects of two degrees of hypoxia(H) were examined in 2-4 day(n=12), 2 week(n=14) and 2 month(n=7) old artificially ventilated swine, anesthetized with 0.25-0.5% halothane in 50% N_2O and O_2(control: PO_2≥100 torr). Moderate(MH), PO_2 61±.7 torr, and severe(SH), PO_2 32±.6 torr, H were produced by decreasing the percent inhaled O_2 with N_2. pH was normal during MH and slightly decreased from control during SH. Aortic pressure(AoP), ECG and phasic mesenteric(Mes), femoral(Fem), carotid(Car) and renal(Ren) blood flows were recorded; means and resistances(R) were calculated. Heart rate responses were variable(V), however, an increase (+20%) was observed during MH in the oldest animals.

AVERAGE PERCENT CHANGE IN CARDIOVASCULAR FUNCTION DURING HYPOXIA

	MH			SH		
	2-4 day	2 weeks	2 months	2-4 day	2 weeks	2 months
AoP	-12	-6	+10	-28	-34	V
MesR	V	-8	+12	V	-26	+132
FemR	-19	V	V	V	-27	V
CarR	-35	-21	V	-59	-59	-29
RenR	V	V	+8	V	V	+55

Immaturity of the cardiovascular regulatory system is evident by the absence and or delayed onset of the adult pattern of response to hypoxia. These findings are of importance to clinicians treating children with chronic hypoxia. (Supported by grants from the American Heart Assoc., Nassau Chapter and NIH HL20864.)

● **131** KAWASAKI DISEASE (KD): ASSESSMENT OF RISK FACTORS FOR CARDIOVASCULAR SEQUELAE. Michele D. Heilbut, Vera Rose, Walter J. Duncan, Teruo Izukawa, C.A.Fred Moes, R. Clifton Way (Spon. by Richard D. Rowe) The Hospital for Sick Children, Toronto, Canada.

Eighty cases of KD were reviewed. The diagnosis was based on Kawasaki's criteria. The aim was to determine whether patients at high risk of developing coronary aneurysms (CA) could be identified noninvasively using the ASAI scoring system, electrocardiograms (ECGs), and two dimensional echocardiograms (2Ds). Most (87%) were <5 years old. There was a 2:1 male dominance. Frequent accompanying symptoms were otitis, arthritis, and diarrhea. Jaundice and neurological involvement rarely occurred but were twice as frequent in patients with CA. Salient laboratory findings included ESR >100 mm/hr; platelet counts >500,000; anemia; and pyuria in about half the patients. Bacterial and viral cultures were positive in only 14%. Ten variables were scored using a modified ASAI system. Thirty-two percent of patients scored ≥6. ECGs were abnormal (rhythm disturbance, chamber enlargement, or pathological Q waves) in 35%. 2D echoes were positive (pathological dilatation or frank aneurysm) in 24%. Fifty-eight aortograms were done. CAs were seen in 7 patients, all of whom had ASAI scores >6, abnormal ECGs, and positive 2Ds. A double blind study of 2D versus angiography showed no false negative and 4 false positive results on 2D. It was concluded that an ASAI score ≥6 identifies patients at high risk of developing CA. 2D echo is a reliable noninvasive means of detecting CA in KD. Angiography might best be reserved for patients with persisting positive 2Ds.

● **132** RELATIONSHIP OF AUTOMATICITY TO MEMBRANE POTENTIAL IN HUMAN ATRIAL FIBERS. Allan Hordof, James Malm,Michael Rosen.(Spon.by Welton Gersony).Columbia University, College of Physicians and Surgeons,Dept.of Pediatrics,New York.

Because of possible cardiac surgical injury to the sinus node, the integrity and function of subsidiary atrial pacemakers has taken on increased importance.The automaticity(auto)of pacemakers in other mammalian cardiac tissue is strongly influenced by membrane potential (MP).We studied human atrial fibers (HAF) from children undergoing open heart surgery to determine the relationship of auto to MP and to determine the effects of pharmacologic agents on auto.Standard microelectrode techniques were used to record action potential (AP)characteristics;and current injection was used to modify MP.Control AP characteristics (X̄±SE):maximum diastolic potential (MDP=-57.7±1.5mV;AP amplitude =66.3±2.3mV; automatic rate=49.5 beats/min (n=12).Hyperpolarization of MP by 10-20 mV induced cessation of auto.Depolarization of MP by 10-20 mV increased automatic rate by 10-40 beats/min. HAF were superfused with tetrodotoxin (TTX) 1 mg/L, which depresses inward sodium current; and verapamil(V) 1 mg/L,which depresses slow inward calcium current.Both significantly decreased automatic rate at the control MDP and enhanced the hyperpolarization induced atrial quiescence.However,the depolarization induced increase in auto was unaffected by TTX but was inhibited by V.In summary,the automatic rate of HAF is sensitive to MP,increasing as MP decreases.Automatic fibers are sensitive to the effects of V over a wide range of MP,but their sensitivity to TTX decreases as MP decreases.Hence,both automatic rate and pharmacologic responsiveness of HAF are modulated by MP.

133 LEFT VENTRICULAR EJECTION FRACTION IN TRICUSPID ATRESIA: ASSESSMENT BY RADIONUCLIDE ANGIOCARDIOGRAPHY
Roger Hurwitz, Alvin Chin, Donald Girod, Randall aldwell, Marlene Rabinovitch (spon. by Morris Green), Indiana niversity Medical School, Department of Pediatrics; Harvard niversity Medical School and Children's Hospital, Departments f Radiology and Pediatric Cardiology, Boston.

Left ventricular ejection fraction (LVEF) has been considered mportant when selecting patients with tricuspid atresia (TA) or a Fontan procedure (Fontan). To assess incidence and ossible age relationship of abnormal LVEF, radionuclide entriculography was performed in 24 unselected patients with A (age range 1 month to 24 years, median 8.0 years). Palliative surgery had been done is 23, and 5 of these also had a ontan. LVEF was measured during supine rest in all, and luring supine isometric exercise (EX) in 10. Mean group LVEF as .56 (range .39-.75); LVEF was similar in the post-Fontan atients. 10 patients (2 with prior Fontan) had an abnormal esting LVEF (<.50). 5 patients studied during EX demonstrated significant decrease in LVEF of >.05; 3 of these 5 had a ormal resting LVEF. There was not a statistical relationship etween age and LVEF for the group without Fontan. However, ean age of the patients with normal LVEF was 8.2 years, and f those with abnormal LVEF, 12.2 years. Both patients with rior Fontan and abnormal LVEF underwent surgery when >10 years. lmost half the patients with TA have an abnormal LVEF; further valuation of the significance of this abnormality is necessary. adionuclide ventriculography can provide a relatively noninvasive method to assess LVEF and its importance.

● **134** NON-INVASIVE RIGHT AND LEFT VENTRICULAR EJECTION FRACTION: RADIONUCLIDE ANGIOCARDIOGRAPHY.
Roger A. Hurwitz, Salvador Treves (spon. by Morris Green), ndiana University Medical School, Department of Pediatrics; larvard University Medical School and Children's Hospital epartments of Radiology and Pediatric Cardiology, Boston.

This study was designed to determine a range of normal for ight and left ventricular ejection fraction (RVEF and LVEF) in ediatric patients. First-pass radionuclide angiocardiography as performed on 74 supine, resting, unsedated patients (age 1 o. to 20 years) undergoing bone scans or investigation for astrointestinal bleeding. Cardiac imaging was performed in the ight anterior oblique projection. Regions of interest were rawn from stroke volume images; ejection fraction was analyzed rom time-activity curves. Mean RVEF was .53±.06 (range .43-.73). wo patients, both under 2 years of age, had andRVEF< .45. 3/5 nder 1 year of age had RVEF< .50. Mean LVEF was .68±.09 range .49-.86). One patient had an LVEF< .50, and only 2/42 atients over 10 years of age had LVEF<.55. Despite these endencies, group means for different age ranges were similar. o evaluate discriminatory ability, clinical utility of this echnique was tested: 10 patients with chronic lung disease, or pulmonale, and "possible congestive heart failure" had VEF=.41±.09 (p< .01 vs. normals); 8 patients with cardiomyopathy nd "left-sided congestive heart failure" had LVEF=.30±.09 (p< .001 vs. normals). This relatively noninvasive radionuclide procedure can thus be used to help identify and follow patients with abnormal pump function.

● **135** CARDIAC ISCHEMIA IN NEWBORNS WITH CEREBRAL ARTERIOVENOUS MALFORMATION (CAVAM) AND CONGESTIVE HEART FAILURE (CHF)
Roy Jedeikin, Richard D. Rowe, Robert M. Freedom, Peter M. Olley, John E. Gillan, Dept. of Pediatrics, Div. of Cardiology, and Dept. of Pathology, Hospital for Sick Children, Toronto.

Myocardial ischemia (MI) and infarction occurs in both structural and non-structural heart disease. Our data suggests that MI complicates the course in neonates with CAVM and CHF. Clinical data from 12 fullterm newborns referred to the Hospital for Sick Children because of severe CHF, and found to have CAVM were reviewed. The mean age of presentation was 40 hrs. Electrocardiographic evidence of MI was found in 11 of 12 patients (pts) studied. Moderate to severe ischemic changes were found in 9 pts and electrocardiograms (ECG) showed T wave changes in more than one lead associated with ST segment changes and/or abnormal Q waves. Mild ischemic changes were found in 2 pts and consisted of T wave flattening or inversion in more than one lead. The ECG showed right ventricular hypertrophy in 5 pts, combined ventricular hypertrophy in 5, right atrial enlargement in 5, and combined atrial enlargement in 4 pts. Post-mortem histologic evidence of MI and infarction was found in material available from 7 out of 9 pts. The above evidence suggests that the neonate with a CAVM has a severely jeopardized and altered myocardium.

136 EXPERIMENTAL BASIS FOR BALLOON VALVULOPLASTY OF CONGENITAL PULMONARY VALVULAR STENOSIS.
Jean S. Kan, John H. Anderson, Robert I. White, Jr. The Johns Hopkins University, Baltimore, Maryland 21205

Balloon angioplasty has successfully been used to open stenotic blood vessels. The feasibility of applying this technique to congenital pulmonary valvular stenosis has not been previously assessed. In an effort to assess the hemodynamic response of the hypertrophied right ventricle (RV) to temporary balloon occlusion, 6 dogs were prepared by banding of the pulmonary artery. Hemodynamic responses to acute balloon occlusion of the pulmonary artery were studied in the 6 banded dogs 3 months after banding, and in 5 control dogs. The following hemodynamic parameters were measured during incremental periods of balloon occlusion of the pulmonary artery: RV systolic pressure (RVSP), RV end diastolic pressure (RVEDP), femoral artery pressure (FAP), cardiac output (CO) by dye dilution, and electrocardiogram.

MEAN PRESSURE VALUES MEASURED DURING BALLOON OCCLUSION (mmHg)

	CONTROL	BANDED
RVSP (initial)	24	57
RVSP (peak)	68	116
RVEDP (max)	21	23

RVSP in both groups peaked at 10 sec after occlusion while RVEDP rose gradually during the occlusion. At occlusion intervals of less than 120 sec, predominately reversible supraventricular arrhythmias were noted. These results suggest that temporary complete occlusion of the pulmonary artery, as would occur during balloon valvuloplasty, is well tolerated by the hypertrophied right ventricle.

● **137** BALLOON VALVULOPLASTY FOR THE TREATMENT OF PULMONARY VALVULAR STENOSIS.
Jean S. Kan, Timothy J. Gardner, Robert I. White, Jr. The Johns Hopkins University, Baltimore, Maryland 21205

Balloon valvuloplasty of the pulmonic valve has been successfully performed in an 8 year old child with congenital pulmonary valve stenosis. A 14 mm maximum diameter polyethylene angioplasty catheter (Medi-Tech, Inc.) was positioned in the pulmonary artery (PA) at the level of the valve. The balloon was hand inflated for 10 sec and then rapidly deflated. During the balloon inflation there was a transient rise in right ventricular pressure (RVP)(to 90 mmHg) and a drop in femoral artery pressure (FAP) (to 24/20 mmHg). Right ventricular cineangiography after the balloon valvuloplasty demonstrated widening of the pulmonary valve orifice.

	PRESSURES (mmHg)				
		RESTING		AFTER CONTRAST MEDIA	
	RVP	PA	FAP	RVP	FAP
Prior to balloon valvuloplasty	60/4	15/6	100/50	76	80/40
Following balloon valvuloplasty	28/4	14/6	100/50	45	90/45

During the time the balloon was inflated, the electrocardiogram (ECG) demonstrated a mild sinus bradycardia with occasional ectopic atrial beats and occasional PVC's. Interval ECG's have shown regression in right ventricular hypertrophy. If the reduction in RVP is sustained and additional patients successfully treated, balloon valvuloplasty may become an effective alternative to open heart surgery for congenital pulmonary valvular stenosis.

● **138** SINUS AND A-V NODE FUNCTION IN ATRIAL SEPTAL DEFECT
L. Khoury, O. Thilenius, D. Ruschhaupt, R. Sulayman, R. Replogle, R. Arcilla; The University of Chicago Hospitals and Clinics, Departments of Pediatrics and Surgery, Chicago, Illinois

Abnormal function of sinus node (SN) or of A-V node (AVN) after open-heart repair of secundum atrial septal defect (ASD) is often ascribed to surgical injury. To check if SN-AVN dysfunction is a pre-surgical or post-surgical abnormality, we conducted electrophysiologic studies (EPS) on 31 children with isolated ASD, age 0.6 to 16 years, before surgery (Gp A), and on 11 children after surgery (Gp B). EPS were obtained using multipolar electrode catheters, and analyzed with H-P digitizer/computer for: A-H and H-V intervals, sinus node recovery time, sinoatrial conduction time, and effective/functional refractory periods. RV and LV volumes, ejection fractions and outputs were derived from angiograms. SN-AVN dysfunction was observed in 42% in Gp A, and in 54% in Gp B. Resting A-H and H-V intervals were normal. Patients in Gp A with NORMAL (Nl) or ABNORMAL (Abl) SN-AVN had comparable hemodynamics (mean, Nl vs Abl): RA pressure (5.4, 6.4), RV systolic (37,.34), PA mean (18, 19), Qp/Qs (2.2, 2.1), RVEDV (159, 143 % PN), LVEDV (86, 86 % PN), and angio RV/LV output ratio (1.94, 1.81). RV and LV ejection fractions were normal. At surgery (19 Gp A, 11 Gp B), ASD size was comparable in Nl vs Abl. However, mean age of Nl was less than Abl (3.3 vs 7.4, $p < 0.02$). Abl SN-AVN was found in 0/10 at age 0.6-2.2, in 7/11 at age 2.5-5, and 6/9 at > 6 yrs. Our study strongly suggests age-related dysfunction of SN-AVN, starting to appear after age 2 yrs. This has obvious therapeutic implications.

139 INOTROPIC EFFECT OF $NAHCO_3$ INFUSIONS IN HYPOXEMIC NEWBORN DOGS. Uma Kotagal, Barbara Fritz, Spon. by Leonard I. Kleinman, University of Cincinnati College of Medicine, Department of Pediatrics

The effect in hypoxemic newborn dogs (PaO_2<38 torr) of an acute infusion (over 5') of $NaHCO_3$ or NaCl (2meq/kg diluted 1:1 with D_5W) were studied on cardiac output (C.O.) and its distribution using radioactive microspheres . Control animals received an infusion of equal volume of D_5W. There was no difference between the groups prior to the infusion in any of the parameters measured. There was no change in heart rate, BP, systemic vascular resistance or distribution of C.O. following any of the infusions.

	C.O. (ml/kg/min)	Stroke Volume (ml)
NaHCO3 (n=10)		
Pre Infusion	275.4±58.7	0.69±0.26
Post Infusion	330.1±88.1**	0.80±0.30*
NaCl (n=8)		
Pre Infusion	222.5±77.6	0.48±0.20
Post Infusion	219.1±63.8	0.46±0.12
D_5W (n=4)		
Pre Infusion	286.3±118.6	0.69±0.40
Post Infusion	268.5±132.3	0.61±0.35

Mean±SD *p<0.05 **p<0.02 comp to Pre Infusion.

Cardiac output and stroke volume increased in animals receiving $NaHCO_3$ but not in those receiving an equiosmolar load of NaCl. $NaHCO_3$ in the hypoxic newborn has an inotropic effect which is not explained by hyperosmolarity and plasma expansion.

140 TORSADES DE POINTES IN ADOLESCENTS. John D. Kugler, John P. Cheatham, William W. Pinsky, Philip J. Hofschire, Paul K. Mooring, Spon. by Robert Nelson, Jr. University of Nebraska College of Medicine, University of Nebraska Affiliated Hospitals, Department of Pediatrics, Omaha.

Torsades de pointes (TP)-multiform ventricular tachycardia-has not been reported in children or adolescents and only rarely has it been described in adults. During intracardiac electrophysiologic studies (EPS) to evaluate suspected or documented ventricular (V) tachycardia (T), TP was induced in 3 pts who had normal QT intervals and no evidence of metabolic disorders. EPS included single (S_1), double (S_2S_3) and bursts (B) of V stimuli. Pt 1 (16 yrs old) had nonsustained (NS) multiform VT-cycle length (Cl) 300 msec-on Holter (H) without symptoms (sx) but had sustained (S) TP (Cl 220) induced by B. After procaineamide (PA), NS TP occurred and Cl ↓ to 200. Because of ↓ LV function (probably 2° to myocarditis) digoxin was given and no VT recurred. Pt 2 (13 yrs old) had Rastelli repair of V inversion, pulmonary stenosis/VSD at age 7. Couplets were found on H; S TP (Cl 185) was induced by B. During serial EPS, S TP was induced after quinidine (Cl 200), NS TP after propranolol (Cl 260), and none after phenytoin. Pt 3 (17 yrs old) with normal heart had bidirectional VT on H (Cl 350) unaccompanied by sx. TP (Cl 200) was induced by B which converted to V fibrillation. NS TP were induced during serial EPS after PA (Cl 250), quinidine (Cl 300, 150), and phenytoin, but propranolol prevented TP. We conclude that inducible TP during EPS in the young has variable characteristics regarding pt population, underlying heart disease, and response to therapy. Serial drug EPS are useful to document therapeutic effect.

141 EFFECT OF PUTATIVE PEPTIDE NEUROTRANSMITTERS ON THE NEONATAL PULMONARY CIRCULATION. Thomas J. Kulik, Dana E. Johnson, Theresa Niemi, Bradley P. Fuhrman, James E. Lock (Spon. by R. Lucas) Dept. Pediatrics, Univ. Minnesota, Mpls MN

Vasoactive intestinal peptide (VIP) and Substance P(SP) may be neurotransmitters in the "peptidergic" nervous system. They occur in the lung, but their effects on newborn pulmonary vascular resistance (PVR) are unknown. Flow probes were placed around the L and R pulmonary arteries (PA) of 3-18 day old lambs; catheters were placed in the aorta (Ao) and either L or RPA 5-12 days later. Bolus injections of 0.1-µg/kg of VIP and SP were made into either PA of unsedated lambs in normoxia (N) and hypoxia (H). L and RPA flows, Ao and PA pressures (AoP, PAP in mmHg) were recorded continuously. A direct effect on PVR of VIP or SP results in a change in the ratio of flow into the injected lung over total pulmonary flow (Q_{inj}/Q_T).

VIP(n=8) is a direct pulmonary vasodilator (Q_{inj}/Q_T increasing from 0.49 to 0.52*) at a very low dose(0.1µg/kg). VIP also lowers AoP(84 to 77*) and increases cardiac output (CO: 1.17 to 1.42 L/min*) at the same dose, indicating systemic vasodilation. Similar effects were seen with H and propranolol(1mg/kg). In contrast, SP(n=6) had variable effects: it increased CO and AoP at 1.0µg/kg, but increased Q_{inj}/Q_T only in H, only transiently, and only at low dose (0.3µg/kg). At 10 µg/kg, SP caused marked agitation. Neither agent showed selectivity as a PA (as opposed to a systemic) vasodilator.

We conclude that VIP is as potent a pulmonary vasodilator as any known, but SP's effects on PVR are weak and variable. Although the non-pulmonary effects of VIP and SP would appear to preclude their use as neonatal PA dilators, they may well contribute to the maintenance of pulmonary vascular homeostasis. (*p<0.05)

● **142** HEMODYNAMIC EFFECTS OF ISOPROTERENOL IN YOUNG ANIMALS WITH A LARGE LEFT-TO-RIGHT SHUNT
Larry A. Latson, John P. Cheatham, Tim Bricker, Robert M. Lewis, Craig C. Hartley, David J. Driscoll.
The Lillie Frank Abercrombie Section of Pediatric Cardiology, Baylor College of Medicine and Texas Children's Hospital, Houston, Texas.

We developed an animal model simulating patent ductus arteriosus to evaluate the effects of isoproterenol (ISO) on hemodynamics in immature animals with a large left-to-right (L-R) shunt. A 6-8 mm conduit from the aorta to the pulmonary artery was placed in seven piglets (4-6 weeks old). After a one to two week recovery period, ISO was infused in these animals and seven instrumented controls. Pressures were recorded via chronic catheters and flows via ultrasonic flow probes (UFP) or green dye curve. Mean values (±1SD) of heart rate (HR), and aortic and pulmonary mean pressure (AMP, PMP) are shown below:

	Resting			After ISO		
	HR	AMP	PMP	HR	AMP	PMP
control	157(29)	92(17)	18(3)	256(11)	80(14)	17(5)
shunt	167(34)	79(15)	36(14)	240(22)	75(6)	24(8)

In shunted animals resting PMP was elevated but fell significantly during ISO infusion. Systemic blood flow (Q_s) increased by 79%. Although Q_p increased slightly in most cases, Q_s was augmented to a greater extent resulting in an average decrease of 34% in Q_p/Q_s. ISO improves hemodynamics in L-R shunt by reducing PMP and increasing Q_s, while reducing Q_p/Q_s.

● **143** PULMONARY MICROTHROMBI SYNDROME IN NEWBORN INFANTS WITH UNRESPONSIVE PERSISTENT PULMONARY HYPERTENSION. Daniel L.Levin, Ronald M.Perkin, Arthur G.Weinberg, Univ. Texas Health Science Center, Department of Pediatrics, Dallas.

Some infants with either primary or secondary persistent pulmonary hypertension of the newborn (PPHN) remain hypoxemic, hypercarbic, and acidotic despite therapeutic efforts. We reviewed autopsies of 23 infants who had PPHN. The most striking abnormality was the presence of diffuse platelet-fibrin thrombi in the pulmonary microcirculation in 8 of these infants. Detailed review of the clinical course in these 8 infants(group A) was done and compared to the 15 other infants(group B) who did not have diffuse thrombi on autopsy. Diagnoses in group A were: pneumonia and sepsis-4, meconium inhalation-3, primary PPHN-1; and group B: pneumonia and sepsis-4, meconium inhalation-4, primary PPHN-4, hyaline membrane disease-2, diaphragmatic hernia-1. The only significant differences between the two groups were the response to tolazoline infusion as assessed by changes in PaO_2 and the platelet counts. Group A responded less favorably to tolazoline (14.8 mmHg vs 83.6 mmHg; $p<0.05$) and had lower platelet counts (51,000/mm^3 vs 128,000/mm^3; $p<0.01$) than group B. No significant differences could be detected in Apgar scores, duration or mode of mechanical ventilation, oxygen requirements, arterial blood gas tensions or pH, systemic arterial blood pressure, coagulation profile or amount of blood product transfusions. Pulmonary microthrombi should be added to the list of mechanisms for PPHN and may explain why some infants do not respond well to therapeutic efforts aimed at vasodilation. Thrombocytopenia and failure to respond to pulmonary vasodilators should suggest the diagnosis.

● **144** EXERCISE BLOOD FLOW(BF) DISTRIBUTION IN LAMB COARCTATION (CO). James E. Lock, Theresa Niemi, Stanley Einzig (Spon. by R. Lucas) Dept Pediatrics, Univ of Minnesota, Mpls.

Although decreased renal BF may underlie CO-associated hypertension both pre- and postop, the impact of CO relief and or exercise(EX) on regional BF hasn't been studied. We made juxtaductal COs in 8 newborn(3-8 day) lambs; 3 lambs(CONT) had thoracotomies without Ao narrowing. After 6-9wks of recovery, cardiac output and BF distribution were measured by LA infusion of radiolabelled 15µ spheres. Treadmill EX(1.6-3 MPH) was performed for 7-9min; BF studies were repeated at 4-5min of EX (PRE-CO). Five lambs then had balloon dilation(BD) of COs using our previously described method, and rest and EX studies were repeated the next day(POST-CO). BD increased CO diameter(5.1 to 8.5mm*), decreased systolic gradient(39 to 8mmHg*) and restored normal (±4%) BP in each lamb. In all three groups, EX increased HR*(46-61%) and cardiac output*(60-72%) by similar amounts. Although the EX-induced rise in mean Ao pressure was only 2-4% in CONT and PRE-CO lambs, Ao pressure rose 26%*(87 to 110mmHg) with EX in POST-CO lambs, suggesting that EX-induced vasodilation is impaired after CO relief. In all lambs, cerebral BF was normal at rest and on EX; GI and liver BF fell similarly on EX. While RBF stayed constant in CONT lambs with EX, RBF fell 18%* in PRE-CO lambs with EX. Significantly, this EX-induced fall in RBF persisted(-20%*) after successful BD.

The major EX-induced BF abnormality in CO is a fall in RBF which persists at least 24hrs after gradient relief. It is associated (in POST-CO lambs) with diminished EX-induced vasodilation. These data suggest that renal vasoconstriction contributes to post-CO hypertension during EX. The cause of this constriction and its persistence after CO relief remain unknown. (*p< 0.02)

145 ABSENCE OF PHASIC SENSITIVITY OF SINOATRIAL NODE TO VAGAL STIMULI IN NEWBORN PUPPIES. Sharon E. Mace, Matthew N. Levy, Jerome Liebman: Division of Investigative Medicine, Case Western Reserve Univ., Depts. of Cardiology and Investigative Med., Mt. Sinai Medical Center, Cleveland, Ohio.

The effect of time of delivery in a cardiac cycle of a vagal stimulus was determined in 8 adult dogs and 8 puppies. Adult dogs had a marked phasic sensitivity with a wide variability in heart rate (HR) depending on the P-St interval (time from P wave to the stimulus). Pups had little, if any, change in HR as a function of P-St interval. Right vagal (RV) stimulation produced a stronger HR response than left vagal (LV) in adults and pups. Differences (adults vs pups, RV vs LV) were significant ($p<0.001$). At the P-St giving a maximum response, PP response (msec) was: RV stim: adults=960, pups=740, LV stim: adults=760, pups=570. Phasic HR may be the result of temporal changes in responsiveness of the sinoatrial nodal cell membrane to acetylcholine. The reason for the absence of phasic HR responses in puppies is not known. However, differences in responsiveness to acetylcholine during the cardiac cycle may not be manifest in the puppy due to a slower breakdown of acetylcholine secondary to inadequate amounts of cholinesterase.

146 UNUSUAL PRESENTATION OF THE TWO-CHAMBERED RIGHT VENTRICLE IN INFANCY. Thomas C.Martin, Alexis F. Hartmann, Jr., David Goldring, Clarence S. Weldon, Fernando R. Gutierrez, Arnold W. Strauss. Washington Univ. School of Medicine, Mallinckrodt Dept. of Pediatrics, Div. of Cardiology & Division of Cardiothoracic Surg., and Mallinckrodt Dept. of Radiology, St. Louis Children's Hospital, St. Louis, MO.

The occurrence of anomalous muscle bundles (AMB) with a ventricular septal defect has been recognized since 1960. Progression in the degree of right ventricular outflow obstruction from AMB has been reported. Cyanosis from right-to-left ventricular level shunting has been described as a complication of late childhood or adolescence.

This report concerns two infants who developed rapidly progressive hypertrophy of AMB and presented with severe cyanotic spells in infancy. Both underwent successful repair of their defects. The clinician should be alerted that AMB may hypertrophy very rapidly, necessitating surgical intervention in the first year of life.

147 CARDIAC DYSRHYTHMIA AFTER THE SENNING PROCEDURE FOR D-TRANSPOSITION OF THE GREAT ARTERIES. Thomas C. Martin, Antonio Hernandez, Clarence S.Weldon, Alexis F. Hartmann, Jr., David Goldring, Arnold W. Strauss, Washington Univ. School of Medicine, St. Louis, MO.

The purpose of this study was to determine the frequency of cardiac dysrhythmia developing after the Senning procedure as compared with that following the Mustard repair. Eighteen patients, 3 to 14 months of age were corrected by the Senning procedure and 16 patients 7 mos to 3½ yrs of age had the Mustard procedure. Both surgical procedures were carried out under deep hypothermia. The preoperative ECG of all patients showed normal sinus rhythm (NSR). These 34 patients were evaluated postoperatively by the 24-hour Holter monitor.

Summary

	Senning	Mustard
No. of patients	18	16
Mean age at operation	8 mos.	19 mos.
ECG during immediate postop period		
NSR	10 (55%)	5 (31%
A-V Dissociation	8 (44%)	11 (68%)
Holter Monitor Findings		
Time interval bet. op & Holter mon.	1 yr	4.7 yr.
NSR	9 (50%)	4 (25%)
Junctional rhythm	2 (11%)	9 (56%)

These results suggest that the Senning repair one year postoperatively may be less arrhythmogenic than the Mustard procedure, but long-term followup is needed for positive confirmation of the above findings.

148 CARDIAC ABNORMALITIES IN HYPERTENSIVE CHILDREN. Sudhir Mehta, Timothy Walsh, Regina Hanson, Robert Bahler, Louis Rakita, (Spons. by Satish Kalhan), Case Western Reserve University, Cleveland Metropolitan General Hospital, Department of Pediatrics and Cardiology, Cleve., Oh.

Documentation of tachycardia in children with mild hypertension (HTN) is generally based on brief periods of observation and has been attributed to anxiety. In order to confirm this observation, heart rates throughout the 24 hour period were measured prospectively in ten ambulatory mildly hypertensive children. Data were compared with 10 controls matched for age, height, weight, sex and race. Twenty-four hour portable ECG were recorded and the heart rate (per minute) data were calculated from the pulse interval time (mean ± S.D.)

	n	Awake	Sleep	24 Hours
HTN	10	96 ± 6.8	72 ± 8.4	87 ± 5.4
Control	10	88 ± 7.8	60 ± 6.0	77 ± 6.06
P Value		< .02	< .02	< .01

To evaluate the presence of anatomical abnormalities -M-mode echocardiograms were done in eight patients and normal matched controls. A significant increase in left ventricular posterior wall thickness (cm.) (1.01 ± 0.13 vs 0.825 ± .14; p= < .02) during diastole; interventricular septum thickness during diastole (1.07 ± 0.2 vs .81 ± 0.13; p= <.01) and systole (1.4 ± 0.2 vs 1.17 ± 0.15; p= < .05) was observed. It is concluded that mild hypertension in children is associated with increased cardiac rate and left ventricular hypertrophy.

● **149** THE EFFECT OF CALCIUM ON MYOCARDIAL MECHANICAL FUNCTION IN THE FETUS OF DIABETIC MOTHER. Toshio Nakanishi, Kenya Nishioka, Tatsuo Shimizu, Naomi D. Neufeld, Jay M. Jarmakani, UCLA and Cedars-Sinai Medical Center, Dept. of Pediatrics, Los Angeles, CA.

This study was designed to evaluate myocardial mechanical function in the fetus of diabetic mother (FDM). Alloxan was given to pregnant rabbits on the 14th day of gestation. Studies were performed on the isolated arterially perfused heart of FDM (n=17) and normal fetuses (NF) (n=15) at 28 days of gestation, and the data were compared with those obtained in the normal newborn (NNB) (n=44). Parameters of mechanical function were recorded at various extracellular calcium (Ca) in the three groups. At 1.5 mM Ca (control), the developed tension, maximal rate of tension development [+dT/dt (max)], resting tension (RT), time to peak tension (TPT), and half time to relaxation(1/2 TR) were similar in the three groups. The maximal inotropic effect [+dT/dt (max)] of Ca was observed at 7.5 mM in NF, at 15 mM in FDM, and at 30 mM in NNB. The inotropic effect at 15 mM Ca in the FDM (144 ± 18% of control) was significantly greater than that in the NF (81 ± 12%) but was not significantly different from that in NNB (158 ± 12%). At 30 mM Ca. significant increases in the RT and 1/2 TR were observed in NF, but not in FDM. Thus in FDM, the inotropic effect of Ca was greater and the toxic effect of high Ca was less than in NF. These data indicate that 1) the capability of Ca sequestration in the heart of FDM and NNB is greater than in NF, and 2) maternal diabetes causes significant changes in development of excitation-contraction coupling in the fetal heart.

● **150** A MODEL OF ALCOHOL CARDIOMYOPATHY IN THE YOUNG. George R. Noren; Frank L. Mikell; Nancy A. Staley; Richard W. Asinger; Stanley Einzig. University of Minnesota, Hennepin County Medical Center, Department of Pediatrics, Minneapolis

In an effort to determine the effect of ethanol (ETOH) ingestion on the function of the preadult myocardium, a group of turkeys were fed 5% ETOH (25% of calories) for the first 56 days of life and compared to control birds. At two months, determination of LV function (by echocardiography), combined ventricular weight/body weight (CVW/BW) and calcium transport of isolated cardiac sarcoplasmic reticulum was done. Examination of cardiac and liver tissue by light and electron microscopy was also performed.

In the ETOH group there was a significant increase ($p<.01$) of CVW/BW (4.92±1.34 vs 3.88±0.27 gm/kg), LV end diastolic diameter (4.74±0.71 vs 3.34±0.54 mm/kg), LV end systolic diameter (2.20±0.50 vs 0.61±0.22 mm/kg) and LV systolic time intervals (PEP/LVET) (0.62±0.06 vs 0.51±0.04). The ETOH birds also had a significant reduction ($p<.01$) of the % change of LV shortening (53.7±7.30 vs 81.2±6.1%), calcium uptake (120±14 vs 165±16 n moles/mgPr/min), and calcium binding (32±3 vs 46±3 n moles/mgPr/4min). Blood pressure heart rate and body weight were not different in the two groups at 56 days ($p>.10$). Microscopic examination of the heart revealed non-specific changes while no cirrhosis was evident in the liver.

The physiologic, morphologic, and biochemical findings of this study are comparable to that found in man with alcoholic cardiomyopathy and suggests that the moderate ingestion of ETOH has significant effects on cardiac function in the preadult heart.

151 LITHIUM-SODIUM (Li-Na) COUNTERTRANSPORT (CT) IN ERYTHROCYTES OF CHILDREN WITH HYPERTENSION (HPT). Laura L. Norling, Michael Landt, David Goldring, Alan M. Robson, Michele P. Monaco, Dept. of Pediat., Washington Univ. Medical School and St. Louis Children's Hospital, St.Louis, MO.

We are investigating the Li-Na CT measurement as a screening test for genetically determined hypertensive disease using the method of Canessa et al.(NEJM,1980:302, 772-6). CT was studied in RBCs of children with primary (1°) HPT and secondary (2°) HPT with comparison to age- weight- sex- and race-matched normotensive controls. Results show a significant increase in the Li-Na CT flux in children with HPT compared with controls. The mean CT(±S.D.) for each group is shown below in mMLi/liter RBCs/hr.

Primary HPT	0.34(±0.13)	n=17	p<.001
Normals	0.17(±0.09)	n=16	
Secondary HPT	0.26(±0.10)	n= 9	p<.025

The difference in CT flux between children with 1° and 2° HPT is not significant (p<.20). There is no correlation of CT values with sex, age, or weight in either HPT or control groups. Black children in both HPT and control groups had somewhat lower CT flux when compared with white children.

	Black		White	
1°HPT	0.27(±0.05) n=7	vs	0.38(±0.15) n=10	p<.10
Normals	0.12(±0.07) n=10	vs	0.25(±0.07) n=6	p<.005

The data indicate that children with 1° HPT have significant elevation of Li-Na CT when compared with normotensive children as has been seen in adults (ref.above). In contrast to adults, children with 2° HPT had increased Li-Na CT. The Li-Na CT has potential in screening for genetically determined HPT in children.

152 LONG-TERM EFFECTS OF SUBCRITICAL PULMONARY ARTERY BANDING Soraya Nouri, D. Glenn Pennington, Hind S. Bashiti (Sponsored by Thomas Aceto, Jr.), St. Louis University School of Medicine, St. Louis, MO Hemodynamic effects of subcritical (S) pulmonary artery banding (PAB) simulating mild pulmonary stenosis (MPS) were assessed 5 years after PAB in 7 mongrel dogs (Group I) and in 6 control dogs (Group II), 3 of which had "sham" PAB. Heart catheterization and hemodynamic measurements were obtained, under sodium thiamylal anesthesia, during baseline (BL) and isoproterenol infusion (ISU) (0.1 mcg/kg/min). All dogs were then killed and autopsies performed. Results:

		Group I	Group II	P Value
Right ventricular (RV) free wall weight as % of total heart weight		28.6±1.0	23.7±0.6	P<.005
Pulmonary arterial lumen (cm^2)		1.96±.80	3.79±.19	P<.001
RV-PA gradient (mm Hg)	BL	15.2±1.7	8.0±0.9	P<.001
	ISU	44.9±9.2	27.7±0.63	P<.001
Cardiac Index ($L/min/m^2$) (Thermodilution)		2.58±0.1	3.35±0.1	P<.001
Stroke Index (cc/m^2/beat)		15.25±.85	20.77±.63	P<.001
RVSWI (Stroke Work Index) ($gm\ m/m^2$/beat)		2.5±0.23	4.1±0.25	P<.001
LV (Left ventricular) SWI		27.08±1.66	40.19±1.26	P<.001
RV dp/dt (mm Hg/sec)		1,054±129	1,555±89	P<.003
LV dp/dt		2,423±210	4,509±399	P<.003

Extensive RV interstital myocardial fibrosis (not LV) was noted only in Group I. Hemodynamic changes due to ISU were similar in both groups. SPAB caused RV hypertrophy and small RV-PA gradients which increased with ISU. These data indicate that SPAB simulating MPS is not ininocuous.

153 SIGNIFICANCE OF VENTRICULAR IMBALANCE IN REPAIR OF COMPLETE ATRIOVENTRICULAR CANAL Soraya Nouri, D. Glenn Pennington, Mark Sivakoff, Su-chiung Chen (Sponsored by Thomas Aceto, Jr.), St. Louis University School of Medicine, St. Louis, Missouri

Between 1977 and 1981, 23 patients (pts) with complete atrioventricular canal (C.A.V.C.) had total repair. Five pts died (21.7%). At autopsy, 4 had a small right ventricle (RV) and 1 had a small left ventricle (LV). Three pts with C.A.V.C. and a small RV have not been submitted for operation (op). In these 7 pts with a small RV (Group S) the RV/LV diastolic ratio (Rd) by M-mode echocardiography (echo) was 0.25-0.35 (mean 0.29 ± 0.03SD), while the Rd in 18 op survivors with adequate echoes was 0.42-1.2 (mean 0.74 ± 0.21SD). Two-dimensional echo in Group S was suggestive of a small RV in 5 pts, equivocal in 1, and inadequate in the 7th. Angiography (Ang) in Group S was distinct from that in balanced C.A.V.C., showing hypoplasia of the trabecular portion of the RV with a normal outflow tract and a normal or large pulmonary artery (PA). In contrast, the 18 survivors had a large LV and a normal or large RV and PA. The pt with the small LV had an echo Rd of 2.3 and by Ang a large RV and PA, small LV, and sub-aortic narrowing. Age, systemic/pulmonary flow ratio, systemic/pulmonary resistance ratio, and RV/LV systolic pressure (RVP/LVP) ratio were similar in the survivors and non-survivors. In both groups RVP/LVP showed a significant and similar reduction immediately after repair. These data show a higher incidence of hypoplastic RV (27%) in C.A.V.C. than in most reported series. In C.A.V.C., RV or LV hypoplasia can be diagnosed by M-mode echo and Ang. In these pts the mortality of complete repair is prohibitive.

154 SPONTANEOUS ECHOGENICITY OF BLOOD IN STASIS AND LOW VELOCITY FLOW: INVIVO AND INVITRO OBSERVATIONS WITH A HIGH FREQUENCY REAL TIME ULTRASOUND SCANNER Soraya Nouri, Michael Wolverson (Sponsored by Thomas Aceto, Jr.) St. Louis University School of Medicine, St. Louis, MO

Observation of spontaneously arising echoes in the lumen of blood vessels at real time ultrasound has not been satisfactorily explained. They are seen most often in large caliber vessels in which flow is relatively slow such as the I.V.C., portal and internal jugular veins, but are seldom seen in the heart or arteries. An invitro model of a blood containing vessel was devised by placing blood in thin rubber tubing immersed in a water bath. Flow in the system was generated by means of an attached syringe and the tubing scanned with an 8 mHz small part instrument. The experiment was repeated using various mixtures consisting of (1) washed red cells suspended in .85% saline in the same concentration as in whole blood. (2) Dilutions of the washed red cell suspension (used in [1] above) with .85% saline of 1:1, 1:4, 1:100, and 1:1,000. (3) Hemoglobin solution of the same concentration as in (1) and (2) above. (4) Particle free plasma. Numerous low level echoes were noted in static and flowing blood and red cell suspensions, but not in plasma or hemoglobin. Formed elements of blood are, thus, the responsible scattering agent. Changing number and amplitude of echoes with changing flow rate, observed clinically, is probably related to red cell aggregation in stasis. Further improvements in ultrasound technology may allow spontaneous echogenicity of blood to be observed more consistently and used to better advantage.

155 CHANGES IN LEFT VENTRICULAR WALL THICKNESS IN OBESE ADOLESCENTS ON A HIGH PROTEIN WEIGHT REDUCING DIET. P. Pencharz, E.Archibald, C.Williams, W.Duncan. (Spon: T. Heim) Hospital for Sick Children, Divisions of Clinical Nutrition & Cardiology, Toronto, Canada.

Sudden death has been reported in obese adults on a liquid protein diet. Thinning of left ventricular myocardial fibres and a fall in total heart weight were noted (Circulation 60:1401,1979). Left ventricular wall thicknesses were measured by echocardiography in 10 obese adolescents studied on a high protein (2.5g/kg/d) weight reducing diet. The diet consisted of lean meat, fish and poultry with complete mineral and vitamin supplements. Measurements were taken during both systole and diastole. The number of subjects (N) for each time period varied due to technical difficulties in the control period and subject failure to attend.

	Diet Period				
Wall thickness (N)	Control (8)	2 weeks (10)	6 weeks (10)	10 weeks (6)	12 weeks (3)
Systole (mm)	13.2±2.5	10.9±1.3	11.1±1.0	11.0'2.0	9.7±1.1
Diastole (mm)	7.2±2.0	6.0±1.3	5.9±1.5	6.0±2.1	5.0±1.1

There was a significant fall in ventricular wall thickness during both systole ($p<0.025$) and diastole ($p<0.05$) in the first 2 wk. Mean weight loss was 5.4±1.0 kg at 2 wk and 14.7±5.3 kg at 12 wk. No electrocardiographic abnormalities or changes were seen. We were unable to demonstrate any loss of body protein in the first 2 wk by nitrogen balance. There was however a significant naturesis and diuresis in the first 2 wk which may have resulted in a reduced blood volume, which in turn may account for the observed reduction in ventricular wall thickness.

156 THE USE OF AMIODARONE IN THE THERAPY OF PRIMARY VENTRICULAR ARRHYTHMIAS IN CHILDREN. Arthur S. Pickoff, Sharanjeet Singh, Grace S. Wolff, Henry Gelband. University of Miami School of Medicine, Department of Pediatrics, Miami, Florida.

Amiodarone is a new antiarrhythmic agent that has been shown to be effective in treating a variety of arrhythmias in both children and adults. We report our experience utilizing amiodarone in the treatment of three children, ages 11-13 years, diagnosed as having anatomically normal hearts and ventricular arrhythmias (2 ventricular tachycardia, 1 multifocal PVC's). All 3 pts were initially treated with standard antiarrhythmic drugs (quinidine, propranolol, procainamide) and either did not respond (2/3 pts) or experienced drug toxicity (quinidine - 1 pt). Amiodarone was administered in a single oral daily dose of 10 mg/kg/day x 1 week, followed by a daily maintenance dose of 5-11 mg/kg/day. All pts have shown a significant clinical response to oral amiodarone with either complete suppression of ventricular tachycardia (1 pt), abolition of multifocal PVC's (1 pt) and near complete suppression of ventricular tachycardia in the third pt (1 short run of ventricular tachycardia in 24 hr ECG). One pt has had corneal microdeposits detected by slit lamp examination and is receiving methylcellulose eye drops; no other adverse reactions have been encountered during the followup of 4 months to 3 years.

Primary ventricular arrhythmias in children are often resistant to standard drug therapy. Amiodarone may be an effective agent in those pediatric pts with primary ventricular arrhythmias in whom pharmacologic suppression is desired.

157 MYOCARDIAL WALL STRESS DURING CATHETERIZATION
William W. Pinsky, John D. Kugler, Philip J. Hofschire, John P. Cheatham, Paul K. Mooring, Harold A. Baltaxe. Spon. by Robert M. Nelson) University of Nebraska College of edicine, University of Nebraska Affiliated Hospitals, Department f Pediatrics, Omaha, Nebraska

Rapid injection of ionic contrast material versus non-ionic ompounds during cardiac catheterization (CC) is known to produce n ↑ osmotic load. However, little information is available oncerning the effects of contrast on LV myocardial wall stress LVWS). Using double blind technique 20 pts. < 3 yrs. of age ndergoing cardiac catheterization were divided equally into roup I receiving Diatrizoate Meglumine, Renografin-76 (R) and roup II a non-ionic radiopaque compound Metrizamide (M). Following baseline LV pressure (P) and echo measurement of LV interval iameter and posterior LVW in systole and diastole an LV injection as performed: Group I receiving 1.41 ± .12 cc/kg, II 1.53 ± .18 c/kg. At one minute intervals the previous indices were recorded nd wall stress calculated for systole and diastole: (GM/CM^2) P < 0.05

		PRE	IMMED-POST	15 MINS. POST
I	SYST	167.5 ± 18.9	187.9 ± 26.9*	194.6 ± 33.8*
	DIAST	50.3 ± 9.1	69.1 ± 14.0*	65.2 ± 12.2*
I	SYST	195.4 ± 32.3	174.6 ± 26.2	165.3 ± 24.4
	DIAST	45.1 ± 7.6	53.6 ± 6.8	39.9 ± 7.2

njection of ionic contrast produces an ↑ in LVWS while non-ionic ontrast allows less of an ↑ in LVWS. We conclude this is dditional evidence to suggest non-ionic contrast may be a safer adio-opaque agent during CC.

158 SYSTOLIC TIME INTERVALS AND RIGHT HEART HEMODYNAMICS IN VENTRICULAR SEPTAL DEFECT.
M.Pinto,P.L.Ferrer,H.Gelband,A.Pickoff,G.Enriquez,G. Wolff,D.Tamer,and O. Garcia. Department of Pediatrics. Jniversity of Miami School of Medicine, Miami.

The value of right systolic time intervals (RVSTI) in predicting pulmonary artery hypertension (PAH)remains controversial. To study this problem M-mode Echo and cardiac cath. were performed in 38 children with VSD. Pts. were divided into 3 groups:A) 14 pts. c̄ RV or PA systolic pressures (RVSP,PASP)<50 mm Hg, and pulmonary vascular resistance (PVR)<3 U/M_2:B) 14 pts. c̄ RVSP or PASP>50 mm Hg,PVR<3 U/M_2:C) 10 pts. c̄ RVSP or PASP>50 mm Hg, PVR>3 U/M_2. 27 normal pts. had only Echo. Results:

RVSTI	Normal	A	B	C
RICT	-4.2±8.6	-7.1±9	25±6*	22±6*
RICT/RVETc	-1.5±2.9	-2.7±4	12±4*	11±4*
PEPc/RVETc	.21±.03	.21±.03	.28±.06**	.32±.07*
RVETc/LVETc	1.14±.08	1.2±.05	1.06±0.1*	1.08±.08*

R=right,L=left,ICT=isovolumic contraction time,PEP=pre-ejection period,RVET=RV ejection time,LVET=LV ejection time,c=corrected for heart rate,intervals=msecs.±SD;*=p<.001,**=p<.005,(as compared c̄ A). Groups B and C behave similarly,but all can be separated from A by ICT and ICT/RVET. The best correlation coefficients for PASP were: RICT/RVETc,r=.824,ICT,r=.800.

In summary,although a comprehensive evaluation of RVSTI (including RICT,RICT/RVETc) can not separate VSD pts. c̄ high and low PVR,is accurate enough in predicting PAH and therefore in helping to indicate cardiac catheterization in pts. with VSD.

159 HEMODYNAMICALLY SIGNIFICANT PDA (hsPDA) IN VERY LOW BIRTH WEIGHT (VLBW) INFANTS - ECHOCARDIOGRAPHIC (ECHO) CORRELATION TO OUTCOME.
Mark D. Reller, John M. Lorenz, Uma R. Kotagal, Richard A. Meyer, Samuel Kaplan, University of Cincinnati, Department of Pediatrics

In order to assess echo criteria in defining hsPDA and correlating these criteria to risk for poor outcome, 51 VLBW infants (750-1500g, 27-34 wks gestational age [GA]) underwent prospective sequential clinical and echo examinations during the first month of life. Echoes were performed on days 1,2,3,5 and 7 and then once/wk. hsPDA was defined as 1) ↑ left ventricular (LV) dimension or ↑ left atrial dimension (LAD) or LAD/Aorta ratio ≥ 1.4 and 2) typical ductal murmur or ↑ shortening fraction or ↓ LV systolic time interval ratio. 32/51 (63%) infants had hsPDA during the first wk of life (early) and did not differ from those without hsPDA in BW or GA. However, infants with early hsPDA had lower Apgar scores (p<0.05) and were more likely to require ventilator support for RDS (p<0.05). A murmur was not audible in 21/32 (66%) infants with early hsPDA. These infants with silent ducts did not differ from infants with murmurs in BW, GA, 5 min Apgar or outcome (duration of ventilation, incidence of BPD). Infants who required ventilator support for RDS with early hsPDA needed ventilation for a mean of 13.8±9.4 days, whereas those without early hsPDA needed ventilation for 3.3±2.6 days (p<.001). Infants with early hsPDA had a higher incidence of BPD and/or death than infants without early hsPDA - 17/32 vs 4/19 respectively, p<0.03. Therefore, the above criteria for hsPDA are useful in identifying the VLBW infant at risk for poor outcome.

160 EVALUATION OF THE GREAT ARTERIES BY LINEAR ARRAY TWO-DIMENSIONAL ECHOCARDIOGRAPHY IN NEWBORNS.
K.H. Rhee, E.W. Nugent, W.D. Wilcox, A.A. Raviele, K.J. Dooley, W.H. Plauth, Jr. (Spon. by: G.W. Brumley) Emory University School of Medicine, Department of Pediatrics, Atlanta.

Early differentiation of sick newborns (NB) with critical congenital heart disease (CHD) from those with non-cardiac illness is essential to the appropriate management of these patients. Linear array two-dimensional echocardiography (LA2DE) provides a technically simple, portable method for assessing cardiac anatomy in NB. Resolution is excellent. LA2DE characteristics of the great arteries were evaluated in 51 consecutive sick NB referred for possible CHD. The median age was one day (0-7) and median weight was 3.2 kg (2.5-4.1). The ratio of the diameters of the large-to-small great vessels was calculated. 24 NB with a ratio greater than 1.4 had CHD with a large shunt in either direction. Of the 27 NB in whom the ratio was less than 1.2, 10 had parallel great arteries (transposition of great arteries), and 17 had normally related great arteries. Of the 17 with normally related great arteries, 6 had a thickened and poorly mobile semilunar valve, and 11 had no evidence of cardiac abnormality. LA2DE findings were confirmed by subsequent cardiac catheterization in all 40 patients with CHD and by clinical course or autopsy in the 11 with no evidence of CHD. Thus, LA2DE is an excellent tool for physicians caring for sick NB to use in non-invasive assessment to distinguish cardiac from non-cardiac disease.

161 ECHOCARDIOGRAPHIC FINDINGS DURING SLEEP IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA.
Thomas W. Riggs, Robert T. Brouillette, Carl E. Hunt, and Sandra K. Fernbach, Northwestern University School of Medicine, Children's Memorial Hospital, Departments of Pediatrics and Radiology, Chicago.

Seventeen infants and children, suspected clinically of having obstructive sleep apnea (OSA), underwent echocardiography (ECHO) examination in both the awake and asleep state to monitor the cardiovascular effects of the exaggerated respiratory variation in intrathoracic pressure. The diagnosis of OSA was established by upper airway fluoroscopy and polygraphic monotoring during sleep with corroboration by transcutaneous PO2 and end-tidal PCO2 determinations in 12 patients, while 5 patients were normal.

Insp./Exp. Ratio	Normals		OSA	
RVED	↑46%	(p< 0.05)	↑62%	(p< 0.001)
RPEP/RVET	↑ 9%	(NS)	↑22%	(p< 0.05)
LVED	↑12%	(p< 0.05)	↑15%	(p< 0.01)
LPEP/LVET	↑ 5%	(NS)	↑23%	(p< 0.01)

During inspiration the RV dimensions were markedly increased, the LV dimensions were decreased and the ventricular systolic time intervals changed in a manner that is consistent with decreasing RV afterload and increasing LV afterload. The converse changes occurred during expiration. Four patients had abnormal ECHO results while both awake and asleep, 5 patients had abnormal ECHO studies only during sleep and the remaining 3 had normal ECHO studies both awake and asleep, while only 4 of these 12 patients had an abnormal EKG. We conclude that ECHO examinations during sleep are more sensitive than either standard ECHO exams or EKG in assessing the cardiovascular effects of OSA.

● **162** DEPRESSED BARORECEPTOR FUNCTION IN CHILDREN WITH EXERCISE-INDUCED HYPERTENSION AFTER COARCTATION REPAIR
Albert P. Rocchini, Robert H. Beekman, Barry P. Katz, Catherine Steffens, (Spon. by Amnon Rosenthal) University of Michigan, C.S. Mott Children's Hospital, Dept. Pediatrics, Ann Arbor

To determine if altered baroreceptor (BR) function may contribute to exercise hypertension following coarctation (COA) repair, BR function was studied in 5 children (age 13.8-19 yr) with repaired COA and exercise-induced upper extremity (UE) hypertension. Data were compared to that from 7 normotensive controls with mild heart disease. Age at COA repair was 10.5±3.4, (mean ± SD) years. UE systolic pressure increased from 130.4±13.2 mmHg at rest to 219.2±16.5 mmHg at peak exercise, compared to 107.9±13.1 mmHg (p<.02) and 146.4±12.2 mmHg (p<.001) respectively for controls. COA gradient was 7.4±9.3 mmHg at rest and 68.8±36.4 mmHg immediately post-exercise. At catheterization, steady state sigmoidal BR curves relating mean arterial pressure (MAP) to R-R interval were derived by increasing and decreasing MAP with small boluses of phenylephrine and nitroprusside. Compared to controls, the BR curves of these postop COA children: 1) are reset about a higher average MAP (110.8±11.1 vs 91.4±8.2 mmHg, p<.01); 2) have a reduced R-R interval range, i.e. difference between R-R interval at the upper and lower plateaus of the sigmoidal BR curve (227.7± 92.3 vs 591.5±165.0, p<.01); 3) have a decreased slope (2.1± 0.6 vs 6.2±1.5 msec/mmHg, p<.01). Thus, in children following COA repair the baroreflex operates at a higher MAP with a markedly reduced gain. We speculate that reduced ability of the baroreflex to regulate blood pressure may contribute to exercise-induced hypertension following COA repair.

163 LEFT HEART MORPHOMETRY IN TOTAL ANOMALOUS PULMONARY VENOUS DRAINAGE (TAPVD). Glenn C. Rosenquist, Joseph L. Kelly III, Roma Chandra, Roger N. Ruckman, Frank M. Galioto, Frank M. Midgley, Lewis P. Scott. Children's Hospital National Medical Center and The George Washington University School of Medicine and Health Sciences, Washington D.C.

Left heart anatomy in 22 heart specimens from infants with TAPVD was compared to normal specimens matched by age, crown-heel length and brain weight. Thicknesses were measured with a Fowler micrometer; lengths and circumferences with needlepoint dividers; diameters with a graduated cone; and atrial surface areas (estimate of volume) with a tablet digitizer after pressing endocardial surfaces against plate glass. Two observers independently graded the left contour of the ventricular septum as 2+ or 1+ concave (normal) and flat or 1+ convex (indicating mild to moderate displacement into left ventricular cavity). Sets of observations were 90% reliable by linear regression (least squares method). Differences between normal and TAPVD specimens were determined by the Student's T test. The left ventricle in TAPVD was longer ($p=.05$) and wider ($p=.001$) than normal. The septum was displaced into the left ventricular cavity in 18 specimens (including newborns, $p=.001$); this suggests that right ventricular preponderance and compression of LV cavity is not always due to increased pulmonary flow after birth. Length of left atrium was decreased from normal ($p=.05$) and surface area diminished ($p=.001$). We conclude that left ventricular cavity in TAPVD may be abnormal in shape. Since left atrium is smaller than normal, appropriate efforts should be made to maximize its effective size at time of surgical correction.

● **164** TWO-DIMENSIONAL (2D) ECHOCARDIOGRAPHIC IDENTIFICATION OF MITRAL AND TRICUSPID VALVE OVERRIDING (MVO,TVO) IN COMPLEX CONGENITAL HEART DISEASE David J. Sahn, Peter W.T. Brandt, John M. Neutze, Louise Calder, Brian Barratt-Boyes, Stanley J. Goldberg, Hugh D. Allen, Lilliam M. Valdes-Cruz, Univ. of Az., Dept. of Pediatrics, Tucson, and Green Lane Hospital, Auckland, New Zealand

In order to evaluate the role of 2D echo for identifying complex MV and TV anatomy, we studied 22 patients who had an overriding atrioventricular valve identified on angiography. Eleven had anatomic verification at autopsy (n=5), or at surgery (n=6). Of 13 with inlet VSD, TVO was subclassified by 2D echo as TVO without straddling in 7, (4 confirmed anatomically), and TVO with straddling in 6, 1 confirmed anatomically. TVO was best evaluated on 4 chamber views. Ventricular inversion in 4 patients or criss-cross heart in 2 did not preclude diagnosis. Three patients had MVO and 2, 1 with and 1 without straddling, were verified anatomically. Short axis views best delineated MV relationships to a more anterior subarterial VSD. Six patients had single ventricle of right ventricular type and a portion of a common AV valve which overrode and straddled into an inferior-posterior blind trabecular pouch, a relationship verified in 4 anatomically. Our study relates the angiographic and echocardiographic views used for evaluation of valve overriding and suggests that angiography and 2D echo are complementary techniques for diagnosing overriding atrioventricular valves. In addition, 2D echo can identify chordal attachments to the septum or those crossing the ventricular septal defect and associated with straddling.

● **165** COMBINED USE OF INTRAVENOUS DIGITAL VIDEO SUBTRACTION ANGIOGRAPHY (DVSA) AND TWO-DIMENSIONAL (2D) ECHOCARDIOGRAPHY FOR EVALUATION OF ABNORMALITIES OF THE AORTIC ARCH PRIOR TO SURGICAL CORRECTION David J. Sahn, Lilliam M. Valdes-Cruz, Theron W. Ovitt, Stanley J. Goldberg, Hugh D. Allen, Jack G. Copeland, Robert B. Mammana, Univ. of Az., Depts. of Pediatrics, Surgery and Radiology, Tucson

This study combined the use of 2D echo and DVSA in 3 patients with double aortic arch and 4 patients with aortic coarctation who subsequently underwent surgical correction without cardiac catheterization. In the 3 children with double aortic arch (ages 4 months to 7 years), the 2D echo corroborated the absence of associated cardiac abnormalities. Additionally, a subcostal left ventricular outflow tract view could be developed which showed the aortic bifurcation high above the aortic valve and the proximal portion of both limbs of the double aortic arch. In the 4 patients with coarctation of the aorta (age 6-11 yrs), clinical examination and 2D echo confirmed nonstenotic bicuspid aortic valve in all 4, and a small ventricular septal defect associated with a ventricular septal aneurysm in 1. Suprasternal notch echo views imaged discrete coarctation distal to the left subclavian artery. DVSA was accomplished with injection of 1 cc/kg of 60% Renovist into a peripheral vein, allowing imaging of the double aortic arch in all 3 patients and diagnosis of atresia of the left arch between the carotid and subclavian in 2. DVSA also confirmed the anatomy of the coarctations prior to surgery. For simple lesions, as in this study, 2D echo and DVSA can provide complete presurgical diagnosis without cardiac catheterization.

166 RADIONUCLIDE EVALUATION OF PATENT DUCTUS ARTERIOSUS. Celia Satterwhite, Giles W. Vick, Joseph R. Logic, Michael V. Yester, Joseph B. Philips, and George Cassady. University of Alabama in Birmingham, Divisions of Perinatal Medicine and Nuclear Medicine, Birmingham.

Conventional diagnosis of left to right persistent ductus arteriosus (PDA) shunting relies on clinical, radiographic, and echocardiographic findings. As these methods err to underdiagnosis, we studied the value of radionuclide angiography in 42 neonates clinically suspected of a PDA.

A mobile gamma scintillation camera was used, and injections of 2 mCi of sodium 99m pertechnetate in 0.2 - 0.3ml volume was injected as a bolus through a peripheral IV.

Birthweights ranged from 640 to 2640 grams; nearly ½ were ≤ 1000 grams, and only 2 were > 2000 grams. Postnatal ages ranged from 1 to 22 days, with nearly 3/4 ≤ 7 days when initially studied. Twenty-five infants had a Qp/Qs ratio ≥ 2.2, 21 of whom needed surgery. Only four of thirteen infants with a Qp/Qs < 2.2 required surgery. Three infants who required surgery had no clinical evidence of a shunt and LA/Ao's were 0.8 to 1.0, yet Qp/Qs was ≥ 2.2. Post-op Qp/Qs ranged from 1.3 to 2.2.

This preliminary experience indicates that radionuclide studies can be performed on tiny, ill infants in the neonatal ICU using a peripheral IV. A Qp/Qs ratio < 2.2 appears to suggest the absence of a significant left to right shunt. Although sole reliance on a Qp/Qs ratio may not be appropriate at this time, the Qp/Qs ratio appears to be a valuable addition to other available diagnostic techniques.

● **167** LEFT VENTRICULAR FUNCTION (LVF) IN CHILDREN ON CHRONIC HEMODIALYSIS (HD). Pilar Soler, Gaston Zilleruelo, Victoria Bennet, Arthur Pickoff, Pedro Ferrer and Jose Strauss. University of Miami School of Medicine, Department of Pediatrics, Miami, Florida.

Echocardiographic assessment of LVF was performed in 11 children of ages 11-20 yrs ($\bar{x}$: 16 ± 2.8 yrs) with end stage renal disease (ESRD) immediately before and after HD. All medications were withheld the night before HD. Predialysis body weight was $\bar{x}$ 2.32 ± 3.7% above dry weight. Based on left ventricular end diastolic dimension (LVED) and posterior wall thickness, patients were categorized as having hypertrophy (LVH) with normal LVED (group I: 7 pts) or LVH with increased LVED (group II: 4 pts). There were no differences between the two groups in duration of ESRD or HD, anemia, hypertension, or bilateral nephrectomy. After HD no consistent changes were found for: LV shortening fraction, electromechanical systole (QS2), pre-ejection period (LPEP) or its ratio to ejection time (LPEP/LVET) in the group as a whole. Group II had significant decrease of QS2 ($p < 0.002$). All patients had left atrial dimension decreased after HD ($\bar{x}$: 11 ± 7%). Patients with no weight loss had significant improvement in LPEP ($p < 0.03$) and LPEP/LVET ($p < 0.001$). Patients with > 2% weight loss had significant prolongation of QS2 ($p < 0.001$) and LPEP ($p < 0.045$), and deterioration of LPEP/LVET ($p < 0.025$). We conclude that children on chronic HD have acute improvement in LV function after HD only when no significant weight loss occurs. This finding suggests that high filling pressures are needed to maintain normal LV performance in patients on chronic HD.

● **168** VASCULAR ACTION OF DIGOXIN AND INDOMETHACIN:A POTENTIALLY DANGEROUS INTERACTION. G.K.Sorensen,E.D.Olsen,R.C.Boerth,(Spon.by T.P.Graham,Jr.);Vanderbilt Univ., Dept. of Ped. & Pharm., Nashville, TN.

Several vasoconstrictors stimulate production of prostacyclin, which attenuates their vasoconstriction.We determined if endogenous prostaglandins modify the vascular response to digoxin.Effects of Indomethacin(I)on changes in systemic vascular resistance(SVR) and coronary vascular resistance induced by digoxin were examined in rabbits.Isolated hearts were perfused at constant flow with blood from donor rabbits so that changes in coronary perfusion pressure(CPP)were proportional to changes in coronary vascular resistance.Effects on SVR were determined in intact rabbits.Digoxin was given IV to donor or intact rabbits in the absence or presence of I(10mg/kg IV).Baseline variables did not differ between groups and I alone did not alter coronary vascular resistance or SVR or change enhanced contractility produced by digoxin.The table shows changes(X̄±SEM)from control in CPP(mmHg)and SVR(mmHg/L/MIN/kg)

		--Digoxin Dose (mg/kg)--				
		0.1	0.2	0.3	0.4	n
ΔCPP	Digoxin	8±1	5±2	1±3	-3±2	6
	Digoxin + I	*25±4	*31±5	*34±5	*39±7	6
ΔSVR	Digoxin	5±3	10±7	15±6	14±8	6
	Digoxin + I	6±4	15±3	*32±7	*47±10	7

(*denotes significance from digoxin at $p < 0.05$)

Digoxin and I interact to produce dramatic increases in systemic and coronary vascular resistances which may be of significant clinical importance if such an interaction occurs in man.This study suggests that digoxin may stimulate prostaglandin synthesis to attenuate vasoconstriction of digoxin in rabbits.

169 CHANGES IN LEFT VENTRICULAR FUNCTION WITH PULMONARY VALVE STENOSIS. Janette F. Strasburger, William W. Pinsky, John P. Cheatham, Philip J. Hofschire, John D. Kugler, Paul K. Mooring, William H. Fleming. (Spon. by Carol R. Angle) University of Nebraska College of Medicine, University of Nebraska Affiliated Hospitals, Department of Pediatrics, Omaha, Nebraska

Although RV dysfunction has been described following operation (OP) for pulmonary stenosis (PS), LV function has not been evaluated. We examined the records of 37 pts. undergoing 38 ops for simple PS between 1975 and 1981. Comparisons were made between the valvulotomy (VO) group and valvulectomy (VE) group by using ejection fraction (EF) as measured by angiography, chamber size, and shortening fraction (%ΔD) by M-mode echocardiography. 16 of 22 VE pts. and 8 of 16 VO pts. underwent followup catheterization at 1 yr. post op (6 mos - 6 yrs). Mean EF, median age at op, and op mortality are outlined below:

	VO	VE
AGE AT OP	5 yrs 6 mos	2 yrs 1 mo
OP MORTALITY	6% (1/16)	0% (0/22)
PRE-OP EF	68.3 ± 2.6	73.6 ± 4.3
POST-OP EF	66.8 ± 2.7	69.5 ± 3.9

Mean EF, chamber size, and %ΔD were not statistically different between the 2 groups, and no significant change in mean EF or %ΔD could be detected at 1 yr post op for either group. However, 5 of 16 VE pts. showed a significant ↓ in EF post op (mean ↓ 13.5%). 2 pts. had ↓ EF pre op and showed return to normal at 1 yr post op (mean ↑ 12%). These findings suggest that LV function is altered by PS and its operative correction and evaluation for LV dysfunction is indicated.

● **170** INDOCIN & RETINOPATHY OF PREMATURITY (ROP). Shyan Sun, Zanaida Aranda, Kamtorn Vangvanichyakorn, Anthony Caputo. (Spon. by R. Levine) New Jersey Med. School. Dept. Neonatology & Ped. Ophthalmology, Newark, N.J.

Flower et al reported that aspirin treated, oxygen exposed Beagle puppies developed retinopathy of significantly greater severity than their unmedicated, oxygen exposed litter mates. Prompted by this observation, we reviewed the outcome of 43 surviving NICU graduates born between 1973-1981 with birthweight of less than 1000 gm.

	No	ROP	Grade	%ROP	Blind	%Blind
Indocin	11	5	III-V	45.5	3	27.3
Control	32	5	I-III	15.5	0	0
Fisher exact P		0.058			0.013	

Ten developed cicatrical ROP Grade I-V (23% of survivals) of which 3 were blind (6.9%). Indocin treated group suffered significantly more severe degree of ROP (Grade III to V, 3 blind) compared to non-medicated group (Grade I-III, non blind). By discriminant analysis the following independent variables were determined to be correlated to the pathogeneses of ROP in order of its significance. (1) Duration of exposure to $PCO_2 > 50$ torr. (2) Duration of exposure to $PO_2 > 100$ torr. (3) Duration of mechanical ventilation. (4) Indocin treatment. (5) Duration of O_2 treatment. Retinal vasoconstriction, if viewed as protective, might be abolished by Indocin, thereby allowing free flow of hyperoxic blood into the retinal tissue which might have increased the severity of ROP. Our experience suggests cause and effect relationship. Further study is urgently needed to clarify the pharmacological effect of Indocin on retinal vessels of human infants.

● **171** POSTNATAL CHANGES IN MYOCARDIAL CONTRACTILITY. D. Teitel, D. Sidi, T. Chin, A. Rudolph, M. Heymann, CVRI, UCSF, Dept. Ped., San Francisco, CA 94143

Previous studies suggesting a high resting contractile state in the newborn lamb have been based upon unreliable indices. We have studied changes in resting contractility, inotropic reserve, and maximal inotropic state over the first month of life in lambs using an in vivo analog of the end-systolic pressure-volume relationship.

A catheter-tip pressure transducer was placed in the left ventricle (LV) and an echo transducer applied to the LV. In the same lambs, at weekly intervals, curves of meridional wall stress (WS) vs LV volume index (LVVI=LV diameter^3) were generated by graded infusions of nitroprusside and phenylephrine to alter LV diameter. Heart rate was maintained by continuous atropine infusion & atrial pacing. A linear regression analysis was performed on the resultant curves. The slope of the WS vs LVVI line has been documented as a reliable index of contractility. Correlation coefficients have been >0.93 in 45 of 49 studies. To assess contractile reserve, studies were performed at rest (R) and during isoproterenol infusion (I) (0.1 μg/kg/min).

Resting contractility was maximal at 1 and 3 weeks, and fell markedly at 4 weeks (31%). Contractility was not affected by isoproterenol at 1 and 3 weeks, but increased at 2 (25%) and 4 (47%) weeks. Maximal contractility was similar at all ages.

These studies demonstrate that the newborn myocardium is operating at maximal performance with no inotropic reserve. Similar findings at 3 weeks may be secondary to the known physiologic anemia.

● **172** TRANSPULMONARY PASSAGE OF BIOLOGICALLY SAFE ECHO CONTRAST AGENTS (E/C) AND POTENTIAL APPLICABILITY FOR DETECTION OF LEFT-TO-RIGHT (L-R) SHUNTS: A CANINE STUDY Lilliam Valdes-Cruz, David Sahn, Suzana Horowitz, Emmanuel Mesel, Daniel Fisher, William Banner, Douglas Larson, Hugh Allen, Stanley Goldberg; Univ. of Az, Department of Pediatrics, Tucson

We evaluated intravenous (IV) agents used in humans which might be capable of achieving reliable E/C in the right ventricle (RV) with transpulmonary passage to the left ventricle (LV). Four agents were tested in 5 open chest dogs: A, a surfactant hypnotic drug; B, a surfactant widely used IV; C, a suspending agent used for IV medications; and D, a bioparticulate mixture for IV use. Injections of 5 cc of each with 5 cc saline flush were made into the superior vena cava while recording an apex 4 chamber view. E/C densities, compared to control, in the RV and LV were quantified by measuring analog video intensities with a waveform monitor. The mean of the maximal video intensities ($\overline{VI}$) for 5 injections of each agent was calculated for LV inflow, ratio of LV:RV-$\overline{VI}$, and LV-$\overline{VI}$ after RV washout. Agent A achieved reliable transpulmonary passage (LV-$\overline{VI}$ = 22.3±4.6(SE); LV:RV-$\overline{VI}$ = .39 ±.1) but with a prolonged RV washout. Agents B and C achieved dense transpulmonary passage (LV-$\overline{VI}$ = 52±5, LV:RV-$\overline{VI}$ = .8±.1 and LV-$\overline{VI}$ = 39 ±9, LV: RV-$\overline{VI}$ = .6 ±.05 respectively) but both also had prolonged RV washout. Only agent D (LV-$\overline{VI}$ = 52±13.5, LV:RV-$\overline{VI}$ = .70±.05) and a gasified electrosolute mixture had potential for detection of L-R shunts, with LV-$\overline{VI}$ values >30 after RV washout. In our study, E/C agents were identified which achieve transpulmonary passage and have potential for positive E/C detection of L-R shunt lesions.

173 HYPEROXIA ALTERS LUNG VASCULAR DEVELOPMENT. Kenneth M. Weesner, John R. Bucher, Robert J. Roberts, Depts. Pediatrics and Pharmacology, University of Iowa, College of Medicine, Iowa City, IA 52242.

An altered ventilation-perfusion (V/Q) relationship is a major functional abnormality noted in infants with chronic lung disease. To examine the possibility that this V/Q abnormality is due to altered lung vascular development due to hyperoxia, we exposed newborn rats to FiO_2 of 0.21, 0.4, 0.8 and >0.95 for the first 6 days of life. Evaluation of the vascular bed was performed after the 6 days of exposure and following 7 and 14 days of air recovery. Structural analysis included capillary counts by light microscopy, barium PA angiography, and methylmethacrylate corrosion casts by scanning electron microscopy (SEM). Functional changes were assessed by $AaDO_2$ in FiO_2 1.0. After 6 days there was a reduction of capillary number/area in the animals exposed to >0.95 O_2. Capillary number/area returned to control values after 1 week and 2 weeks recovery in air. The pattern of PA branching was similar in both hyperoxic and control animals. SEM casts of the lung vascular bed revealed differences in the microvasculature between control and hyperoxic lungs. Maximal PaO_2 in FiO_2 1.0 showed a dose-related reduction in the hyperoxic exposed animals. After 1 week recovery in air, the dose response relationship reversed. With 2 weeks of recovery there were no differences between the groups. We conclude that hyperoxia alters pulmonary vascular development in the newborn rat. This may serve as a model for the V/Q abnormality noted in premature infants with chronic lung disease. Supported by NIH Grants GM12675 and HL07413.

174 ECHOCARDIOGRAPHIC ASSESSMENT OF CHILDREN WITH HEAD INJURY. Randall C. Wetzel and Mark C. Rogers. Departments of Anesthesiology/Critical Care Medicine and Pediatrics, Johns Hopkins University, Baltimore, MD 21205

To detect early hemodynamic changes in children with head trauma of varying severity, we undertook a prospective, non-invasive echocardiographic study of children following isolated closed head trauma. Echocardiographic determination included shortening fraction and ventricular time intervals (PEP: pre-ejection period and ET: ejection time) for both left and right ventricles. Glasgow coma scores, degree of intrapulmonary shunting, respiratory status and outcome were determined for all patients. Sixteen patients were studied on admission to the PICU and followed serially until discharge or death.

Our findings include a significant difference ($p < .05$) in the ratio of RVPEP/RVET in survivors (.24 ± .015) versus non-survivors (.44 ± .095). No statistically significant difference was demonstrated for LVPEP/LVET or SF between groups. Furthermore in the survivors, over time, RVPEP/RVET fell significantly ($p < .01$) (.24 ± .015 to .17 ± .006). In contrast, this ratio increased in non-survivors (.44 ± .095 to .543 ± .12, $p < .02$). We also found significant correlation between the RVPEP/RVET and the degree of intrapulmonary shunting (R = .69) and severity of injury (R = .69), as determined by the GCS.

We conclude that echocardiography demonstrates significant hemodynamic alterations in children with isolated head injury. Further, that in children with head injury there is early elevation in pulmonary vascular resistance and that patients in whom this is most severe, have a poor prognosis.

Withdrawn Prior to Publication

Withdrawn Prior to Publication

177 EFFECTS OF HYPOXIA AND REOXYGENATION ON MITOCHONDRIAL RESPIRATION AND CA^{2+} UPTAKE IN NEONATAL MYOCARDIUM Helen H. Young, Tatsuo Shimizu, Kenya Nishioka, Toshio Nakanishi, Jay M. Jarmakani, UCLA Medical Center, Dept. of Pediatrics, Los Angeles, California.

This study was designed to evaluate the effects of hypoxia (N_2) and reoxygenation (re-O_2) on mitochondrial respiration and mitochondrial Ca uptake in isolated, arterially perfused newborn (NB) and adult (A) rabbit heart. After perfusion, mitochondria were isolated, and mitochondrial function and Ca uptake were determined by polarograhic and Millipore filtration techniques, respectively. In the control muscle, rate of State 3 respiration (QO_2), ATP-dependent and respiration-dependent Ca uptake in NB were greater than in A. After 60 min N_2, State 3 QO_2 decreased significantly in both NB (64 ± 4% of control, n=8) and A (60 ± 7%, n=10). After re-O_2 following N_2, State 3 QO_2 recovered to control in NB (96 ± 6%, n=8), but not in A (56 ± 3%, n=12). In A, ATP-dependent Ca uptake was not affected by 60 min N_2 but decreased significantly ($P<0.01$) after re-O_2 (62 ± 3%, n=6). ATP-dependent Ca uptake in NB was unchanged during N_2 and re-O_2. Respiration-dependent Ca uptake was significantly ($P<0.001$) decreased after hypoxia (62 ± 4%, n=4) and re-O_2 (51 ± 3%, n=4) in A, but not in NB. Mitochondrial Ca content increased after re-O_2, and the increase in A was greater than in NB.

These data suggest that 1) the effect of N_2 and re-O_2 on State 3 QO_2 and Ca uptake in NB is less than in A, 2) the decrease in respiration-dependent Ca uptake during N_2 and re-O_2 in A may be due to decreased State 3 QO_2, 3) the decrease in ATP-dependent Ca uptake in A may be due to increased mitochondrial Ca content.

DEVELOPMENTAL BIOLOGY

178 PROSTAGLANDIN(PG) METABOLISM BY THE CANINE LUNG DURING DEVELOPMENT. Billy S. Arant, Jr. and William H. Stephenson. Southwestern Med. Sch.,Dept. Ped., Dallas,TX

Degradation(D) of PGE_2 and PGF_{2a},but not PGI_2, is nearly complete across the adult lung in which synthesis(S) of each PG can occur. To investigate changes in pulmonary metabolism of PG during development, simultaneous blood samples were obtained from right atrial(V) and aortic(A) catheters in unstressed conscious(C) and pentobarbital anesthetized(B) puppies 1-60 days old. PG were measured by RIA. Preliminary results are presented in the Table as ratios of A:V plasma PG concentrations (X±SEM).

AGE		n	PGE_2	PGF_{2a}	6ketoPGF$_{1a}$	TXB_2
1	C	4	0.90±0.15	0.71±0.11	0.93±0.10	0.92±0.09
	B	4	0.99±0.10	0.94±0.04	1.12±0.18	1.09±0.07
3	C	5	0.66±0.08	0.77±0.04	0.86±0.08	0.79±0.15
	B	3	1.18±0.27	0.91±0.003	0.81±0.16	0.94±0.57
30	C	4	0.68±0.07	0.73±0.09	1.21±0.16	1.22±0.33
	B	11	0.92±0.12	1.36±0.17	1.04±0.16	1.02±0.15
60	C	9	0.55±0.07	0.82±0.07	1.14±0.29	1.36±0.40
	B	8	1.44±0.41	1.53±0.52	1.07±0.05	0.85±0.13

Although relative contributions of pulmonary D and S were not investigated in these studies, we conclude that net D of PGE_2 and PGF_{2a} remains constant in C puppies after the first day of life and that net S of PGI_2(6ketoPGF$_{1a}$) and thromboxane(TXB_2) can occur as a result of stimuli that produce parallel changes in their metabolism. Consequences of B on PG metabolism was to increase delivery of PGE_2 and PGF_{2a} into the systemic circulation,suggesting caution in interpreting PG effects even in animals stressed only by anesthesia. (Supported by NIH RO1-HD14706)

179 ADULT (HbA) AND FETAL (HbF) HEMOGLOBIN SYNTHESIS IN NEWBORN INFANTS OF INSULIN DEPENDANT DIABETIC MOTHERS. Harry Bard and Janie Prosmanne. University of Montreal, St. Justine's Hospital, Department of Pediatrics, Montreal, Quebec, Canada.

Elevated levels of erythropoietin and increased erythropoiesis have been reported in the cord blood from infants of diabetic mothers. It has also been shown by others that de novo synthesis of HbF is enhanced by erythropoietin when human erythroid stem cells from adults with no HbF are grown in clonal cultures. To determine whether the reported conditions of the increased erythropoietin in fetus of the diabetic mother can effect the proportion of HbA and HbF synthesis, studies were carried out on cord blood obtained from term newborn infants of insulin dependant diabetic mothers. Cord blood samples from infants of diabetic mothers ranging from 36-38 weeks of gestation, were incubated in an amino acid mixture containing {^{14}C} leucine followed by column chromatography on DEAE Sephadex which separated the radioactive HbA and HbF. Globin chain separations were carried out on some samples using carboxylmethylcellulose chromatography in order to determine if the HbF separated was contaminated by a significant amount of Hblc. The data obtained to date showed that these newborns are synthesizing significantly more HbF than would be expected for their period of human development (n=6, $\bar{x}$ = 82.0 ± 5.5% vs 67.5 ± 9.9%). It is thus conceivable that the levels of erythropoietin plus other unknown factors in the fetus of the diabetic mother stimulate erythroid precursor cells than contain HbF.

180 THE POSTNATAL FETAL AND ADULT HEMOGLOBIN SYNTHESIS IN PRETERM INFANTS WHOSE BIRTH WEIGHT WAS LESS THAN 1000g. Harry Bard and Janie Prosmanne. University of Montreal, St. Justine's Hospital, Department of Pediatrics, Montreal, Quebec, Canada.

To determine if environmental factors could effect the switchover from fetal hemoglobin (HbF) to adult hemoglobin (HbA) synthesis, studies were carried out on blood samples from 8 infants born at less than 1000g, when they had reached their postconceptional age corresponding to term. All of these infants required prolonged intensive care, multiple blood transfusions. Several were ventilated mechanically for 60 days and 2 infants had bronchopulmonary dysplasia at the time of the study. The blood samples were incubated in an amino acid mixture containing {^{14}C} leucine followed by column chromatography on DEAE Sephadex for separation of radioactive HbA and HbF. In spite of the extreme prematurity and poor growth of these sick infants, the proportional synthesis of HbF and HbA, as determined by the incorporation of {^{14}C} leucine during the red cell incubations, was characteristic of the period of human development from which the red cells were obtained.

181 NUTRIENT AND ENERGY COMPOSITION OF HUMAN MILK FROM MOTHERS DELIVERING PRETERM INFANTS (PT) AND MOTHERS DELIVERING TERM INFANTS (FT): IS THERE A DIFFERENCE? Eileen D. Brewer, Richard Caprioli, and Eugene W. Adcock. Univ. of Texas Med. Sch. at Houston, Dept. of Pediatrics and Analytical Chem. Cnt., Houston, Texas.

Recent studies of PT milk and FT milk have suggested nutrient differences during the first month of lactation. Nutritional appropriateness of PT milk remains controversial because of inconsistencies among the results of the various investigations. We compared nutrient and energy composition of milk from 12 mothers delivering PT and 11 mothers delivering FT, each studied three times during the first six weeks of lactation, and found no consistent differences. An Egnell breast pump was used to empty completely the breast for each morning sample. Total lipid concentration, fatty acid composition, total calorie concentration and total protein to energy ration did not differ significantly between the two groups at any time interval. The values for total nitrogen and lactose concentrations differed as follows:

		2-5 days	6-16 days	21-38 days
Total N (mg/dl)	PT	370±31	302±27	252±19
(*PT v FT, $p < 0.01$)	FT	785±160*	298±23	263±21
Lactose (g/dl)	PT	5.42±.27	5.47±0.30	6.25±0.21
(**PT v FT, $p < 0.05$)	FT	4.53±0.51	6.40±0.22**	6.64±0.34

The differences noted were not correlated with sample volume. We conclude that although our values agree closely with values for nutrients and energy reported by others, we could find no clear difference or biologic advantage for PT milk. The wide ranges of values make it unlikely that consistent differences exist between PT and FT milks.

182 BODY WEIGHT, STATIC AND DYNAMIC SKINFOLD THICKNESS IN SMALL PREMATURE INFANTS DURING FIRST MONTH OF LIFE. Sergio Bustamante, Patricia Jacobs and John Gaines (Spon. by Otakar Koldovský). University of Arizona, Department of Pediatrics, Tucson, Arizona.

The growth of prematurely born infants is different from the growth of fetuses of the same age remaining in utero. This is in part due to changes in body composition that occur after birth. We obtained data in two anthropometric studies that included 180 premature infants of 750 to 1750g weight at birth and analyzed the relationships between weight, static skinfold thickness (SSFT) and dynamic skinfold thickness (ΔSFT) (the percentage of change in skinfold thickness between 15 and 60 seconds after application of the Harpenden caliper). The table shows that the SSFT increases steadily after birth inspite of a significant decrease in weight and ΔSFT.

Age	2 days	1 wk	2 wk	3 wk	4 wk
Weight (g)	1344(261)*	1251(247)	1360(283)	1510(350)	1622(347)
SSFT (mm)	2.06(.41)	2.20(.49)	2.46(.61)	2.75(.66)	2.93(.73)
ΔSFT (%)	15.35(3.6)	10.17(3.1)	8.52(2.8)	8.24(2.4)	8.22(1.9)

*mean (SD)

Serial correlations of measures obtained at each period indicate that weight and SSFT have a good correlation to same measures in subsequent weeks ($p<.01$). ΔSFT, however, showed only a weak correlation ($p=.05$). The ΔSFT follows the general pattern of known changes in total body water but it is not accurate enough to determine changes in individual infants; further studies are thus needed to find a practical method to evaluate changes in total body water and body composition in premature infants.

183 THE LYMPHOCYTE AS A BIOPSY TISSUE TO DIAGNOSE MAGNESIUM (Mg) DEFICIENCY. Joan L. Caddell, Curtis Tinsley, and Evelyn Kanter. (Spon. by Thomas Aceto, Jr.), St. Louis U. Sch. Med., Dept. Pediatr./Adol. Med., St. Louis, MO and NICHD, Bethesda, MD.

The lymphocyte has been suggested as a biopsy tissue for assessing the cation status of patients, but we could not find a study to show whether or not the lymphocyte Mg decreases in Mg deficiency. Male 45±0.7 g weanling Sprague-Dawley rats were fed a purified diet containing 150 mg of added Mg/100 g (150-Mg) or no added Mg (0-Mg) for 6 d. We removed plasma from 5 ml heparinized pooled blood, replaced it with phosphate buffered saline, and isolated lymphocytes using Histopaque^{R}-1077 (Sigma Co.). Plasma, femur, and lymphocytes (97%) in suspension were analyzed for Mg using an atomic absorption spectrophotometer. (We noted a rapid change in the lymphocyte count of 0-Mg but not 150-Mg rat blood in a preliminary study).

TISSUE STUDIED	150-Mg		0-Mg		P VALUE
Plasma Mg (mg/dl)	2.11 ±0.07(8)*		0.49±0.01	(10)	0.001**
Bone Mg (mg/kg dry)	3,639±54.7(15)		1,449±19.5	(21)	0.001
Lymphs isolated/mm^3	4,162±329 (8)		12,612 ±2,004	(10)	0.005
Lymph. Mg (ug/10^6)	109.3±12.2(8)		62.02 ±3.82	(10)	0.005

* Mean ± SEM (Number in sample); ** Two-tailed Student's t test

We conclude that the lymphocyte does reflect acute Mg deficiency in the weanling rat. Because a lymphocytosis develops in Mg-deficient rats, values were expressed per 10^6 lymphocytes; it appears to be preferable to study a homogeneous cell population rather than a mixed leukocyte population. (Supported by the Life Seekers and the Cardinal Glennon Memorial Hospital Research Fund).

184 METABOLISM OF THE FETAL LAMB GROWTH RETARDED BY MATERNAL MALNUTRITION. Valerie E. Charlton and Michael J. Johengen, University of California at San Francisco, Department of Pediatrics, San Francisco.

The response of the fetus to inadequate nutrition is unclear. We studied umbilical uptake in fetuses of malnourished ewes.

Five ewes with singleton gestations,117±1 SE days,had catheters placed in the maternal artery,fetal femoral artery,femoral vein and umbilical vein. After five days of recovery and ad lib eating, 2 baseline measurements were made of umbilical blood flow,using labelled microspheres,and of umbilical uptake of glucose,lactate and oxygen. The ewes were then placed on a diet of less than 50% of their protein and calorie needs. The diet was continued until delivery. Maternal weight was stable and did not show the normal increase.Umbilical flow and nutrient uptake were measured weekly. The lambs were born small at 143±2 days;weights were 2644±131 gm and C-R lengths 40.9±1.5 cm.Large brain to body ratios,a sign of growth retardation,were present, 1.9±0.1%.Between the baseline period and week of delivery,fetal and maternal glucose levels fell, 22.3±0.8 to 15.1±1.5($p<.025$)and 54.1±2.3 to 45.5±2.3($p<.1$)mg/dl, respectively. Umbilical blood flow increased slightly,486±75 to 582±118 ml/min(NS).There were no real changes in umbilical uptakes ofglucose(12.1±4.1 vs 14.7±2.1 mg/dl),lactate(3.9±1.2 vs 3.5±1.3 mg/dl) or oxygen(16.1±1.1 vs 16.9±1.7 ml/min).These findings contrast sharply with the large increasesin umbilical flow and glucose,lactate and oxygen uptakes reported for normal,well nourished fetuses, over the same period of gestation.

The fetus copes with limited nutrient availability by halting its normal increase in umbilical blood flow and nutrient uptake.

● **185** METABOLIC CONSEQUENCES OF INTRAUTERINE GROWTH RETARDATION. Philippe Chessex,Brian Reichman,Gaston Verellen, Guy Putet,John Smith,Tibor Heim,Paul Swyer. Dept Paed & Med Eng, U of Toronto, Res Inst, Hosp for Sick Children Toronto.

By the combination of energy & macronutrient balances, continuous open-circuit indirect calorimetry & anthropometry we have compared the metabolizable energy intake(MEI), energy expenditure(EE) storage of energy & macronutrients & growth of normally grown(AGA) with those of growth retarded(SGA)very low birthweight infants.22 studies in 13 AGA infants(M±SE: Gest Age 29.3±0.4wk; birthwt 1.15 ±0.04kg; study age 21±2d; study wt 1.27±0.06kg)& 14 studies in 6 SGA infants(Gest Age 33.1±0.3wks; birthwt 1.12±0.03kg; study age 26±3d; study wt 1.55±0.05kg)were performed. Results of energy balances(M±SE; kcal/kg.d):

	Intake	Losses	MEI	EE	Storage
AGA	148.6 ± 3.8	18.2±1.5	130.4 ± 3.5	62.6 ± 0.8	67.8 ± 3.0
SGA	155.8 ± 2.2	30.0±2.8	125.7 ± 3.5	67.4 ± 1.3	58.2 ± 3.7
P	ns	< 0.001	ns	< 0.005	< 0.05

The SGA infants had decreased absorption of fat & protein & hence increased energy loss in excreta. The significant hypermetabolism of SGA infants(by 4.8kcal/kg.d)was associated with increased fat oxidation. Despite lower energy storage, SGA infants were gaining wt(19.4±0.9g/kg.d), length(1.25±0.14cm/wk)& head circ(1.16±0.08cm /wk)at higher rates than the AGA group(wt 16.8±1; length 1.02±0.1; head circ 0.94±0.08). The energy storage/g of wt gain was lower in the SGA group(3.0±0.14 vs 4.26±0.26kcal/g wt gain; $p < 0.001$)reflecting higher water, lower fat(22±2% vs 33±2.5%; $p < 0.001$)& lower protein contents(8±0.6% vs 12.5±1; $p < 0.001$) of wt gain in the SGA group.

● **186** CHARACTERIZATION OF BETA ADRENERGIC RECEPTORS IN FETAL RABBIT BROWN ADIPOCYTES. Paula J. Chou, Anita L. Reviczky, and Alan H. Klein. UCLA School of Medicine, Harbor-UCLA Medical Center, Department of Pediatrics, Torrance, CA

During a cold stress, brown adipose tissue (BAT) respiration is increased in response to neurosympathetic stimulation. [^{3}H] dihydroalprenolol, a potent beta adrenergic antagonist, was used to identify and characterize beta adrenergic binding sites on fetal rabbit brown adipocyte membrane preparations. 11 litters of 31 day gestation rabbit fetuses were obtained by hysterotomy. After decapitation, BAT was removed from the paracervical and interscapular regions. Tissue from fetuses in 1-2 litters was pooled for membrane preparation. Adipocytes were isolated by collagenase digestion, then homogenized and fractionated to yield the plasma membrane fractions. Binding of [^{3}H] dihydroalprenolol was rapid, reaching saturable equilibrium within 10 minutes. Binding was linear between 70 and 280 mcg membrane protein per tube. Scatchard analyses with high degree of linearity ($r=.954$) indicate that DHA binds to a single class of receptors. The dissociation constant and maximal binding (mean ± SEM) were 1.71±0.21 nM and 119±14 fmole/mg protein. β adrenergic agonists competed for DHA binding sites with potency characteristic of β_1 adrenergic receptors: (-)isoproterenol > (-)norepinephrine ≈ (-)epinephrine. Binding was stereospecific, (-)propranolol inhibition being 100 fold more potent than (+)propranolol. Conclusion: Brown adipocytes from term fetal rabbits demonstrate high affinity, low capacity, readily saturable, stereoselective β_1 catecholamine receptors.

● **187** HEPARIN INHIBITS THE PROLIFERATION OF FETAL PULMONARY ARTERY SMOOTH MUSCLE CELLS IN VITRO. John D. Coulson and Merton R. Bernfield, Stanford University, Dept. of Pediatrics, Stanford, California

In normal development, the relative mass of small pulmonary artery smooth muscle cells (PA-SMC) declines sharply after birth (Naeye, Arch. Pathol. 71:121, 1961). In syndromes such as persistance of the fetal circulation this decline does not occur (Murphy, et al. J. Peds. 98:962, 1981) and PA-SMC proliferation seems to continue. Because heparin, or the heparin-like molecules secreted by endothelial cells, inhibits the induced growth of adult systemic vascular SMC in vivo and in vitro (Castellot, et al., J. Cell Biol. 90:372, 1981), we have studied whether heparin also inhibits the proliferation of fetal PA-SMC. Primary cultures of calf aorta, and calf and fetal calf PA-SMC were arrested in G_0 by placing them in medium containing 0.2% calf serum. After 72 hrs, medium was changed to include 20% fetal calf serum with or without 30 µg/ml heparin. Cells were counted at 24-hr intervals. The growth of calf PA-SMC was inhibited to the same extent as reported for aortic SMC (Castellot, op cit). Heparin similarly inhibited the growth of fetal calf PA-SMC. This inhibition was not due to toxicity as it was reversed by removing heparin 48 hrs after stimulation. Thus, fetal PA-SMC can be stimulated to proliferate and this effect can be reversibly inhibited by heparin. Heparin-like molecules, ubiquitous on cell surfaces, may be involved in regulating pulmonary arterial development. Supported by the United States Navy and NIH Grant HD-06763.

● **188** PERSISTENT GLUCOSE PRODUCTION (Ra) DURING CONSTANT GLUCOSE INFUSION IN THE HUMAN NEWBORN. Richard M. Cowett, William Oh, and Robert Schwartz. Brown Univ., Women & Infants Hospital, Dept. of Pediatrics, Providence, RI.

Diminished hepatic glucose production is the adult response to exogenous glucose. To document the degree of suppression and characterize the maturation of neonatal glucose control, Ra was measured in infants previously infused with glucose. Twenty-three well preterm AGA infants (PT) [1999±67 gm BW (M±SEM); 34.3 ±0.3 wks GA] were studied at 37.5±5.3 hrs of age, and 11 well term AGA infants (T) [3304±108 gm BW; 38.9±0.4 wks GA] at 35.8± 4.7 hrs. Nineteen continued to receive glucose infusion (Glu. Inf.). After 3 hr NPO, plasma glucose and insulin, and Ra were determined following a prime constant infusion of 4 µg/kg/min D-[U-^{13}C] glucose during the turnover period. Ra was compared to data obtained in 10 normal adults (A).

	SALINE TURNOVER PERIOD				GLUCOSE TURNOVER PERIOD				
		Pl Glu	Pl Ins	Ra		Glu.Inf.	Pl Glu	Pl Ins	Ra
	N	mg/dl	µU/ml	mg/kg/min	N	mg/kg/min	mg/dl	µU/ml	mg/kg/min
PT	10	64±5	11±1	3.0(1.8-4.1)	13	5.6±0.3	97±5§	19±3*	1.4(0-4.4)
T	5	75±8	15±3	3.4(2.8-4.7)	6	5.7±0.3	88±4	31±8	0.4(0-2.6)
A	6	87±1	14±1	2.0(1.5-2.4)	4	3.1±0.2	107±8†	29±4ʃ	0.1(0-0.3)

Unpaired T - *p <.05 †p <.02 ʃp <.01 §p <.001 (range)

The PT and A had elevation in plasma glucose and insulin during glucose infusion. Eight of 13 PT, 5/6 T and all A suppressed Ra during glucose infusion. The preterm neonate was less efficient in control of glucose homeostasis, which may explain the occurrence of hyperglycemia in some low birth weight infants receiving intravenous glucose.

● **189** EPIDERMAL GROWTH FACTOR (EGF) RECEPTORS IN NEWBORN RABBIT LUNG. Uday P. Devaskar, (Spons. by Dr. William J. Keenan). Division of Neonatal Perinatal Medicine, Dept. of Pediatrics, St. Louis University School of Medicine, St. Louis, MO 63104.

Several endogenous compounds influence fetal pulmonary maturation. EGF, when administered in vivo, has been shown to accelerate pulmonary differentiation in fetal rabbit and sheep (Peds. Res. 13:104-108, 1979). EGF binding was investigated in lung plasma membranes (LPM) of term newborn (< 12 hours of age) New Zealand White Rabbit lungs. For each assay, lungs from pups within each litter were pooled. LPM were prepared by differential centrifugation. Specific binding of 125 I-EGF (NEN, sp. activity 150-180 µ Ci/µg) was assessed by competitive displacement in the presence of increasing concentration of unlabeled EGF. The number of receptor sites/mg LPM protein and Kd were derived by Scatchard analysis. In all experiments (pooled NB=5) rabbit LPM specifically bound 125 I-EGF; the specific binding was saturable, time (60 minutes), and temp. dependent (37°C). Optimal pH=7.45. All Scatchard plots indicated one order of binding sites. The number of receptor sites/mg of LPM protein and Kd were 276.88 ± 19.18 X 10^{10} (X ± S.E.M.) and 0.27 ± 0.019 X 10^{-10}M respectively. We conclude that newborn rabbit LPM possess high affinity receptors for EGF and propose a direct rather than an indirect role of EGF in neonatal pulmonary maturation.

190 DIFFERENTIATIVE DEVELOPMENT OF THE ENTEROCYTE IN THE PRE- AND POSTWEANED RAT INTESTINE. Arthur D'Harlingue, Linda K. Kwong, Aiko Tsujimoto, and Kenneth K. Tsuboi (Spon. by Philip Sunshine). Dept. of Ped., Stanford Univ. Sch. of Med., Stanford, CA.

The developmental changes along the crypt to villus tip of intestinal enterocytes have been studied previously, using protein as a reference in determining specific activity of cellular constituents. Since the enterocyte accumulates large amounts of protein, the measured changes expressed on a cellular basis (i.e. DNA) should provide a better picture of developmental processes occurring during migration. Serial fractions of jejunal and ileal enterocytes were collected by a modified Weiser technique from preweaned and postweaned Wistar rats. The percentage of cells in each fraction was determined by DNA analysis and compared with estimates based on protein. All animals undergo a 3-6 fold linear increase in the ratio of protein to DNA from crypt to tip. The disaccharidases increases in activity from crypt to tip with little decline in specific activity at the tip when referenced to DNA; whereas there is usually a marked decline when referenced to protein. In preweaned animals the total cellular RNA remains generally constant from crypt to tip. Postweaned animals, however, demonstrate continuous accumulation of RNA. Protein synthesis as measured by ^{3}H-leucine incorporation declines from crypt to tip in preweaned animals, but initially rises and then declines in the adult. Membrane bound alkaline phosphatase accumulates along the crypt to tip gradient without loss of specific activity. Measurement of DNA provides a constant reference point for assessing functional changes accompanying differentiative development of the enterocyte.

● **191** AORTIC FLOW MEASUREMENTS IN THE HUMAN FETUS BY NONINVASIVE, PULSED DOPPLER TECHNIQUE. Marlowe W. Eldridge, P. Reilly, William Berman, Jr. Lovelace Medical Center, and University of New Mexico School of Medicine, UNM Affiliated Hospitals, Dept. of Pediatrics, Albuquerque, N.M.

We developed a method of quantitating abdominal aortic blood flow noninvasively in the human fetus. A 5 MHz, real-time, 2-dimensional pulsed Doppler duplex scanner (DS) was used both to image the fetal aorta and record a Doppler shifted frequency from the abdominal aortic blood flow stream. Measurements were made serially in 16 uncomplicated pregnancies, ranging in gestational age (GA) from 14 weeks to term. Each fetus was studied 4 to 8 times, at monthly intervals. GA and fetal weight (FW) were estimated from biparietal and transverse abdominal diameters. Aortic velocity (V) was calculated from the Doppler shifted frequency; the Doppler incidence angle and the aortic diameter (d) were measured directly from the DS image. Both $\bar{V}$ and d increased with GA. Abdominal aortic blood flow ($\dot{Q}_A$ ml/min) was computed as $\bar{V}$ (cm/sec) x π $d^2/4$ (cm^2) x 60 (sec/min). $\dot{Q}_A$ increased with FW and GA from 175 ml/min at 26 weeks to 516 ml/min at term. The mean (±SD) $\dot{Q}_A$/FW was 185 ± 38 ml/kg/min and showed little change with GA. Currently, assessment of fetal well-being relies on fetal heart rate monitoring and analysis of blood samples from the fetal scalp. Several studies suggest umbilical blood flow patterns may reflect changes in fetal status more accurately. Because the vast majority of fetal abdominal aortic flow is destined for the placenta, this noninvasive approach to umbilical blood flow determination may prove a simple and useful adjunct in the serial assessment of fetal growth and development.

192 FOLLOW-UP OBSERVATIONS ON A BOY WHO HAD IATROGENIC CUSHING'S DISEASE IN INFANCY. Lytt I. Gardner. SUNY Upstate Medical Center, Dept. of Pediatrics Syracuse, New York.

This boy was misdiagnosed as having sodium-losing virilizing adrenal hyperplasia, and was treated from the newborn period until age 4 years with mineralocorticoids plus massive doses of corticosteroids. Growth almost ceased between ages 1 and 4 years. Bilateral glaucoma developed. Studies revealed poor pituitary ACTH reserve. Bone x-rays showed striking abnormalities, with a bone-age of 1 9/12 years (J. Pediat. 83:69, 1973). When steroid therapy was withdrawn there was catch-up growth. After the latter ceased, growth velocity fell to 10th-25th percentile (Tanner) in years 6 to 12. Normal puberty occurred at age 14-15 years, with a growth spurt velocity of 75th percentile. Bone x-rays no longer showed the dense epiphyseal zone of spicules of calcified cartilaginous matrix seen in infancy, and bone age was normal. The only residual x-ray finding was minimal lateral bowing of the tibiae. Final achieved height was 153.6 cm (5 ft. 1/2 in). Glaucoma had resulted in blindness in the right eye and very limited vision in the left.

The corticoid-induced changes in the cartilage of growing bones may have been primary to the severe growth failure observed during the first 4 years of life. In spite of this metabolic insult to the mechanisms of growth, this case demonstrates that they can recover enough during childhood to permit a normal adolescent growth spurt, even though ultimate height may have been compromised by early growth failure.

193 CELL LINEAGE ANALYSES OF PREIMPLANTATION MOUSE EMBRYOS AFTER BLASTOMERE INJECTIONS WITH HORSERADISH PEROXIDASE. John Gearhart, Rose M. Shaffer, James M. Musser, Mary L. Oster-Granite. (Spon. by John W. Littlefield) Developmental Genetics Laboratory, Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore.

Single blastomeres of 4-, 8-, and 16-cell embryos (with zonae) were pressure injected with horseradish peroxidase (HRP). The embryos were cultured to blastocysts, fixed, stained for peroxidase activity, serially sectioned, and the number and distribution of cells containing HRP determined. The presence of HRP did not inhibit cell divisions and although the distribution of HRP-labelled cells varied among embryos, labelled cells remained contiguous. The allocation of cells to the inner cell mass(ICM) or trophectoderm(TE) became evident at the 16-cell stage. Individual cells of the 4-cell embryos contributed progeny to the ICM and TE; approximately half of the blastomeres of the 8-cell embryos contributed progeny to both the ICM and TE while progeny from the other half produced only TE. Single "outside" cells of the 16-cell embryos occasionally contributed cells to the ICM while none of the "inside" cells at this stage produced TE. Embryos treated with pronase or acid Tyrode's to remove the zonae resulted in the rapid spread of HRP among blastomeres. Our results demonstrate that HRP can be used effectively as a tracer for cell lineage studies in preimplantation mouse embryos; that cells of a common lineage remain contiguous during this period; and that the allocation of blastomeres to ICM or TE in intact whole embryos occurs progressively to the 16-cell stage at which time it is almost complete. (Support: NICHD 16303, MOD 1-723)

194 ALTERATIONS IN PLACENTAL GLYCOGEN METABOLISM IN STREPTOZOTOCIN DIABETIC (DM) RATS. I.H. Gewolb, C. Barrett, and J.B. Warshaw, Dept. of Peds., Yale Univ. Sch. of Med., New Haven, CT.

Placental glycogen metabolism was investigated in rat pregnancy complicated by streptozotocin induced DM. Placental glycogen concentration (ug/mg protein) rose until day 16 and then declined in both control (C) and DM animals. DM placentas had significantly increased glycogen concentration from day 16-22.

GLY	DAY	14	16	18	19	20	21	22
	C	48±7	87±10	33±8	14±6	8±2	1.3±.7	2±.4
	DM	70±16	155±18*	126±17**	92±8**	67±6**	46±10**	29±5**

The activity of the glycogenolytic enzyme phosphorylase A (nmol/min/mg protein) was significantly diminished in the DM placentas late in gestation. Glycogen synthase A activity was paradoxically lower in the DM group.

PHOS-A	DAY	14	16	18	19	20	21	22
	C	.55±.05	.15±.04	.08±.05	.13±.06	.11±.03	.14±.03	.06±.03
	DM	.68±.05	.13±.02	.16±.09	0*	.01±.01**	.02±.01**	.09±.03

Marked placentomegaly was noted in the DM placentas after day 19. DNA content plateaued after day 19 in the DM group, one day later than the controls.

Thus, DM results in increased size and a prolonged period of growth in the placenta. The increase in glycogen may be the result of persistent hyperglycemia, and may be mediated by the decrease in phosphorylase A activity.

*p<.05 **p<.01

195 PULMONARY NUCLEAR T_3-RECEPTORS: BINDING CAPACITY AND OCCUPANCY CHANGE DURING FETAL RABBIT DEVELOPMENT. Linda W. Gonzales and Philip L. Ballard. Dept. of Peds. and Cardiovas. Res. Instit., Univ. Calif., San Francisco, CA.

The effects of thyroid hormone on fetal lung maturation are likely mediated by nuclear T_3-receptors. Therefore we studied both binding capacity (BC) and occupancy of receptors by endogenous thyroid hormone during development. Nuclei were incubated under optimal conditions (fetal, 90 min at 37°C; adult 4 h at 25°C) with various concentrations of $[^{125}I]T_3$ in the presence or absence of unlabeled T_3. BC rose 44% between 21 days (0.267 ± 0.021 fmol/μg DNA) and 28 days (0.384 ± 0.011 fmol/μg DNA) of gestation, then decreased 30% by term (0.273 ± 0.018 fmol/μg DNA), before declining to the adult level (0.238 ± 0.013 fmol/μg DNA). Receptor release, relative binding potencies of T_3-analogs and K_d (fetal, 84 ± 12 pM; adult, 67 ± 6 pM) did not change. Occupancy of fetal receptors was estimated with an in vitro assay based on (1) the lower equilibrium binding of T_3 to nuclei at 2°C than at 37°C and (2) the slower dissociation rate of the T_3-receptor complex at 2°C ($t_{½}$ = 24 h) than at 37°C ($t_{½}$ = 30 min, n = 4). We validated the assay by altering the nuclear T_3 content both in vivo and in vitro, and by RIA. Receptor occupancy increased from 11% of BC at 21 days to 23% at 28 to 31-days of gestation. Based on the changes in BC and occupancy, the average total number of occupied receptors increased threefold between 21 days (110 sites/cell) and 28 days (330 sites/cell) of gestation. We conclude that both BC and occupancy increase in late fetal life, supporting a direct role of endogenous thyroid hormones in the maturing of fetal lung.

196 DEVELOPMENTAL CHANGES IN OXIDATIVE PHOSPHORYLATION IN GUINEA PIG LIVER MITOCHONDRIA. Daniel E. Hale, Barbara E. Corkey, Charles A. Stanley and John R. Williamson. University of Pennsylvania School of Medicine, Depts. of Peds. and Biochem/Biophys., Philadelphia, PA.

Although developmental changes in the activities of a number of mitochondrial enzymes have been observed, the effects of these changes on oxidative phosphorylation are unknown. Rates of O_2 consumption and adenine nucleotide concentration were determined in mitochondria isolated from newborn and adult guinea pig liver. Mitochondria from both groups of animals were similarly well coupled. Rates of O_2 consumption in the presence of ADP and a variety of substrates (state 3 respiration) were (natoms/min/mg protein) M± SEM):

	Newborn (4)	Adult (5)
glutamate/malate (5mM/1.25mM)	24.8 ± 2.1	51.9 ± 7.4
succinate (5mM)	52.4 ± 8.2	77.6 ± 8.2
ketoglutarate (1mM)	21.7 ± 5.0	42.3 ± 6.1
pyruvate/malate (1mM/1.25mM)	23.8 ± 3.7	33.5 ± 6.1
palmityl carnitine (40uM)	25.5 ± 1.9	35.7 ± 3.3

Oxygen consumption from all substrates except succinate were similar in the newborn period. Intramitochondrial ATP content (0.89±.04 nM/mg protein) and ATP:ADP (0.24) were lower in the newborn than in adult (6.86 ± .44 nM/mg; 1.89). These data suggest that neonatal oxidative phosphorylation is sluggish, with a low rate of site I (NADH linked) oxidation. It is possible that the differences in ATP and ATP/ADP ratio between the newborn and adult guinea pig are important in controlling developmental changes, since the phosphorylation state of adenine nucleotides are known to play an important regulatory role in mitochondrial metabolism.

197 FETAL GLUCOSE UPTAKE, UTILIZATION, AND PRODUCTION AS A FUNCTION OF GLUCOSE CONCENTRATION. William W. Hay, Jr., John W. Sparks, Randall B. Wilkening, Giacomo Meschia, Frederick C. Battaglia, University of Colorado School of Medicine, University Hospitals, Division of Perinatal Medicine, Departments of Pediatrics, Ob-Gyn and Physiology, Denver.

Under normal physiologic conditions the fetus uses mainly exogenous glucose. However, it may resort to endogenous glucose production (PR) if the transfer of gucose from placenta to fetus (TR) decreases. To test this hypothesis in chronically catheterized fetal lambs we measured simultaneously TR and the fetal glucose utilization rate (UR), and calculated PR (PR=UR-TR). UR was determined simultaneously by two different methods by comparing fetal glucose specific radioacitivty with net fetal tracer uptake from (1) a fetal intravenous infusion of ^{14}C-U-glucose and (2) by a transplacental fetal infusion during a maternal IV infusion of ^{3}H-6-glucose. The mean UR ($mg \cdot min^{-1} \cdot kg^{-1}$ ± SEM) from the two infusions (3.39 ± 0.27 fetal inf.; 3.04 ± 0.32 maternal inf.) were similar, validating the tracer methods for calculating UR. TR was measured by the Fick principle. Both UR and TR were positively correlated with maternal plasma glucose (r=0.92 and 0.82, respectively) and UR with fetal plasma glucose (r=0.82). At TR <3.0 $mg \cdot min^{-1} \cdot kg^{-1}$ corresponding to plasma $(glucose)_{maternal}$ <40.0 mg/dl and plasma $(glucose)_{fetal}$ < 15.0 mg/dl, UR was significantly greater than TR, documenting a mean endogenous glucose production of 1.22 ± 0.27 $mg \cdot min^{-1} \cdot kg^{-1}$. We conclude that hypoglycemia and the resulting low TR can induce fetal glucose production; this PR is small and cannot prevent a decrease in the rate of fetal glucose utilization.

198 EARLY DEVELOPMENT OF INSULIN RECEPTORS IN LIVER AND BRAIN OF CHICK EMBRYO. S. Anne Hendricks and Jesse Roth. (Spon. by Michael Frank) Diabetes Branch, NIADDK, NIH, Bethesda.

The first indications of both insulin secretion and sensitivity to insulin in chick embryo appear at day 5 of incubation; this study showed that insulin receptors are present in embryo heads as well as bodies by day 4. In addition, crude membrane preparations of embryonic brain and liver from day 8 to 18 of incubation showed sequential increases in insulin binding; levels seen in the last week of development were equivalent to those seen in similar preparations of adult rat tissues. However, binding over this period (expressed below as percent of the binding to day 18 brain) increased according to distinct developmental patterns in the two tissues:

TISSUE	DAY OF INCUBATION 4	8	14	16	18	TISSUE
-HEADS	33%	28%	23%	51%	100%	BRAIN
-BODIES	31%	12%	49%	61%	74%	LIVER

In liver, binding was low at day 8 and increased markedly during mid-development (p<0.005, day 8 vs 14), while late rises were less impressive. However, in brain substantial binding was present quite early, levels remained stable through the second week, and a marked rise was seen late in development (p<0.0025, day 14 vs 18). Interestingly, brain tissue bound higher levels of insulin at day 18 than did liver, a known target tissue for insulin.

SUMMARY: Insulin receptors are present in both bodies and heads of chick embryo before demonstrable insulin secretion occurs. Developmental increases in insulin binding occur via tissue specific patterns, suggesting complex mechanisms of control.

199 IMPAIRED BRAIN AND BODY GROWTH FOLLOWING SHORT-TERM ETHANOL EXPOSURE IN NEONATAL RAT PUPS. Donald E. Hill, Thomas J. Sziszak, Linda G. Sziszak, J. Mark Boughter, Louis W. Chang, William Slikker, Jr. Dept. Pediatrics and Pathology, Univ. of Arkansas for Medical Sciences and National Center for Toxicol. Res., Jefferson and Little Rock, Arkansas.

Neonatal rat pups were raised artifically ("pup-in-cup") and exposed to ethanol from postnatal day 4-8 inclusive to determine the effect of ethanol on the developing neonatal brain. The experiment was replicated four times with 4 cup raised controls (CRC) and 6 ethanol exposed pups (EE). Ten pups served as mother raised controls (MRC). The CRC pups were fed a diet isocaloric to the EE pups and body weight as well as nutrient intake was recorded daily. Ethanol dose was 3%, 4%, 6% and 5% v/v respectively for day 4-8. Both groups were returned to the dam on day 9-18. Blood ethanol concentrations varied from 150-250mg%.

GROUP	BODY WT.(N)		BRAIN WT.		CEREBELLUM WT.
MRC	35.7±3.6(16)	>NS	1.38±0.04	>p<0.001	0.182±0.018
CRC	34.5±2.6(16)	>p<0.001	1.27±0.04	>p<0.001	0.176±0.010 >NS
EE	30.4±2.6(16)		1.16±0.06		0.139±0.016 >p<0.001

Light microscopy of the EE cerebellum at day 18 revealed delayed granular cell migration, thicker external granular layer, thinning of the cerebellar cortex, disorganization of migrating neurons, and failure to develop axonal connections when compared to the CRC or MRC groups. We conclude that short term exposure to ethanol has a profound effect on somatic growth and brain development. These data confirm and extend the findings of Diaz and Samson. (Science 208:751, 1980)

200 DIFFERENTIAL DEVELOPMENT OF THE CAT'S UPPER INTESTINAL TRACT. Craig Hillemeier, Joyce Gryboski, Richard McCallum and Peter Biancani, Yale Univ. Sch. Med., Dept. of Pediatrics, New Haven, CT

The lower esophageal sphincter (LES) and pylorus of various aged kittens were identified and 1.75 mm wide rings were cut transversely and studied in vitro. Force length curves were obtained in a muscle bath with standard, potassium-rich and calcium free EDTA tyrode to determine basal, total and passive forces respectively. Active force was obtained as the difference between the total and passive force.

	LES area		Pyloric area					
	MAF	t	MAF in gm			t in mm		
Age	gm	mm	A	P	D	A	P	D
3 day	2.8	0.27						
1 week	3.5	0.29	4.5	3.6	3.3	.47	.33	.34
3 weeks	5.3	0.34						
6 weeks	8.3	0.47	7.2	6.3	6.0	.63	.40	.40
Adult	12.2	1.80	7.3	7.4	6.4			

t - thickness circular smooth muscle, MAF - max. active force, A - antrum, P - pylorus, D - duodenum.

Forces generated in vitro at the LES and pyloric region increase with age. Unlike the adult, the MAF of the kitten is greater in the antrum than pylorus due to lack of muscle thickening. The MAF in the antrum is equivalent to the adult, slightly less in the pylorus, and markedly less in the LES of the 6 week old kitten. Differential rates of development throughout the upper GI tract may affect coordination of intestinal motility and play an important role in the pathogenesis of reflux during infancy.

● **201** EFFECT OF TRIIODOTHYRONINE (T3) ON EPIDERMAL GROWTH FACTOR (EGF) IN NEONATAL MOUSE SKIN. SYNERGY OF T3 AND DEXAMETHASONE (DEX) IN EPIDERMAL MATURATION. Steven B. Hoath, Jayaraman Lakshmanan, Susan M. Scott, Delbert A. Fisher. UCLA School of Medicine, Harbor-UCLA Medical Center, Department of Pediatrics, Torrance, CA

EGF is a 6045 MW protein which accelerates normal epidermal maturation in newborn mice; i.e. eruption of the incisors and opening of the eyelids. Similar acceleration is seen following exogenous thyroxine (T4) administration. To relate the T4 and EGF effects we measured immunoassayable EGF in skin cytosols following daily postnatal administration of T3 to crossfostered litters of Swiss Webster mice. Additional litters received either normal saline (controls), Dex or T3 + Dex. Mice were sacrificed on the 6th postnatal day. Only mice in the T3 + Dex group (N=16) had erupted incisors. Results (mean ± SEM) and dosages are shown:

N	T3 (ng/d)	Dex (ng/d)	Body Weight (g)	Skin EGF Content (pg/mg protein)
16	--	--	3.9 ± .1	152 ± 11
16	200	--	3.7 ± .2	408 ± 57
16	1000	--	2.9 ± .2	575 ± 61
16	1000	100	3.2 ± .15	515 ± 48
16	--	100	3.2 ± .2	224 ± 17

Conclusions: 1) T3 markedly increases EGF in newborn mouse skin; 2) Dex produces a small but significant ($p<.01$) increase in skin EGF but no additive effect with T3; 3) T3 and/or Dex reduce body weight; 4) T3 + Dex markedly accelerates incisor eruption. Speculation: Epidermal maturation induced by T3 ± Dex may be mediated by local levels of EGF.

● **202** SULFHYDRYL OXIDASE (SHO) IN HUMAN MILK AND INDUCTION IN KIDNEY AND SKIN AT WEANING. Charles E. Isaacs, Charles E. Wright, Theresa A. Pascal and Gerald E. Gaull. Dept. Hum. Devel. Nutr., NYS Inst. Basic Res. Devel. Disab., Staten Island, N.Y. 10314.

SHOs are a recently-defined class of enzymes that catalyze the net synthesis of disulfide bonds using O_2 and producing H_2O_2; such bonds are essential for the structure, function and transport of proteins. Human milk SHO oxidizes the low-molecular thiols cysteine and dithiothreitol but not glutathionine; bovine milk SHO oxidizes all three. SHO activity in human milk is greater early in lactation. Other human secretions, including saliva, sweat and semen, also have SHO activity.

A survey of adult rat tissues shows SHO activity to be present in kidney and skin, but not in liver and brain. SHO activity was not present in the kidney of suckling rats until 18 days of age. Weaning occurs at 21 days, and SHO activity remained at a low level until 23 days of age at which time there was a 3-fold increase in kidney SHO above the 18 day level. SHO in rat skin was initially detected at 23 days of age. The results indicate that SHO in rat kidney and skin are induced following weaning and that this enzyme follows a developmental pattern similar to that of rat kidney ornithine aminotransferase and alkaline phosphatase. The metabolic roles of SHO in milk and other secretions, its induction at weaning and their relevance to human development and nutrition will be discussed.

203 DIFFERENCES IN LIVER FOLATE ENZYME PATTERNS IN PREMATURE AND FULL TERM INFANTS. Aida Kalnitsky, David S. Rosenblatt, and Stanley Zlotkin, McGill University-Montreal Children's Hospital Research Institute and Department of Nutrition and Food Sciences, University of Toronto.

The specific activities of four folate enzymes have been measured in livers from preterm infants (Group 1), full-term infants (Group 2), and from control subjects (Group 3). The four enzymes studied were methylenetetrahydrofolate reductase (EC 1.1.1.68), methionine synthetase (EC 2.1.1.13), methylenetetrahydrofolate dehydrogenase (EC 1.5.1.5), and glutamate formiminotransferase (EC 2.1.1.5). The specific activities for methylenetetrahydrofolate reductase were 6.62±0.51, 4.42±0.31, and 2.60±0.40 (nmoles formaldehyde/mg protein/h, $\bar{x}$±SEM) for groups 1, 2 and 3 respectively. The specific activities for the three groups for methionine synthetase were 0.99±0.11, 0.64±0.06, and 0.42±0.05 (nmoles methionine/mg protein/h, $\bar{x}$±SEM). The specific activities for the three groups for glutamate formiminotransferase were 84.1±10.7, 108.6±14.6, and 104.3±17.8 (nmoles methenyltetrahydrofolate/mg protein/min, $\bar{x}$±SEM). The specific activities for the three groups for methylenetetrahydrofolate dehydrogenase were 0.16±0.03, 0.39±0.07, and 0.92±0.16 (nmoles methenyltetrahydrofolate/mg protein/min, $\bar{x}$±SEM). Thus, during development the specific activities of methylenetetrahydrofolate reductase and methionine synthetase decreased whereas the specific activity of methylenetetrahydrofolate dehydrogenase increased and that of glutamate formiminotransferase remained constant.

● **204** INSULIN RECEPTORS IN TYPE II PNEUMOCYTES AND FIBROBLASTS FROM FETAL LUNG. Solomon A. Kaplan, Marilyn Scott and Cynthia T. Barrett, UCLA School of Medicine, Center for Health Sciences, Department of Pediatrics, Los Angeles.

Previous studies have shown that excess insulin secretion in vivo and high physiologic concentrations in vitro inhibit formation of surfactant by the fetal lung. To determine which cell is primarily responsive to insulin action type II pneumocytes and fibroblasts were grown from organotypic cultures obtained from fetal rabbits at 27 days of gestation. Cells growing in monolayers that were over 80% type II pneumocytes or fibroblasts were exposed to I-125 insulin in a buffered medium and specific binding of insulin was measured. Optimum binding conditions were established (incubation at 20°C, pH 7.4 for 1 hour). Analysis of the binding data showed Scatchard plots that were curvilinear, consistent with negative cooperativity or at least two populations of binding sites. Under optimum conditions type II cells have about 30,000 high affinity and about 230,000 low affinity sites per cell. Kd of the high affinity sites was approximately 2 nM and of the low affinity sites was approximately 150 nM. Fibroblasts had many fewer high affinity sites never exceeding 5000 per cell.

The large number of high affinity receptors in the type II pneumocytes indicates that this is the primary cell through which insulin inhibits surfactant production in infants of poorly controlled diabetic mothers.

● **205** CELL SURFACE INTERACTIONS OF NORMAL AND VARIANT H6 TERATOCARCINOMA CELLS. Sreedharan Kartha and Jeanette S. Felix, (Spon. by John W. Littlefield), Developmental Genetics Lab., Department of Pediatrics, Johns Hopkins University, School of Medicine, Baltimore.

Mouse teratocarcinoma cell cultures share many characteristics with the early mouse embryo and are a suitable model for studying aggregation and compaction during preimplantation development. H6 cells form uniform, grape-like clusters of adhering cells when rotated in medium (MEM) with 10% fetal calf serum. These aggregates are induced to compact within 1 hour when additional calcium (5mM) is supplied, resulting in a tight mass of cells with obscure cell boundaries and a smooth outer surface. Compaction can be reversed by removal of calcium and inhibited by cytoskeletal poisons and by the lectins concanavalin A and wheat germ agglutinin. This behavior is similar to compaction in the 8 cell morula. Mutants of H6 with altered aggregation or compaction will be useful for studying the molecular nature of these processes. We have isolated 3 aggregation-deficient variants which have lost the ability to form intercellular adhesions. Since cell surface glycoproteins are implicated in cell adhesions, agglutination by eight lectins was tested. Only peanut agglutinin (PNA) had a significantly reduced effect on all 3 variants compared to parental cells. Measurement of fluoresceinated-PNA bound to the cell surface confirmed this deficiency; the mean fluorescence value for parental cells was reduced to 1/3 in the variant lines, suggesting that a galactose-rich glycoprotein is defective or missing in the variants and is associated with aggregation. (Supported by NCI Grant no. 16754.)

● **206** ROLE OF SODIUM TRANSPORT DEPENDENT RESPIRATION IN THE DEVELOPMENT OF BROWN ADIPOSE TISSUE (BAT) THERMOGENESIS IN THE RABBIT. Alan H. Klein, UCLA School of Medicine, Harbor-UCLA Medical Center, Department of Pediatrics, Torrance, CA.

Basal (B) and norepinephrine (NE, 10^{-6}M) stimulated BAT respiration (QO_2) were measured ± ouabain (1mM) using cells from fetal rabbit litters at 24 (Group I, n=4) and 31 (Group II, n=4) days gestation and at 10 days postnatal age (Group III, n=4). Cell volume also was determined. Mean (±SEM) B QO_2 ($\mu l\ O_2/10^6$ cells·hr) increased from 12.9±1.6 (Group I) to 47.2±5.5 (Group II) and 89.0±6.8 (Group III). Volume increased from 4.6±0.5 picoliters (pl) (Group I) to 34.7±4.0 pl (Group III). After volume adjustment, B QO_2 in Group III > Groups I and II, Group I = Group II. Ouabain did not suppress basal respiration. NE QO_2 increased from 41.7±6.6 in Group I to 845±142 in Group II with no further increase in Group III (836±78). Ouabain suppression of NE QO_2 increased from 42.8±4.4% (Group I) to 61.9±2.9% (Group II) with no further change in Group III (69.9±1.6%). Sodium transport dependent NE QO_2 increased from 17.8±3.6 (Group I) to 533±104 (Group II) with no further increase in Group III (561±51). Non-transport dependent NE QO_2 (ouabain suppressed) increased from 24.0±4.3 (Group I) to 312±41 (Group II) with no further change in Group III (250±24). Adjustment for cell size did not change the pattern of development of NE QO_2. Conclusions: The increase in fetal B QO_2 is dependent on increased volume and not on changes in transport dependent QO_2. In contrast, maturation of NE QO_2 is independent of volume and dependent on changes in both sodium transport dependent and independent respiration.

207 DEVELOPMENT OF BROWN ADIPOSE TISSUE (BAT) THERMOGENESIS IN THE FETAL AND NEWBORN LAMB. Alan H. Klein, Anita L. Reviczky, Paula J. Chou, James F. Padbury, Calvin J. Hobel and Delbert A. Fisher, UCLA School of Medicine, Harbor-UCLA Medical Center, Department of Pediatrics, Torrance.

Basal (B), norepinephrine (NE) and dibutyryl cAMP (dBCAMP) stimulated oxygen consumption (QO_2) were measured in isolated BAT cells from fetal sheep at 121-124 days gestational age (GA) (Group I, n=4), 136-140 days GA (Group II, n=5) and 2-4 days after birth (Group III, n=4). BAT cell volume also was determined. Mean (±SEM) B QO_2 (in $\mu l\ O_2/10^6$ cells·hr) increased from 10.5±1.0 in Group I to 31.4±2.1 in Group II and 38.5±2.8 in Group III. Cell volume increased from 9.0±0.74 picoliters (pl) in Group I to 13.4±2.0 pl in Group II and 18.4±2.3 pl in Group III. B QO_2 (adjusted for cell volume) for Group II was greater than for Group I ($p<0.005$) and equal to Group III. Maximal NE (10^{-6}M) QO_2 increased from 74.4±16 in Group I to 294±47 in Group II. Maximal NE QO_2 in Group III (111±27) was < Group II and = Group I. dBCAMP stimulated QO_2 increased from 51.3±12 in Group I to 175±22 in Group II and 172±29 in Group III. Summary: 1) Basal BAT QO_2 (adjusted for changes in cell size) increases between 120 and 140 days GA but not after delivery. 2) Maximum NE QO_2 occurs at 140 days GA and decreases after delivery. 3) Post-receptor stimulated BAT QO_2 (dBCAMP) increases between 120 and 140 days GA but does not decrease after delivery. Conclusions: 1) Full maturation of BAT thermogenesis occurs prior to delivery near term in the ovine fetus. 2) In the neonatal lamb a decrease in BAT sensitivity to NE occurs at the receptor-adenyl cyclase level.

208 FASTING NEONATAL CANINE OXIDATIVE METABOLISM FOLLOWING MATERNAL STARVATION. R.Kliegman, E.Miettinen, G.Campbell, M.Patel (Spon.by A.Fanaroff). Case Western Reserve Univ., Depts. Pediatrics & Biochem., Cleveland, OH

Maternal canine starvation(MCS) produces diminished fetal(F) growth and neonatal(NEO) hypoglycemia. To investigate the effects of MCS, 11 pregnant dogs were starved for 72 h prior to term delivery while 9 controls were fasted overnight. Circulating substrates and GLU, palmitate(PAL) and alanine(AL) turnover plus AL appearance in GLU were determined as was VO_2 and RQ in pups fasted for 3,6,9 or 24 h. MCS ↓ F growth (251±7 vs 271±7 g).* MCS ↓ maternal(M) (2.3±0.4 vs 5.3±0.3mM), F (2.2±0.5 vs 4.5±0.2) and NEO GLU at 3,6 and 9 h. MCS ↑ M and F levels of ketones(K), while K was ↓ after 24 h of fasting in MCS pups. FFA was ↑ after MCS in the M (10.3±0.9 vs 3.3±0.4) and F (0.8±0.1 vs 0.3±0.1). FFA levels in MCS pups were similar to controls at 3 and 6 h but ↓ at 9 and 24 h when they became lower than control values. MCS or 24 h of NEO fasting had no effect on AL levels or turnover. GLU production was ↓ in MCS pups at 3 (21.2±1.8 vs 26.0±1.6μmol/kg/min), 6 (24.0±2.0 vs 29.5±1.8) and 9 (26.6±1.1 vs 34.7±2.8) h, AL incorporation into GLU ↑ during 24 h of fasting in both groups but was ↓ at 3,6 and 9 h after MCS. PAL turnover was unaffected by MCS between 3-9 h but ↓ in both groups at 24 h. VO_2 was unaffected by MCS and ↑ in both groups between 3 and 9 h. However, at 24 h VO_2 ↓ in both groups. Control RQ ↑ from 3-24 h (0.79±0.02-0.87±0.02). MCS RQ was ↑ only at 3 h (0.84±0.02). Conclusion: NEO canine fasting results in ↓ VO_2 due to ↓ FFA oxidation; MCS produces fasting NEO ↓ GLU due partly to ↓ GLU production, due in part to ↓ AL incorporation into GLU. *Mean ± SE

209 CEREBRAL SUBSTRATE A-V DIFFERENCES FOLLOWING MATERNAL CANINE STARVATION. R.Kliegman, E.Miettinen, A.Sutton, M.Patel (Spon.by A.Fanaroff)CWRU,D.Peds & Bioch,CLEVE

Maternal canine starvation(MCS) results in ↓ fetal weight (250.8±6.8 vs 270.5±6.7g) and neonatal hypoglycemia. To determine the effects on cerebral oxidative metabolism, simultaneous artery to superior sagittal sinus(A-V) differences were determined for glucose(GLU), lactate(LAC), FFA, ß-hydroxybutyrate (BHBA), acetoacetate(AC) and oxygen(O_2) content after 3,6,9 and 24 h of neonatal fasting. GLU A-V diff were always positive and were unaltered by MCS or neonatal fasting (range 0.231-0.527mM). LAC was released by the brain in all pups at each time. However, the cerebral LAC A-V diff was less in MCS pups at 3(-0.07±0.05 vs -0.20±0.05),*6(-0.04±0.01 vs-0.13±0.06) and 9(-0.01±0.01 vs -0.12±0.08) h. A negative A-V diff for BHBA was noted only at 3 h whereas the extraction of BHBA and AC were small and not affected by MCS. FFA A-V diff were small but positive at each time. At 6 h however, FFA A-V diff was ↑ after MCS (0.34±0.14 vs 0.09±0.03). At 24 h FFA A-V diff ↓ (0.016±0.011 MCS vs 0.036±0.013). The cerebral GLU/O_2 ratio was between 0.78 and 1.08 and was not affected by MCS or fasting. Conclusion: 1) In the presence of low circulating GLU levels, cerebral GLU A-V diff are unaffected and suggest enhanced GLU clearance by the neonatal canine brain; 2) Uptake of GLU may account for 78-100% of cerebral O_2 consumption. Additionally, less GLU was released as LAC suggesting more complete cerebral GLU oxidation in MCS pups. Except in MCS pups at 6 h, alternate fuel uptake accounts for a small fraction of O_2 uptake, emphasizing the central role of GLU for cerebral energy production. *Mean ± SE

● **210** MATURATION OF CIRCULATORY RESPONSES TO METHIONINE-ENKEPHALIN. E.F.LaGamma, J.Itskovitz, and A.M.Rudolph Cardiovas. Res.Inst.,Univ. of CA.,S.F. and The Perinatology Ctr., N.Y.Hosp.-Cornell Med. Ctr., N.Y.(SPON: P.A.M.Auld)

Endogenous opiates are widely distributed in the autonomic nervous system. To assess their potential role in influencing the maturing circulation, we studied the effects of methionine-enkephalin (15 nanomole/kg, IV) on heart rate and mean aortic blood pressure (MAP) in 20 chronically instrumented fetal (120-130 d.gest.), 5 newborn (2-4 wks/old), and 15 adult sheep. Methionine-enkephalin caused a 40% decrease in heart rate ($p<0.002$, n=5) and a 30% decrease in MAP ($p<0.002$, n=5) in fetuses, and a 26% decrease in heart rate and MAP ($p<0.001$, both, n=5) in newborns. On electrocardiogram, the bradycardia was sinus. Cardiovascular effects were unrelated to volume of administration or pH and showed tachyphylaxis. In contrast, in adults, the peptide increased heart rate by 21% ($p<0.001$, n=5) and MAP by 24% ($p<0.001$, n=5). The fetal responses were blocked by naxolone (n=4), atropine (n=4), trimethaphan (n=4), and by acute vagotomy (n=3). In adult sheep, the heart rate effect was blocked by propranolol (n=4), whereas the MAP response was reversed by phentolamine (n=3) or phenoxybenzamine (n=3). These studies demonstrate 1) that opiate receptors are functional in fetal, neonatal, as well as in adult sheep, 2) that the effects of methionine-enkephalin mature postnatally and 3) that they are mediated by autonomic nervous system efferent nerves. (supp. in part NHLBI # 5KO8-HL00756).

211 PLASMA ARGININE VASOTOCIN (AVT) IN NEWBORN INFANTS. Rosemary D. Leake, Henry G. Artman, and Delbert A. Fisher, UCLA School of Medicine, Harbor/UCLA Medical Center, Department of Pediatrics, Torrance, CA.

Arginine vasotocin is a nonapeptide with antidiuretic and oxytocic action and is widely distributed in lower vertebrates. Its presence in mammalian blood has remained controversial due to the lack of adequate extraction and assay methods. Sep-Pak cartridges (ODS silica) were used to extract AVT from human blood and AVT was measured by radioimmunoassay (RIA) in the eluates. Mean (±SEM) recoveries of unlabeled AVT by RIA from pooled human plasma were 65±1% with the addition of 5, 10, 50 or 100 pg/ml of peptide (N=51). AVT and AVP levels were measured serially in umbilical arterial and venous plasma (N=17) and in peripheral blood at 2 hr (N=9) and 24 hrs (N=9) of age. Mean (±SEM) plasma AVT levels were 5.2±2.4 pg/ml, 5.5±1.1 pg/ml, 3.2±1.9 pg/ml, and 3.9±2.3 pg/ml, respectively. Plasma AVP levels were 24.0±10.6 pg/ml,29.2±15.6 pg/ml, 6.2±0.6 pg/ml, and 6.8±1.0 pg/ml, respectively. The AVT antiserum shows approximately 5% cross reaction with either arginine vasopressin (AVP) or oxytocin (OT). However, high performance liquid chromotography (HPLC) of cord blood demonstrated that the AVT immunoreactivity localized similarly to synthetic AVT; AVP and OT were well separated from the AVT peaks. Thus, we report 1) an extraction method and RIA allowing measurement of pg quantities of AVT in human newborn plasma; 2) characterization of the AVT by HPLC; 3) significant levels of AVT in cord blood persisting through 24 hours; and 4) differing plasma levels of AVP and AVT in the first 24 hrs of life.

212 DIFFERENCES IN HEART AND BRAIN MITOCHONDRIAL RESPIRATORY RESPONSE TO ISOVOLEMIC ANEMIA IN FETAL LAMBS IN-UTERO. Robert M. Liston, Linda M. Sacks, Endla K. Anday, David W. Herbert and Maria Delivoria-Papadopoulos. Univ. of PA. Sch. of Med., Depts. of Physiol., Ped. and Ob-Gyn, Phila., PA.

Tissue mitochondria adapt to in-vivo hypoxia by increasing state 3 respiratory rate (RR). The present study compares the adaptive response of fetal heart and brain mitochondria to acutely induced anemic hypoxemia in 10 chronically catheterized fetal lambs. Five animals were subjected to varying degrees of anemia by blood replacement with Dextran 70 (5%) while 5 served as controls. Blood gases, O_2 sat, [Hb], cerebral and myocardial blood flow (microsphere technique) were measured before and after 2 hrs of anemia. Heart and brain mitochondrial state 3, state 4 RR (nmol O_2 min^{-1} $nmol^{-1}$ cytochrome oxidase ± SEM), and O_2 delivery to segments of heart and brain tissue from which mitochondria were isolated were assayed. Oxygen delivery fell from 27.3 to 5.2 ml/min/100g in heart and from 9.7 to 3.7 ml/min/100g in brain. Heart state 3 RR rose from 115 nmol O_2 at O_2 delivery of 30 ml/min/100g to 490 nmol O_2 at 5 ml/min/100g ($r=-.9, p<.01$). Hearts of anemic animals had higher state 3 RR than controls (554±104 vs 232±34 nmol O_2, $p<.025$). Brain state 3 RR rose from 75 nmol O_2 at O_2 delivery of 14 ml/min/100g to415 nmol O_2 at 3 ml/min/100g ($r=.7, p<.05$). These data indicate that while both fetal heart and brain mitochondria adapt to anemia-induced hypoxia there is a distinct difference in their respective response curves; the variability may be intrinsic to tissue-specific fetal mitochondria or may reflect inherent characteristics of fetal microcirculatory (autoregulatory) adjustments to organ-specific O_2 requirements.

● **213** SECRETION OF PLASMINOGEN ACTIVATOR BY CBA MOUSE TERATOCARCINOMA CELL LINE (H6) DURING TERMINAL DIFFERENTIATION INDUCED BY RETINOIC ACID. John W. Littlefield, Developmental Genetics Laboratory, Department of Pediatrics, Johns Hopkins Univ. School of Medicine, Baltimore.

Mouse teratocarcinoma cell lines provide a model system in which aspects of early embryogenesis can be studied in detail. Differentiation of essentially all H6 teratocarcinoma cells to endoderm-like cells occurs following exposure to retinoic acid ($3x10^{-6}$ M) for even as short a time as a few minutes. During the subsequent 1-2 weeks the H6 cells divide up to 6 times, but then cannot be passaged further. At this point the culture is composed entirely of large flat cells, which soon degenerate. Flow cytometric analysis indicates these cells are not polyploid. Differentiated H6 cells resemble endoderm on the basis of morphology, increased secretion of plasminogen activator, and analogy with other teratocarcinoma cell systems. After 3-4 days of exposure to retinoic acid, plasminogen activator secreted by mass cultures is increased about 5-fold, and then does not increase further. Treatment with dibutyryl cAMP (10^{-3} M) alone does not increase the secretion of plasminogen activator, but when combined with retinoic acid it causes about a 5-fold further increase in secretion. Study of plasminogen activator secretion by individual cells suspended in casein-agarose suggests that retinoic acid, and especially retinoic acid plus dibutyryl cAMP, increases both the number of cells transiently or permanently secreting plasminogen activator and probably also the amount of plasminogen activator secreted per cell.

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● **214** VASOACTIVITY OF NEUROENDOCRINE CELL PRODUCTS IN NEWBORN LUNGS: BOMBESIN(B), GRP, LEU-ENKEPHALIN(L.E), SEROTONIN(S). James E. Lock, Thomas J. Kulik, Dana E. Johnson, Theresa Niemi(Spon. by R. Lucas) Dept of Pediatrics, U. of Minnesota, Mpls.

Because of their unique anatomic position in the lung, pulmonary endocrine cells are thought to influence pulmonary vascular resistance(PVR) by secreting certain agents; i.e. B, GRP(gastrin releasing peptide), LE, and S. These agents' effects on PVR in the newborn lung are largely unknown. L and R pulmonary artery(PA) flow probes and LA lines were implanted in 3-18day old lambs; catheters were placed in the aorta(Ao) and either L or RPA 5-12days later. Bolus injections of 0.1-10ug/kg of the 4 agents were made into either PA of the unsedated lambs in normoxia(N) and hypoxia(H). L+RPA flows (cardiac output[CO]), LA, Ao, and PA pressures(P) in mmHg were recorded continuously. A direct effect of an agent on PVR changes the ratio of flow to the injected lung to total lung flow(Q_{inj}/Q_T).

B(n=5) and GRP(n=6) had no effect on AoP, PAP, CO, systemic or PVR, in N or H at any dose. In contrast, LE(10μg/kg,n=7) increased PAP in N and H(14%*, 25%*), with a threshold of 0.1μg/kg. AoP, LAP, CO and Q_{inj}/Q_T did not change, suggesting the rise in PVR was not due to a direct effect of LE on pulmonary vessels. S(n=6) caused a rise in AoP(86 to 96*) and a fall in Q_{inj}/Q_T(0.30 to 0.25*) without changing CO, indicating direct systemic and PA vasoconstriction, in both N and H, at a threshold of 3.0μg/kg.

B and GRP are unlikely to be mediators of neonatal PVR. However, both LE and S show PA and/or systemic vasoactivity, even at low doses. In addition, LE appears to act indirectly on pulmonary vessels, perhaps via the central nervous system. The importance of S and LE in maintaining neonatal PVR remains unknown. (*$p < 0.05$)

215 DEFECTS IN BRAIN-STEM AUDITORY EVOKED POTENTIAL RESULTING FROM LEAD POISONING. Steven M. Marcus, Janet M. Purn, Spon. by Franklin C.Behrle,College of Med. & Dent. of N.J.- N.J. Med. School,Newark Beth Israel Medical Center, Newark, N.J.

Numerous reports in the literature suggest lead poisoning produces significant CNS dysfunction even at levels below encephalopathogenic. Previous works suffer from various biasis among the many of which is the relatively subjective nature of the measured parameters. Many of the reports suggest that defects may involve primarily the auditory pathways when effecting learning abilities. We used brainstem auditory evoked potentials to determine if lead poisoning can be shown to damage auditory or CNS functioning. Patients were used as their own controls; they were tested prior to and subsequent to chelation therapy.

pt.	pre-Rx Pb	pre-Rx FEP	ABR(I-V)	post-Rx Pb	post-Rx FEP	ABR(I-V)
1.	59	156	4.72	27	138	4.32
2.	64	262	4.32	30	233	3.92
3.	46	649	4.66	26	70	4.30

Lead poisoning appears to produce an easily measured, reversable effect on auditory evoked potential. Defects of this nature may be responsible for some of the behavioural and academic problems associated with children who have suffered from lead poisoning.

● **216** CHANGES IN CORTISOL-RESPONSIVENESS OF FETAL RABBIT LUNG TISSUE DURING GESTATION. Carole R. Mendelson, John M. Johnston, and Jeanne M. Snyder. (Spon. by Charles R. Rosenfeld) The Univ. of Texas Southwestern Med. Sch., Cecil H. and Ida Green Ctr. for Reprod. Biol. Sci., and the Depts. of Biochem., Ob-Gyn. and Cell Biol., Dallas, TX.

The capacity of lung tissue from fetal rabbits of different gestational ages to respond to glucocorticosteroids was investigated. Lung tissue obtained from 19, 21, 24, 26 and 29-day gestational age fetal rabbits was maintained for up to 7 days in organ culture in the absence or presence of cortisol (F, 10^{-7} M). The rate of phosphatidylcholine (PC) synthesis was assayed by the incorporation of [^{3}H]choline into PC after 1, 3, 5 and 7 days of culture. When lung tissue from 19-day fetuses was used, F increased choline incorporation 3-fold on days 5 and 7. No effect of cortisol was observed on days 1 and 3. When the same experiment was conducted with lung tissue from 21-day fetuses the stimulatory effect of F was first observed on day 3 and persisted through days 5 and 7. A similar effect occurred when lung tissue from 24-day fetuses was utilized, but when 26-day fetal lung was used the effect of F was attenuated. Lung tissue from 29-day fetal rabbits was unresponsive to F. These findings are suggestive that a critical period exists during gestation in which the fetal lung has the capacity to synthesize increased PC in response to glucocorticosteroids. These changes in cortisol-responsiveness were not reflected in significant changes in the binding capacity or affinity of glucocorticosteroid receptors.

217 THE EFFECT OF CHRONIC HYPERINSULINEMIA ON OVINE FETAL GROWTH. J. Ross Milley (Spon. by Paul M. Taylor). Univ. of Pittsburgh School of Med., Magee-Womens Hosp. Department of Pediatrics, Pittsburgh, PA.

A fourfold increase in cord insulin concentration has been associated with fetal macrosomia in the infant of the diabetic mother. In this study, a similar degree of hyperinsulinemia has been induced in the ovine fetus to study the possible effects of hyperinsulinemia on fetal growth. Catheters were placed in 4 ewes and their nondiscordant twin fetuses at 110-118 days' gestation. Insulin was continuously infused for 18±1.8 days intravenously at 24±16 μU/kg/hr to one fetus (I) while its twin (C) was simultaneously infused with saline. During infusion, insulin-infused fetal plasma insulin was 22±9 μU/ml while the control was 6±2 μU/ml (P=0.037). Serum glucose concentrations were lower in the hyperinsulinemic fetuses (C=1.08±0.15 mM; I=0.82±0.18 mM; P=0.038). Although pH was slightly but significantly lower in the hyperinsulinemic fetuses (C=7.38±0.02; I=7.36 ±0.01; P=0.014), there were no differences in PO_2, PCO_2 or hematocrit. Following infusion, no differences between the body weights or weights of placenta, liver, heart, lung, brain, and kidney of the infused and control fetuses were noted. Adrenal weight was significantly greater in the insulin-infused fetuses (P=0.044). There were no changes attributable to insulin infusion in the water content of the organs tested or in the glycogen content of fetal liver. Hyperinsulinemia (to 3.7 times normal concentrations) when accompanied by mild hypoglycemia does not result in alterations of fetal somatic growth. Higher concentrations of insulin, glucose or both may be necessary to induce ovine fetal macrosomia.

218 ONTOGENY OF OVINE FETAL LIVER AND KIDNEY PLASMA MEMBRANE INSULIN RECEPTOR-HORMONE INTERACTION. Frank H. Morriss, Cherylann Tuchman, and Sharon S. Crandell. Univ. of Tx. Med. Sch. at Houston, Dept. of Ped., Houston.

To characterize insulin hormone-receptor interaction in fetal liver and kidney plasma membranes during gestation, 22 sheep were sacrificed at 94-147 d gestational age (GA). I125-insulin and varying conc. of unlabelled insulin were incubated for 20 hr at 4°C with the 40,000xg fraction of plasma membrane preparations. Specific binding of insulin, Bsp, to ovine fetal liver and kidney membranes increased as gestation approached term, at which time it was 2-4x greater to fetal than to the respective maternal tissues (22±3 vs. 10.6±1.4% for liver; 20 vs. 4.9±0.9% for kidney). Increased Bsp was associated with late gestational increases in affinity for receptors in both fetal liver and kidney and with an earlier increase in insulin receptor concentration in fetal kidney. The increase in Bsp to male (M) fetal liver membranes was exponential (ln Bsp=0.68+0.016 GA); there was no increase in Bsp to female (F) liver membranes. These results are consistent with reports of progressively decreasing Bsp from fetus to adult in many tissues and of increased Bsp to M of F rbcs and monocytes in adult humans, and suggest that the fetal increased Bsp is primarily a function of increased affinity. We speculate that increased binding of insulin to hepatic and kidney plasma membranes in late gestation may contribute to hepatic storage of glycogen, to diminution of gluconeogenesis, and to differential growth rates between M and F if insulin binding to other tissues is greater in M than in F. (Supported by NIH RO2 HD11337).

219 HUMAN ENDORPHIN LEVELS IN THE PERINATAL/NEONATAL PERIOD. Immanuela R. Moss, Helen Conner, William F.N. Yee, Paola Iorio and Emile M. Scarpelli. Pediatric Pulmonary Division, Albert Einstein College of Medicine, Bronx, New York 10461.

To examine whether endorphins might influence postnatal respiratory control, we measured endorphin levels in maternal-fetal-neonatal compartments. Venous samples were drawn from control adult men and women, 19-37 week pregnant women not in labor and pregnant women, who were both at term and in labor. Umbilical venous and arterial blood as well as amniotic fluid were collected at delivery. In addition, 43 venous or arterial samples were drawn from 18 infants (203-294 gestational days at birth) from <1 up to 24 days of age. They had no apnea or other overt respiratory control disturbances. Endorphins were measured in unextracted samples by radioimmunoassay (Human β-endorphin Kit, New England Nuclear Co., Boston, Ma.). Maternal plasma endorphin levels were elevated during pregnancy and were highest at labor and delivery. Endorphins were elevated in umbilical and early neonatal blood and did not correlate with gestational age at birth. The increased endorphin levels of the infants were sustained for the first 4 days of postnatal life, beyond which they decreased to control (adult) levels. Because our previous work has demonstrated the suppressor effect of endorphin on respiratory control in adult and fetal subjects (Moss and Scarpelli, J. Appl. Physiol. 47:527, 1979 and 50:1011, 1981), we propose that the elevated levels of endorphins in the early postnatal period may contribute to the subtle immaturity (suppression) of respiratory drive that is known to exist during that time. Supported by NIH RCDA grant #HL 00688 (IRM) and research grants # HL 07060 and # HL 23995.

● **220** SURFACTANT SYNTHESIS IN THE FETAL LUNG: EFFECT OF PROLACTIN AND DEXAMETHASONE ON PHOSPHOLIPID SYNTHESIS IN ORGAN CULTURES OF FETAL RAT LUNG. Darlene K. Mullon, Yolande F. Smith, Laura L. Richardson, Margit Hamosh and Paul Hamosh. Georgetown University Medical Center, Washington, D.C. (Spon. by J.W. Scanlon.)

Lung explants from 18 day fetal rats were maintained in serum-free organ culture for 48h with either 2 μg/ml prolactin (PRL) (NIH or Sigma) or 10^{-6} M Dexamethasone (DEX) or with a combination of DEX (first 24 h) followed by PRL (last 24 h). Lung DNA, protein, total phospholipid (PL) and dipalmitoyl phosphatidylcholine (DPPC) were quantified after 48 hrs of culture.

	CONTROL	PRL (NIH)	PRL (Sigma)	DEX	PRL+DEX (NIH)	PRL+DEX (Sigma)
PL†	9.98	14.2*	15.60*	11.3	20.0*	20.6*
DPPC†	2.09	4.67*	5.46*	2.83	8.0*	8.96*
Protein/DNA††	8.80	8.71	8.91	8.07	8.70	8.80

†μg P/mg protein; ††mg/mg; *Significantly different ($P < 0.05$) from control values.

The data show that exposure of fetal lung explants to PRL results in a significant increase in PL and DPPC levels and higher incorporation of ^{3}H-choline (+ 34%) and ^{14}C-glycerol (+ 44%), while DNA and protein levels are not affected. A synergistic effect of PRL and DEX on lung maturation is suggested by a further increase in PL and DPPC levels and in the incorporation of labeled precursors (+64 & 76%) in the presence of both hormones. (Supported by NIH Grant HD 11353.)

● **221** INFLUENCE OF SEX KARYOTYPE ON THE SEX DIFFERENCE IN FETAL PULMONARY SURFACTANT PRODUCTION. Heber C. Nielsen, John S. Torday (Spon. by Chester Fink) Harvard Medical School, Dept. Ped., Boston, MA.

The sex difference (female > male) in fetal pulmonary surfactant production in the rabbit is related to the hormonal regulation of fetal sexual differentiation. Manipulations of fetal sex hormones to induce sexual masculinization or feminization also masculinize or feminize the pattern of fetal pulmonary surfactant production. We tested the hypothesis that the sex difference in fetal pulmonary surfactant production is affected by the genetic determinants of sex by studying surfactant production in the chicken embryo. In avian species the sex karyotype is reversed from that of mammals (avian males are homogametes XX, females are heterogametes XZ). Leghorn eggs were incubated and the embryos sacrificed on days 15, 16,17,18, and 19 of gestation (term = 21 days). The lungs were removed, weighed, and homogenized. Pulmonary surfactant was measured as saturated phosphatidylcholine (SPC) and expressed as μg SPC/100 mg wet lung weight (SPC ratio). On days 17,18, and 19 the SPC ratio was significantly higher in males than in females (day 17: male SPC ratio 76±4; female SPC ratio 55±2; mean ± SE; p<.001). Injection of estradiol (250μg) into the yolk sac at day 5 of gestation resulted in a lowering of the male SPC ratio and the sex difference was eliminated. This pattern of sex difference in fetal pulmonary surfactant follows the pattern of fetal sexual differentiation in birds and is reversed from that of mammals. We conclude that the sex difference in fetal pulmonary surfactant production is modulated by chromosomal as well as hormonal factors, and is linked with the process of fetal sexual differentiation.

● **222** EFFECTS OF CONGENITAL HYPOTHYROIDISM ON THE ONTOGENY OF MYOCARDIAL α_1-ADRENERGIC RECEPTOR(α_1AR). Akihiko Noguchi (Spon. by Wm. J. Keenan) Dept. Peds, Univ of Cincinnati, College of Med, Cincinnati, OH.

α_1-Adrenergic agonists increase myocardial inotropic response independently of β-adrenergic mechanisms and is thought to primarily involve α_1AR present on sarcolemmal membranes in the heart. Effects of congenital hypothyroidism on the postnatal development of α_1AR and myocardial growth in the neonatal hearts were examined since thyroid hormone is a potent regulator of both cell growth and adrenergic receptors. α_1-Selective radioligand ^{3}H-prazobinding to ventricular membranes from control (C) and PTU treated (17 day of 22 day gestation onwards) newborn rats were as follows:

Age	fmole mg^{-1}prot	fmole mg^{-1}DNA	fmole per heart
1d C	45 ± 10	521 ± 73	68 ± 11
PTU	54 ± 2	675 ± 14	87 ± 4
15d C	154 ± 7*	1615 ± 51§	1332 ± 92Δ
PTU	112 ± 6*	712 ±114§	458 ± 45Δ
28d C	83 ± 6	2335 ±210▲	1521 ±196†
PTU	76 ± 4	671 ± 96▲	931 ±160†

MEOE, each group n=4, *§Δ▲† $p < 0.01$(t-test) C and PTU compared. Affinity (K_D) did not change with age or with PTU treatment and was approximately 0.12nM for all pups. PTU pups had significantly less ventricular protein content ($p < 0.001$) with normal DNA content at 15 and 28 days. Thus, the difference of α_1AR between C and PTU was more marked when expressed per DNA or per heart after 15 days. We conclude that α_1AR and normal hypertrophic cellular growth in the heart are dependent on thyroid hormone during the neonatal period.

● **223** THE EFFECTS OF THYROIDECTOMY AND TRIIODOTHYRONINE (T3) INFUSION ON OVINE FETAL NEUROSYMPATHETIC DEVELOPMENT James F. Padbury, Alan H. Klein, Robert E. Lam, Calvin J. Hobel, and Delbert A. Fisher. UCLA School of Medicine, Harbor UCLA Medical Center, Department of Pediatrics, Torrance, CA

Thyroid hormones may be important in the development of the neurosympathetic system (NSS). To assess the effect of altered thyroid status on ovine fetal NSS, thyroidectomy and insertion of a constant infusion pump was performed at 119-121 days gestation followed by 8 days of infusion with either T3 (4 animals, Group I 24 mcg/hr) or vehicle (4 animals, Group II). Fetuses were delivered by cesarian section and tissues were removed and extracted in perchloric acid for tissue catecholamine (CAT) levels or homogenized for beta adrenergic receptors (BAR). CATs were measured by radioenzymatic assay and BAR with [^{3}H] dihydroalprenolol.

	Adrenal		Atria		Ventricles		Lung		Brown Fat	
Gp	I	II	I	II	I	II	I	II	I	II
NE	NC		NC		NC		NC		NC	
E	184*δ	99δ	NC		NC		NC		NC	
DA	NC		4.1*	12.4§	2.9*	14.4	5.6	14.5*	NC	

(Norepinephrine=NE, Epinephrine=E, Dopamine=DA, No Change=NC)
*p < .05 δμgm mg protein^{-1} §ng mg protein^{-1}

Lung BAR was 240±10 fmole mg protein^{-1} in Group I and 221±19 in Group II (p>0.1), Ventricular BAR was 285±26 in Group I vs 355±55 in Group II (p>0.1). Conclusions: a) Fetal T3 infusion accelerated adrenal medulla maturation, e.g. increased adrenal epinephrine content; b) T3 decreased tissue concentration of dopamine in the heart and lung but did not affect BAR.

● **224** IDENTIFICATION OF PHENYLETHANOLAMINE-N-METHYL TRANSFERASE (PNMT) IN THE OVINE FETAL LUNG. James F. Padbury, Robert E. Lam, Calvin J. Hobel, and Delbert A. Fisher. UCLA School of Medicine, Harbor-UCLA Medical Center, Department of Pediatrics, Torrance, CA

Adrenergic mechanisms are important in the synthesis and release of pulmonary surfactant but the nature of these mechanisms is unclear. PNMT is the terminal enzyme in epinephrine (E) biosynthesis; its activity has been considered restricted to adrenal medulla. We have identified PNMT activity in the ovine fetal lung. A radiometric assay was used and results are expressed as pmole product formed mg protein^{-1} hr^{-1} X 10^3. Km for purified fetal lung PNMT (9.91 X 10^{-6}M) was similar to adrenal PNMT (4.17 X 10^{-6}M) as was the order of substrate specificity; phenylethanolamine > normetanephrine >> phenylethylamine. Similar elution profiles were noted during sephadex chromatographic purification but not cullulose ion-exchange chromatography. Polyacrylamide gel chromatography of the purified lung PNMT showed partial but not complete homology with the adrenal enzyme. Pharmacologic inhibitors of adrenal PNMT did not inhibit the purified lung enzyme. Lung PNMT was measured in 5-100 day (d), 4-120 d, and 4-140 d fetuses and in 7 newborn sheep at 3.6±0.8 d. Activity increased from 132±18 at 100 d to 326±26 in NB. The correlation with advancing age (r=.570) was significant (p<.05). Conclusions: 1) PNMT is present in ovine fetal and newborn lung; 2) Chromatographic and pharmacologic properties of lung PNMT are different from the adrenal enzyme. Speculation: 1) Local production of E by lung PNMT may be important in regulation of surfactant metabolism.

225 EFFECT OF BLUE LIGHT ON ANTIBIOTIC SENSITIVITY OF KLEBSIELLA & E. coli ORGANISMS: K.V.C. Rao, C. Yonkin; Pontiac Gen'l. Hosp., Dept. Pediatrics, Pontiac, Mich. (Spon. by T.R.C. Sisson)

The effect of blue light irradiation upon the sensitivity of 3 organisms to two dose levels of CHLORAMPHENICOL SUCCINATE was studied. K. pneumoniae, K. oxytoca, and E. coli, ATCC #25923 (all chloramphenicol-sensitive) were put in broth suspensions of saline, 20 mg/ml and 40 mg/ml concentrations of chloramphenicol. Suspensions of each mixture were plated on 2 sheep blood agar plates and incubated for 100 hrs., one in dark, one under blue fluorescent light (F20T12/BB) at a distance of 18 inches. Radiant intensity of light (420-470 nm) was 5.6 μw/cm^2. Sensitivities were then determined by the Kirbey-Bauer method.

E. coli	in dark	in light	chlor.20 in dark	chlor.20 in light	chlor.40 in dark	chlor.40 in light
K.oxytoca	"	"	"	"	"	"
K.pneum.	"	"	"	"	"	"

There was no change in the sensitivity of the various organisms to chloramphenicol at the end of the study period in the dark or in fluorescent light.

It was concluded that under in vitro conditions, light of the type used for phototherapy of hyperbilirubinemia does not cause antibiotic resistance to develop.

● **226** ONTOGENY OF c-AMP PHOSPHODIESTERASE AND CALMODULIN ACTIVITY IN DEVELOPING RAT LUNG. Ward Rice, Jeffrey Whitsett, University of Cincinnati College of Medicine, Department of Pediatrics

Surfactant release and smooth muscle tone in the lung are regulated by increases in intracellular c-AMP and shifts in intracellular calcium (Ca). Calmodulin (CDR) is known to regulate both c-AMP and Ca levels in certain cell types by interacting with c-AMP phosphodiesterase (PDE) and by stimulating Ca transport. Inhibition of c-AMP-PDE by treatment of the fetus with PDE inhibitors increases c-AMP and lung compliance and decreases the incidence of RDS in premature neonates. To understand the role of c-AMP and CDR in the regulation of pulmonary maturation and surfactant release, characteristics of c-AMP-PDE and CDR activity were determined in developing rat lung. Cytosolic PDE activity was 1.28±0.24 nmoles c-AMP hydrolyzed/min/mg protein (±SEM, n=5) at 18 days gestation, before surfactant production begins. PDE activity decreased to 0.48±0.09 at 20 days gestation, reached a nadir in the newborn animal of 0.17±0.04 and increased to 0.41±0.12 in the adult. At 18 days gestation c-AMP-PDE was inhibited by Ca-CDR, an effect not apparent in older animals. While lung PDE changed during development, CDR activity remained constant: 293±42 ng of CDR actvity/mg protein (±SEM, n=6) at 18 days gestation, 262±35 at 20 days, 229±36 in the newborn, and 203±28 in the adult. A significant (p<0.05) fall in PDE activity is associated with perinatal lung maturation. Although total CDR activity did not change with age, functional changes in Ca-CDR interactions with c-AMP-PDE were demonstrated during perinatal lung maturation.

227 THE EFFECT OF THEOPHYLLINE ON THE HYPOXIC RESPONSE OF CEREBRAL BLOOD FLOW IN THE NEONATAL LAMB. Adam A. Rosenberg, M. Douglas Jones, Jr. and Mitchell G. Karlowicz, Department of Pediatrics, The Johns Hopkins Hospital, Baltimore.

Adenosine has been demonstrated to be a mediator in the increase in cerebral blood flow (CBF) in hypoxic states. Theophylline can inhibit the production of adenosine. We studied seven unanesthetized lambs aged 3-10 d. to ascertain theophylline effect during hypoxia. Catheters were placed under pentobarbital anesthesia into the left ventricle, brachiocephalic artery, sagittal sinus, abdominal aorta, and inferior vena cava. Animals were studied on the first postoperative day. CBF was measured with radioactive microspheres. Cerebral oxygen consumption ($CMRO_2$) was obtained from the product of CBF and cerebral arteriovenous difference in O_2. Each animal had measurements made in room air and moderate hypoxia before and after the onset of an infusion of theophylline. Animals had theophylline levels of 10-20mg/dl. Baseline CBF was depressed by theophylline [106.3 ± 5.60 ml·100g^{-1}·min^{-1}(± SEM) to 87 ± 5.81[p<.01)]. However, $CMRO_2$ was unchanged (6.55 ± .63 ml·100g^{-1}·min^{-1} ± SEM to 6.10 ± .48). The hypoxic response was not altered by theophylline (CBF = 920/CaO_2 + 39; r = .95 (control) and CBF = 980/CaO_2 + 22; r = .95 (theophylline) (p>.05). Thus, theophylline depresses baseline CBF, but does not alter the response to hypoxia. The importance of adenosine as a mediator for the increase in CBF with hypoxia cannot be determined from these data. (NIH Grant HD-13830)

● **228** OXYHEMOGLOBIN DISSOCIATION AND CEREBRAL O_2 DELIVERY IN FETAL SHEEP. Adam A. Rosenberg, M. Douglas Jones, Jr., Richard J. Traystman, Raymond C. Koehler. Departments of Pediatrics, and Anesthesiology and Critical Care Medicine, The Johns Hopkins Hospital, Baltimore.

Exchange transfusion with adult blood produces an acute rightward shift in the oxyhemoglobin dissociation curve in the fetus. We studied six fetal sheep at 125-130 days of gestation. Catheters were placed under halothane anesthesia, and the animals studied on the third post-operative day. Baseline measurements of respiratory gases, cerebral blood flow (CBF) and cardiac output (microsphere technique), cerebral O_2 delivery (CBF x carotid arterial O_2 content), cerebral O_2 consumption ($CMRO_2$) and the cerebral fractional O_2 extraction (carotid-sagittal sinus arteriovenous O_2 content difference ÷ carotid O_2 content) were made. Exchange transfusion with adult blood was performed and the measurements repeated. In four animals the P_{50} changed from 16.7 ± .78 (± SEM)mmHg to 35.4 ± 2.2mmHg. In two animals intermediate P_{50} values (23 and 27mmHg) were chosen to investigate non-specific effects of the exchange; none were found. The P_{50} shift had no effect on $CMRO_2$ (3.86 ± 0.28 ml/100g/min), but produced a significant (P<.02) fall in O_2 delivery (ml/100g/min; y = -0.31P_{50} + 19.43; r = -0.77) and a consequent rise (P<.01) in cerebral fractional O_2 extraction (y = 0.01P_{50} + 0.08; r = 0.96). A rise in cardiac output was not significant. Fetuses have higher cerebral O_2 delivery than adults (Science-in press); some of this difference may be due to a difference in P_{50}. (NIH Grants HD 13830, HL 10342).

229 PHYLOGENIC COMPARISON OF PRIMATE SUPEROXIDE DISMUTASE I (SOD). Louise S. Saik, William H. Baricos, Emmanuel Shapira. Tulane Univ. Sch. of Med. Hayward Genetics Center. Depts. of Biochem., Path. and Peds.. New Orleans.

Cytosolic SOD preparations were compared by their electrophoretic mobility and immunological reactivity. The following primate species were compared: chimpanzee (Pan), baboon (Papio), Rhesus (Macaca), African green monkey (Cercopithecus), Patas monkey (Cercopithecus), owl monkey (Aotus), squirrel monkey (Saimiri) and spider monkey (Ateles). Human SOD was purified and monospecific antiserum was raised in rabbits. Using double gel diffusion, an antigenic identity was revealed between human, chimpanzee and spider monkey SOD preparations. Marked antigenic dissimilarities were detected between human SOD and the other primate SOD preparations. The degree of structural divergence between the different species was determined by comparing the ratio of the antigenically cross-reacting material (as determined by single radial immunodiffusion) to the enzymatic SOD activity. This index of divergence was shown to be: human 1.00,chimpanzee 1.80,owl monkey 2.32,African green monkey 2.60,Patas monkey 2.72, squirrel monkey 2.72, spider monkey 2.72,baboon 3.36 and Rhesus 3.36. The net electrical charge of the various SOD preparations were compared by isoelectric focusing and immunoelectrophoresis. The SOD preparations from the chimpanzee and the spider monkey were very similar to human SOD, whereas the other old world and new world monkeys showed dissimilarities. However, in general, the migration patterns of the new world monkeys were more similar to human SOD than were the old world monkeys. The findings suggest that a random, not directional, evolutionary pattern of SOD occurred.

230 NERVE GROWTH FACTOR (NGF) TISSUE CONCENTRATIONS AS A MARKER OF THYROID HORMONE EFFECT ON SUBMAXILLARY GLAND (SMG). Susan M. Scott, Paula Chou, Steven B. Hoath, Jayaraman Lakshmanan, Delbert A. Fisher. UCLA School of Medicine, Harbor-UCLA Medical Center, Department of Pediatrics, Torrance, CA

Studies in our laboratory using the Swiss-Webster (SW) mouse have shown 1) the SMG NGF tissue concentrations have a logarithmic increase between 17-18 days of postnatal life, and 2) that this increase can be accelerated by injections of thyroxine for the first twelve days of postnatal life. These results verify a responsivity of NGF tissue concentrations to exogenous thyroid hormones but do not demonstrate dependency. Thus using a newly developed genetically conditioned congenitally hypothyroid mouse model (hyt/hyt), we are examining the use of NGF as a marker of thyroid hormone effect and the interrelationship of NGF and thyroid hormones on normal development. In preliminary studies, examination of both euthyroid (E) and hypothyroid (H) pups at 21 days of postnatal life reveals low tissue concentrations of NGF in the SMG (<.081 ng/mg tissue) relative to mean values (10 ng/mg) in SW mice. At 30 days H mice had low SMG NGF values (<.081 ng/mg) relative to E (1.89±1.59 ng/mg) or SW (200±20 ng/mg) values. The early biological effect of thyroid hormones on SMG was reflected in a decrease in the SMG/body weight ratio in H ($.64\pm X10^{-2}$) relative to E ($.87\pm X10^{-2}$) mice. Conclusions: 1) The increase in SMG NGF tissue concentrations in SW is delayed in (E) controls of the hyt/hyt mutant; 2) This species difference is further obtunded in association with decreased SMG mass in the hyt/hyt mouse; 3) SMG NGF serves as a marker for hypothyroidism in this species.

231 CHARACTERIZATION OF NEWBORN (NB) INTESTINAL GOBLET CELL MUCIN (GCM) BY ^{125}I-LECTINS: A POSSIBLE CLUE TO INADEQUACY OF MUCOSAL BARRIER IN NEONATES. Mitchell Shub, Kam Pang, Jean Bresson and W. Allan Walker, Harvard Medical School, Massachusetts General Hospital, Dept. of Pediatrics, Boston, MA. 02114

GCM acts as a protective barrier for the gastrointestinal tract. Many of the physiologic properties attributed to GCM are due to the complex carbohydrate coat. Recently, lectin studies have shown maturational differences in the rat intestinal cell surface components. To further investigate these differences small intestine GCM was isolated from NB (<24 hrs) and adult (Ad) rats using reported techniques. GCM purity was documented by carbohydrate and amino acid analysis. In SDS-agarose-acrylamide slab gel electrophoresis both mucins appear as a single broad band with the NB GCM moving ahead of the Ad GCM. After electrophoresis, lectin binding to GCM was done by incubating ^{125}I-lectins with the gel. Gel slices were counted for radioactivity and the degree of each lectin bound was calculated by integration of the total cpm bound to the gels. In comparing the lectin binding to Ad and NB GCM (5µg of protein/gel), 3 different patterns were observed: 1) Dolichos biflorus bound only to Ad GCM and not to NB GCM, 2) Wheat germ agglutinin bound 6 times more avidly to NB GCM and 3) Ulex europeus I and Lotus tetragonolobus had the same degree of binding to both mucins. These preliminary results suggest that the carbohydrate coat may be different in Ad and NB GCM, due to either incomplete glycosylation or a different glycosylation pathway in the NB. These alterations may affect adequate protection of the mucosal barrier in the developing intestine.

232 EFFECTS OF BETA ADRENERGIC BLOCKADE ON RESPONSE TO ACUTE HYPOXEMIA IN NEWBORN LAMBS. D. Sidi, J. Kuipers, D. Teitel, A. Rudolph, M. Heymann, CVRI, UCSF, Dept. Ped., San Francisco, CA 94143

We have shown that acute hypoxemia causes an increase in heart rate(HR) and cardiac output(CO), a fall in O_2 consumption(VO_2), and decreased subendocardial perfusion suggestive of left ventricular(LV) ischemia. To assess the role of beta adrenergic stimulation in these responses, we studied the effects of propranolol (P)(1mg/kg) during acute stable hypoxemia in the chronically-instrumented lamb (1-14 days of age).

Acute hypoxemia alone caused the expected responses as tabulated below. LV work, calculated from the product of HR and peak aortic systolic pressure (rate-pressure product), and LV-VO_2 increased markedly, in association with a decrease in subendocardial:subepicardial flow ratio to 1.03:1 (radionuclide-labelled microsphere method). With propranolol, there was an abolition of the tachycardia and a fall in CO, with a subsequent further fall in systemic O_2 transport(SOT). However, LV-VO_2 and LV work decreased markedly and LV endo-epi flow ratio returned to normoxic values (1.26:1). Acidbase status remained normal and mixed venous O_2 saturation increased. Percentage changes during hypoxemia from normoxic values were (m±SD):

	VO_2	HR	CO	SOT	LV WORK	LV-VO_2
HYPOXEMIA	-15±9	43±19	10±8	-39±7	+41	+38
HYPOXEMIA + P	-28±9	-6±13	-15±9	-52±6	-15	-21

These studies indicate that beta adrenergic stimulation during hypoxemia increases CO and SOT, thus facilitating O_2 delivery to tissues. However, this benefit is outweighed by the deleterious effects on body VO_2 and the increase in LV work and O_2 consumption

233 GLUCOCORTICOID-INDUCED MATURATION OF DUODENAL EPITHELIUM IN VITRO: ROLE OF THE MESENCHYME. Barry T. Smith, Howard M. Zinman, Harvard Medical School, Department of Pediatrics, Boston, MA

Glucocorticoids induce biochemical (alkaline phosphatase, alk pase) and morphological differentiation of the developing duodenum in vivo. In organ culture systems, such induction has been difficult to detect. We have observed that growth of trypsin-dispersed chick embryonic (17d) duodenal cells for 4 days in the presence of 10% fetal bovine serum (FBS) followed by one day in 6% chicken serum:4% FBS results in a confluent bilayer, with epithelial cells overlying fibroblasts. Incubation of such cultures with 10^{-6}M cortisol (F) increased alk pase activity (47.18±4.07 vs 38.22±5.87 U/mmol DNA; t=2.81, p<.02). Alone, triiodothyronine (T3) had no effect, but in the presence of F, T3 (10^{-8}M)marginally further enhanced alk pase (54.75±11.46; f=3.827, p=.06).

Induction seen in this epithelial-fibroblast bilayer system is in contrast to many organ culture systems, where marked disruption of the villus mesenchymal core is observed. It suggests that, as in another foregut derivative, the lung (Science 204: 1094, 1979), glucocorticoid effect on duodenal epithelium may be mediated by mesenchyme.

Recent development of techniques to isolate the uppermost, epithelial layer of these cultures with collagenase and to culture each layer separately will allow us to test this hypothesis directly.

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234 SOMATOMEDIN C AND COMPENSATORY ORGAN GROWTH: POSSIBLE PARACRINE MECHANISM. I. Sosenko, A. Stiles, A. Boyer, A.J.D'Ercole, B. Smith. Dept. of Pediatrics, Harvard Medical School and U. of North Carolina, Boston, MA and Chapel Hill, NC.

Pneumonectomy and nephrectomy result in organ specific compensatory growth of the contralateral organ. Somatomedins may play a role in this phenomenon (Am. Rev. Resp. Dis. 121:701,1980). To explore whether serum Somatomedin C (Sm-C) levels are related to organ growth, left pneumonectomy, left nephrectomy or sham chest surgeries were performed on 11, 11, and 10 rats respectively. Serum was collected on post-op days 3 and 5 and at sacrifice on day 7 and Sm-C levels were determined by radioimmunoassay.

GROUP ($\bar{x}$±S.E.)	DAY 3 (units/ml)	DAY 5	DAY 7
Pneumonectomy	1.65±0.26	1.40±0.14	1.61±0.19
Sham	2.12±0.15	1.86±0.23	1.39±0.16
Nephrectomy	1.31±0.13	1.25±0.12	1.34±0.15

Sm-C levels appeared to fall in all groups during first 5 post-op days, presumably due to the stress of surgery. From days 5 to 7, sham rats continued to show a fall in Sm-C levels; Sm-C levels were rising significantly (p<0.05) in both pneumonectomy and nephrectomy rats (paired t-test). At no time did pneumonectomy or nephrectomy rats have serum Sm-C levels significantly elevated over sham rats. These findings suggest that serum Sm-C does not reflect ongoing organ growth and that any influence on compensatory organ growth exerted by Sm-C probably occurs via a paracrine (i.e. local secretion, diffusion and action) rather than an endocrine mechanism.

● 235 SIMULTANEOUSLY MEASURED LACTATE UTILIZATION RATE (LUR) AND LACTATE UMBILICAL UPTAKE (LUU) IN THE FETAL LAMB. John W. Sparks, William W. Hay, Jr., Giacomo Meschia, and Frederick C. Battaglia, University of Colorado School of Medicine, Division of Perinatal Medicine, Departments of Pediatrics, Ob-Gyn and Physiology, Denver.

Lactate oxygen quotients have suggested the nutritional importance of lactate in the unstressed fetal lamb. The present study compared the net fetal LUU with the simultaneously measured fetal LUR. We studied fourteen late gestation sheep with catheters maintained chronically in the maternal artery and uterine vein, and the fetal artery and umbilical vein. Uterine and umbilical blood flows were measured using antipyrine, and net uterine and umbilical lactate uptakes were calculated by the Fick principle. Placental lactate production averaged 11.8 ± 0.7 mg/min (mean ± SEM). Placental lactate distributed preferentially towards the fetus, with the net fetal LUU averaging 1.95 ± 0.16 mg/kg/min. Using primed, continuous infusion of ^{14}C-(U)-Lactate in 6 animals, simultaneously measured fetal lactate turnover averaged 6.5 ± 0.8 mg/kg/min. Correcting lactate turnover for non-metabolic umbilical diffusional tracer loss, the fetal LUR averaged 5.9 ± 0.7 mg/kg/min. Fetal lactate production rate (LPR), calculated as the difference between LUU and LUR, averaged 4.5 ± 0.7 mg/kg/min. Infusion of ^{3}H-glucose into the fetus demonstrated that approximately 3 mg/kg/min of the fetal LPR was derived ultimately from glucose and 1.5 mg/kg/min from non-glucose precursors. We conclude that under unstressed conditions, 1) lactate is quantitatively a major exogenous nutrient for the fetal lamb, and 2) fetal lactate utilization is the result of a large exogenous lactate umbilical uptake from the placenta plus an even larger endogenous fetal lactate production.

236 IMPAIRED FATTY ACID OXIDATION IN THE NEWBORN GUINEA PIG - IN VIVO STUDIES. Alan R. Spitzer, Charles A. Stanley, Joseph M. Egler, Lester Baker. Univ. of Pa. Sch. of Med., and Dept. of Peds., Children's Hospital of Philadelphia, Philadelphia, PA.

Previous studies have suggested that newborn infants are unable to oxidize free fatty acids for hepatic ketogenesis during the first 8 hours after birth. In vitro studies in newborn guinea pig have shown a similar delay in development of hepatic fatty acid oxidation postnatally. To assess the onset of total body fatty acid oxidation, the utilization of labelled palmitate was measured in vivo in groups of newborn guinea pig pups and compared to fed and fasted adult animals. (1-^{14}C) palmitate was injected intracardiac. The time course of label excretion as $^{14}CO_2$ was followed for 2 hours. Results are expressed as percent dose recovered (M ± SEM):

Age of Animal	60 minutes	120 minutes
1-4 hr (n=5)	7.1 ± 1.4*	13.7 ± 1.6*
16-24 hr (n=6)	23.5 ± 4.5	36.0 ± 3.8
24-72 hr (n=5)	20.7 ± 4.4	33.8 ± 4.6
Adult fed (n=7)	8.6 ± 1.4	18.1 ± 2.8
Adult-fasted (n=5)	27.9 ± 2.7	39.3 ± 2.9

*$p < .001$ - compared to 16-24 and 24-72 hour old animals.

Conclusion: The in vivo oxidation of plasma fatty acids in the newborn guinea pig is significantly reduced during the first 4 hrs of life, with rate approximating that of fed adult guinea pigs. After 16 hrs of age, there is an increase in rate to levels similar to that of fasted adult animals. These in vivo results are consistent with our previous in vitro studies suggesting that ability to utilize free fatty acids is not developed in the guinea pig until several hours after birth.

● 237 HYPOTHYROIDISM (HYPO) AND GLUCOCORTICOIDS (GC) MODULATE THE DEVELOPMENT OF HEPATIC INSULIN RECEPTORS. Bruce Sterman, Supriya Ganguli & Mark Sperling. Univ. of Cincinnati, Child. Hosp. Med. Ctr. Dept. of Peds., Cincinnati.

Since insulin mediates many fetal growth processes which may also be affected by HYPO and GC, we invectigated the characteristics of the insulin receptor (IR) of liver plasma membranes (LPM) during maturation and the effect of HYPO and GC in fetal/neonatal rabbits. In control fetuses (n=6), specific binding of ^{125}I-insulin per 50 µg of LPM protein increased progressively from d22 to a peak of 27 ± 4% at birth (31d). Administration of propylthiouracil (PTU) plus thyroxine (T4) to maternal drinking water from d23 onwards induced fetal but not maternal HYPO (fetal free T4 undetectable; maternal free T4 normal) since PTU but not T_4 crosses the placenta. Normal fetal IR number of 7 ± 0.9 x 10^{-10} M/L was reduced by 50% ($p<0.01$). When HYPO was maintained for the first 6d of life, specific binding of ^{125}I-insulin was 30% less than control ($p<0.02$) and the normal pattern of changes in postnatal IR was prevented. Restoration of euthyroidism by supplemental T4 to neonatal HYPO rabbits restored insulin binding and IR patterns to normal. Betamethasone, 0.17 mg IM to mothers late in gestation markedly suppressed maternal and fetal corticosterone levels by 80 to 90%; fetal IR on d28 was only 50% of control ($p<0.01$). Receptor number but not affinity was altered by HYPO or GC. Conclusions: Fetal HYPO or GC exposure impairs normal development of hepatic insulin receptors. Changes induced by HYPO are reversible when euthyroidism is restored post-natally. Impairment of insulin receptor development may in part explain the mechanism by which HYPO and GC influence growth.

238 Histomorphometry of the human placenta in class B diabetes mellitus. François Teasdale. Pediatric Research Center, Hôpital Ste-Justine, Montreal, Canada.

The purpose of this study was to evaluate with quantitative analyses the morphological changes in the functional structure of the placenta in diabetes mellitus class B, and to determine their possible impact on placental function and fetal growth. Ten placentas of diabetic mothers, divided in two groups based on the growth characteristics and neonatal outcome of the infants at birth were compared to a group of placentas collected from normal pregnant women. It has shown that the placentas of the appropriate for gestational age infants were morphologically very similar to the controls, except for a well-developed villous capillarity (11.13 ± 0.84 vs 7.66 ± 0.81 m^2; $p < 0.02$). In contrast, the placentas of the large for gestational age infants (LGA) were shown to differ from the controls by having heavier placentas (627 ± 31 vs 462 ± 30g; $p < 0.01$), due mainly to a significant accumulation of non-parenchymal tissue (363 ± 9 vs 256 ± 21g; $p < 0.005$). Consequently, the surface areas of exchange between mother and fetus in terms of capillary (9.94 ± 1.01 vs 7.66 ± 0.81 m^2; p = NS) and villous (11.18 ± 1.36 vs 9.21 ± 0.79 m^2; p = NS) surface areas were only moderately enlarged in these placentas, due to a relatively lower number of villi filled with connective tissue (145 ± 15 vs 84 ± 5g; $p < 0.01$). On a functional basis, despite these morphological differences, these findings suggest that placental function is probably not adversely affected in class B diabetics. However, the placental changes described in the placentas of the LGA infants may represent a less successful adaptation to the maternal disease, which may worsen in the more severe forms of diabetes during pregnancy.

● 239 STREPTOZOTOCIN-INDUCED MATERNAL DIABETES AND ITS EFFECTS ON FETAL RAT LUNG INSULIN RECEPTOR BINDING. R.E. Ulane, R. Steinherz, J.E. Graeber, M. Cornblath, NICHD, NIH, Bethesda, MD 20205. (SPON: Joseph D. Schulman).

Maternal diabetes induces fetal hyperglycemia and hyperinsulinemia and it has been proposed that either or both of these conditions may produce the reduced synthesis of dipalmitoylphosphatidylcholine (DPC) and phosphatidylglycerol (PG) observed in the fetal lung of diabetic rat pregnancies. We produced maternal diabetes in Sprague Dawley rats at 9 days gestation after a single I.P. injection (60 mg/kg) of streptozocin. (Maternal serum glucose: 521 ± 35 [SD] mg/dl, diabetic vs. 92 ± 2 mg/dl, control; maternal serum insulin: 0.3 ± 0.1 ng/ml diabetic vs. 1.2 ± 0.1 ng/ml control, n ≥ 12). Pregnancies were allowed to progress to 21 days gestational age when fetuses were removed by Caesarian delivery. Fetal serum glucose levels were 375 ± 31 mg/dl in streptozotocin-treated animals (FS) compared to 39 ± 2 mg/dl in control pregnancies (FC). However, insulin concentrations in both groups of fetuses were indistinguishable (2.5 ± .2 ng/ml in FS vs. 2.7 ± .3 ng/ml in FC). ^{125}I-insulin binding to lung membrane preparations of FS was significantly reduced (220 ± 50 fmoles insulin bound/mg DNA) when compared to FC (580 ± 80 fmoles insulin bound/mg DNA). The data do not support the hypothesis that hyperinsulinemia causes reduced synthesis of DPC and PG. On the contrary, the down-regulation of insulin receptor binding in the face of normal circulating insulin levels is noteworthy and suggests an impairment of insulin effects on fetal lungs in diabetic rat pregnancies.

● 240 CHRONIC HYPERGLYCEMIA REDUCES SURFACE ACTIVE MATERIAL FLUX IN TRACHEAL FLUID OF FETAL LAMBS. David Warburton, (Spon. by Alan B. Lewis). University of Southern California School of Medicine, Childrens Hospital of Los Angeles, Department of Pediatrics, Neonatal-Respiratory Disease Division, Los Angeles.

Chronic hyperglycemia was induced by continuous intravenous infusion of glucose (14±2 mg/Kg/min, M±SE) into 4 chronically catheterised fetal lambs from which tracheal fluid was collected from 112 through 133, 135, 143 and 145 days gestation respectively. Serum glucose levels (32±2 mg/dl) and serum insulin levels (48±12 µU/ml) in these fetuses were higher than serum glucose levels (18±2 mg/dl, $p < 0.001$) and serum insulin levels (12±3 µU/ml, $p < 0.001$) in 4 chronically catheterised control fetuses of the same gestational age. Glucose infusion to the fetuses did not alter the maternal serum glucose (60±3 mg/dl) or serum insulin levels (35±4 µU/ml). Surface active material (SAM) measured on a surface balance, began to appear in tracheal fluid of control fetuses at 120 days and was present in all 4 controls at 129 days gestation. SAM did not appear at all in tracheal fluid of 3 glucose treated fetuses and appeared in the fourth fetus at 142 days gestation. SAM flux was significantly reduced in the tracheal fluid of the glucose treated fetuses (M < 1 µg/Kg/Hr) in comparison with the control fetuses (60±7 µg/Kg/Hr, $p < 0.001$). I conclude that chronic hyperglycemia reduces SAM flux in tracheal fluid of fetal lambs. A similar mechanism may operate in utero to cause respiratory distress in infants of diabetic mothers whose glucose homeostasis is poorly controlled.

241 POSTNATAL PULMONARY STUDIES ON THE PREMATURE RABBIT EXPOSED IN UTERO TO BETAMETHASONE.

Jill A. Ward, Allen Erenberg, and Robert J. Roberts. Depts. Pediatrics and Pharmacology, College of Medicine, University of Iowa, Iowa City, IA 52242.

Pregnant rabbits were dosed with betamethasone (B) or saline (S) I.M., on days 26 and 27 of gestation. Pups were delivered on day 29 via C-section and killed prior to breathing, or allowed to live 6, 24, or 48 hours. B-treated pups exhibited reduced body weights, dry lung weights, and lung protein. Maximum lung volume/gm dry lung weight was not altered with B treatment. Pressures at 30%, 80%, and 30% maximum lung volume on inflation (i) and deflation (d), derived from air pressure/volume (P/V) curves showed lower P_{30i} at 6 hours, and higher P_{30d} at 0 hours in the B pups. No other P/V measurement was affected by B treatment. Lavage phospholipid (PL) phosphorus was greater in B pups at 6, 24, 48 hours with a 57% increase in PL/body weight by 48 hours. Relative percent lavage PL components were altered with B at time 0, but only phosphatidylglycerol remained lower than with S treatment after the onset of breathing. Light and electron microscopic evaluation of lungs indicated B-associated increase in number and size of lamellar bodies in Type II alveolar cells at 6 hours, which was less evident by 24 hours. This study shows that B treatment increases alveolar surfactant PL levels which are maintained through 48 hours of life in the premature rabbit. This increase in PL correlated with morphologic changes in Type II cells, but was not associated with corresponding alterations in P/V curves. These observations would support the conclusion that factors in addition to B-induced elevated PL levels are important in determining P/V relationships. Supported by NIH Predoctoral traineeship #GM07069.

242 THE EFFECT OF EARLY MECONIUM EVACUATION ON TOTAL SERUM BILIRUBIN LEVELS.

Leonard E. Weisman, Marilyn T. Digirol, Carolyn Hudgins and Gerald B. Merenstein (Spon. by Donald G. Corby), Department of Pediatrics, Fitzsimons Army Medical Center, Aurora, Colorado.

Delayed passage of meconium is associated with hyperbilirubinemia. To determine if early evacuation of meconium was effective in reducing peak serum bilirubin, 70 term healthy neonates were randomly assigned to 4 groups. Group I suppositories, breast fed. Group II breast fed. Group III suppositories, bottle fed. Group IV bottle fed. Suppositories were given at 1 hr. and then every 4 hrs. until transition stool. Bilirubin was determined every 12 hrs. IDM's, neonates with positive Coombs or polycythemia were excluded.

GROUP	n	PEAK BILI (mg/dl)		1ST MEC (hrs.)		1ST TRANS (hrs.)	
I	20	9.4	NS	4	(.01)	20.4	(.03)
II	20	7.8		8		28	
III	15	6.8	NS	3.2	NS	15.7	(.05)
IV	15	6.7		4.7		23.7	

Time to first feed, gestational age and class, birth weight, sex, race, neonatal weight loss at 3 days, method of delivery, maternal oxytocin, analgesia and anesthesia, history of "pill" contraception, parity, and ethnic background were not different between groups. No mothers received phenobarbital or steroids.

Conclusion: Suppositories resulted in early evacuation of meconium in both breast and bottle fed neonates. No significant effect was noted in peak bilirubin levels in the first 5 days of life. Routine use of suppositories to decrease peak serum bilirubin cannot be recommended for term healthy neonates.

243 DEVELOPMENT OF c-AMP DEPENDENT PROTEIN KINASE(S) IN THE RAT LUNG.

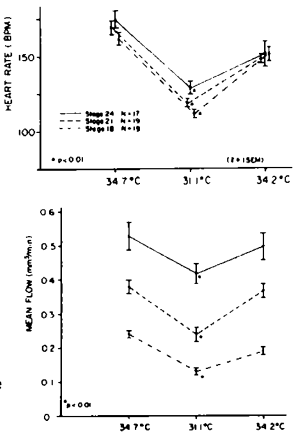
Jeffrey A. Whitsett, Susan Matz, Charlotte Beckerman, Children's Hospital, Cincinnati

Catecholamines regulate smooth muscle tone and surfactant release by the stimulation of c-AMP synthesis in pulmonary cells. The effects of c-AMP on the cell are thought to be mediated by protein kinases (PK) activated when c-AMP binds to its regulatory subunit releasing the catalytic subunit. The catalytic subunit phosphorylates regulatory proteins within the cell altering their function. The present study describes the ontogenic changes of c-AMP-protein kinase activity, c-AMP binding proteins, and phosphoprotein substrates in the rat lung from day 17 of gestation to adulthood. c-AMP dependent protein kinase was demonstrated at all ages studied. Phosphorylation activity was present in both cytosol and membrane of the lung and was enhanced by c-AMP, c-GMP and Ca. c-AMP protein kinase activity in the presence of histone was 5.5±.87 nmole·mg^{-1} on day 18 of gestation and decreased postnatally to 2.75±.57 nmoles·mg^{-1}, p<.01 in the adult. Phosphatase activity did not change with age. The regulatory subunit of c-AMP-PK was identified with [^{3}H] c-AMP which bound to a single class of sites in lung cytosol, K_D 3.3±0.3nM. [^{3}H] c-AMP binding capacity was also highest in the prenatal period, decreasing postnatally from 4.6±1.2 on day 18 of gestation to 2.62±.4 pmoles mg^{-1} in the adult, p<0.01. Marked developmental changes in the phosphoprotein substrates of c-AMP-PK were also identified by audoradiography after polyacrylamide gel electrophoresis. The high c-AMP-protein kinase activity observed during late gestation is associated with increased lung β-adrenergic receptor density and the activity of other aspects of the c-AMP dependent response system. These regulate surfactant release, glycogen mobolization and smooth muscle relaxation in the lung.

244 THE EFFECT OF HYPOTHERMIA ON HEART RATE AND DORSAL AORTIC BLOOD FLOW IN THE CHICK EMBRYO

J.R. Wispé, N. Hu and E.B. Clark, Division of Pediatric Cardiology, Department of Pediatrics and the Cardiovascular Center, University of Iowa Hospitals and Clinics, Iowa City, Iowa

The developing chick embryo is poikilothermic and exposed to varying environmental temperatures during incubation. We studied the cardiovascular effects of hypothermia on Stage 18, 21 and 24 embryos. Mean dorsal aortic blood velocity was measured using a 20 MHz pulsed-doppler flow meter. Blood flow was calculated. Heart rate and embryo temperature were measured. We applied 0.5 ml, 20°C Ringer's lactate to reduce environmental temperature and then rewarmed the embryo to baseline. 38°C Ringer's lactate was applied to control embryos which were similarly studied. We observed no change in heart rate, dorsal aortic blood flow or diameter among control embryos. Heart rate and dorsal aortic flow are directly related to temperature in experimental embryos. Stroke volume remains constant. These data indicate temperature effects pacemaker rate but not myocardial function. This is a protective cardiovascular mechanism.



245 COLLOID OSMOTIC PRESSURE: VARIATIONS IN NORMAL PREGNANCY AND PREGNANCY WITH DIABETES MELLITUS AND TOXEMIA

Paul Y.K. Wu, Vikram Udani, Linda Chan, Franklin C. Miller and Carol C. Henneman. Univ. of So. Calif. Sch. of Med., Dept. of Peds., Family and Preventive Med., Obstet & Gynec., L.A.

Pregnancy is associated with changes in both the volume and composition of fluid in body water compartments. In order to study the forces which regulate fluid flux, colloid osmotic pressure (COP), hematocrit (HCT), serum total solids (STS), mean blood pressure (MBP) and MBP-COP gradient (M-C) were measured in 184 women with normal uncomplicated pregnancy. COP fell gradually during the first and second trimesters, and reached its nadir at 30-34 weeks, thereafter it rose. These changes were significant, p <.0001. The relationship of COP and gestational age (GA) was best described by the quadratic equation. The pattern of changes of HCT and STS during pregnancy were similar to COP. MBP and M-C were linearly correlated to GA. COP correlated directly with STS (r=0.71). Stepwise multiple regression analysis of COP on GA, STS, HCT, MBP and M-C showed that STS was the most significant variable, with GA, M-C and MBP followed in order. With the exclusion of HCT, the variables explained 100% of the variations of COP in normal pregnancy. In 90 pregnant women with diabetes mellitus, the COP and STS were lower, and M-C was higher than in women with normal pregnancy. COP in 9 women with toxemia of pregnancy was lower than both the above groups. The increase in M-C with advancing GA would promote fluid flux from the intra to extra vascular space in normal pregnancy and this process is further aggravated in pregnancy with diabetes mellitus and toxemia.

246 EFFECT OF INDUCED HYPOVOLEMIA (HV) ON SUPERIOR MESENTERIC ARTERY BLOOD FLOW (MBF) RESPONSE TO FEEDING IN PIGLETS.

A.C. Yao, P.M. Gootman, N. Gootman, P.E. Pierce, and S.M. DiRusso, Downstate Med. Ctr., SUNY, Depts. of Pediatrics & Physiology, Brooklyn, New York

The effect of HV on the MBF response to feeding was examined in term <2 day old (n=7) and 2-4 weeks old (n=10) piglets. Phasic blood flow was measured using the experimental preparation previously described*. Temperature, EKG, and aortic pressure (AP) were monitored. Mesenteric vascular resistance (MVR) was calculated from mean AP and MBF. HV was induced by 15% reduction in estimated blood volume by blood withdrawal via jugular and/or femoral catheter. MBF in the younger group showed a significant increase from control value 15-45 minutes after feeding (23.6 ml/kg of sow's milk or commercial formula) which was not sustained through the 2 hour measurement period. MVR showed no significant change. In contrast, the older group, fed 26.5 ml/kg, showed a significant decrease in MVR. These findings differed from responses of normovolemic pigs of comparable ages where feeding under controlled conditions in the younger group showed a significant increase in MBF usually accompanied by a decrease in MVR, while the older group showed a significant postprandial MBF increase with an insignificant decrease in MVR. These results suggest an immaturity of the cardiovascular regulatory system in the younger pigs with induced HV and feeding.

*1981 Ciba Foundation Symposium 83, Dev. Autonomic NS p. 70-93
Supported by NIH HL20864

247 MINIMAL DAILY ENERGY EXPENDITURE IN PREMATURE INFANTS <1500GMS. T.F. Yeh, S.T. Leu, S. Voora, M. Admani, M. Tan, R.S. Pildes. Cook County Hosp. Dept. of Ped. Univ. of Ill., Chicago, Ill.

Daily energy expenditure is difficult to estimate in infants during ongoing nursery care unless continuous O_2 consumption (VO_2) and CO_2 production (VCO_2) can be measured. In this study, VO_2 and VCO_2 were measured continuously for 24 hrs. using indirect calorimetry. The daily energy expenditure was derived from daily VO_2 and VCO_2; both were calculated from the area under the O_2 and CO_2 concentration-time curve of the expired mixed gases. The accuracy of the method was tested in vitro by burning 100% ethyl alcohol and the average error between measured and the theoretical values for VO_2 was 4.9% and for VCO_2 was 4.7%. Ten studies were performed on 8 healthy premature infants (mean±SD BW 1189±231gms, GA 31.2±2.1wks, postn. age 8.4±4.2 days) who were nursed under: 1) neutral thermal environment; 2) heat shield; 3) continuous NG drip feeding (70-110cal/kg/day); 4) prone position, 5) minimal handling including no medical care procedures.

	VO_2 (L/24hrs)	VCO_2	VO_2 (ml/kg/min)	VCO_2	R.Q.	Energy Expen. (Kcal/kg/24 hrs)
Mean±SD	8.8±3.6	7.6±3.1	5.2±1.1	4.6±0.9	0.88±0.06	41.4±6.1
Range	4.1-14.5	3.5-13.6	3.5-6.8	3.5-6.4	0.83-1.0	29.2-50.7

There were minimal fluctuations in VO_2 and VCO_2 throughout the 24 hr period in each infant. This study provides data of daily energy expenditure in tiny premature infants under ideal conditions available in the nursery.

DEVELOPMENTAL PHARMACOLOGY

248 THE IATROGENIC INTRAVENOUS INJECTION OF ISOPROPYL ALCOHOL (IPAL): TOXICITY AND MANAGEMENT. David H. Adamkin, Renita Price, Roger J. Shott, (Sponsored by Billy F. Andrews), University of Louisville, School of Medicine, University Hospital, Department of Pediatrics, Louisville, Kentucky.

This case describes the clinical events that occurred after 3-5ml of IPAL (mistaken for saline) were injected IV during a venous cut down procedure. We review the acute toxicities and suggest a management plan.

An 1100gm, 30wk black female convalescent from HMD received the IPAL on eighth day of life. Within minutes she manifested acute hypoventilation, hypotension and bradycardia. She was areflexic and nonresponsive. Cardiopulmonary resuscitation including atropine and adrenalin and placement on assisted ventilation while vasopressors and alkalinization were begun. A double volume exchange transfusion (DVET) for removal of IPAL was done after the initial level exceeded the toxic range levels of 50-100. The following table summarized the levels and lab values:

Time after injection	IPAL level	pH	HCO_3	pCO_2
45 min	175	6.93	4	23
4hrs (immediately post DVET)	115	6.89	12	68
5hrs	83	7.15	17	52
7hrs	none detectable	7.46	16	23

Hemorrhagic pulmonary edema was also noted. Despite this, within 24hrs this neonate was apparently well and at age four months is thriving and has a normal Denver Developmental Screening Test.

Acute supportive care including ventilation, alkalinization and vasopressors and exchange transfusion utilizing IPAL is recommended.

● **249** EFFECT OF CAFFEINE(C) ON VAGAL REFLEXES AND BREATHING PATTERN IN INFANTILE APNEA. J.V. Aranda, J. Davis, T. Trippenbach. Depts Pediatr, Physiol, Pharmacol, McGill University- Montreal Children's Hospital, Montreal, Quebec, Canada

To determine mechanism(s) underlying the efficacy of C in apnea, we further evaluated the effect of C on breathing pattern and the Hering-Breuer inspiratory inhibitory reflex in 12 infants (ages 12d - 6 mo, gest age 30-41 wks, bt wgt 1.04 - 4.8 kg) with apneic spells consistent with near-miss crib death. Ventilation (V_E) was measured using a face mask attached to a pneumotachometer to measure flow and electronically integrated to give tidal volume (V_T) before and after C (10 mg/kg IV). Airway pressure was also measured in 8 infants with a strain gauge pressure transducer during airway occlusions at end-expiration (FRC) before and after the drug. Inspiratory and expiratory times during non-occluded breathing (T_I^C, T_E^C) and during occluded breathing (T_I^O, T_E^O) were obtained directly from these recordings. Results show that $\dot{V}_E$ significantly increased with C (from 350.3±42.7 to 444.2± 39.3 ml/kg/min p<0.005). Relationship of V_T and T_I before C (r = 0.04, p = NS) was considerably improved after C (r = 0.51, p = 0.08) indicating that instantaneous $\dot{V}_E$ was held more constant after C. T_E correlated with T_I before C (r = 0.58, p<0.05) and after C (r = 0.54). The ratio of T_I^O/T_I^C was increased before C ($\bar{x}$ ±SE = 1.21± .08) and in 4/8 babies, but the increase was slightly greater after C (1.37±.14) and in 6/8 babies. In contrast T_E^O/T_E^C was slightly prolonged only before C (1.25±.17) and in 6/8 infants and was close to unity (1.01±.12) after C. Data suggest that C produced greater vagal contribution to inspiratory inhibition and increase in irritant receptor and/or chest wall reflexes.

● **250** DEVELOPMENTAL CHANGES IN SYSTEMIC VASCULAR RESISTANCE (SVR) COMPARED WITH PROSTAGLANDINS (PG) AND ANGIOTENSION II(AII) CONCENTRATIONS IN ARTERIAL PLASMA OF CONSCIOUS DOGS. Billy S. Arant, Jr. and William H. Stephenson. Southwestern Med. Sch., Dept. of Pediatrics, Dallas, TX.

Mean arterial pressure(MAP) in the neonate is low compared to the adult when circulating AII is elevated. Moreover, Indomethacin therapy in the human neonate is complicated by hypertension. To examine possible relationships between circulating PG, AII and cardiovascular function during development, 20 puppies and 3 adult dogs had measurements of cardiac output(CO)(CG dye), MAP and heart rate(HR); stroke volume(SV) and SVR were calculated. Plasma PG and AII were measured by RIA. Results are presented in the Table as mean±SEM for each age group.

Age, days(n)	1(4)	14(3)	30(4)	60(9)	Adult(3)
MAP, mmHg	49±0.6	55±6	76±4	100±3	115±5
CO, ml/min/kg	451±78	333±39	320±31	317±16	171±21
HR, per min	207±6	164±4	156±9	159±3	136±22
SV, ml/kg	2.2±0.4	2.0±0.2	2.1±0.3	2.0±0.1	1.3±0.2
SVR, units	0.12±0.02	0.17±0.04	0.23±0.02	0.33±0.02	0.70±0.1
AII, pg/ml	373±94	201±50	16±8	15±5	14±5
$6kPGF_{1\alpha}$, pg/ml	620±59	254±42	206±11	175±34	140±8
PGE_2, pg/ml	417±38	195±49	91±14	78±31	62±25

The relatively high CO and low SVR in the neonate suggest an important role for prostacyclin in cardiovascular function during development since changes in concentrations of its metabolite $6kPGF_{1\alpha}$ in the arterial plasma were related directly to CO (r=0.63, p<0.01) and inversely to SVR (r=-0.60, p<0.01).
(Supported by NIH RO1-HD14706)

● **251** DEPRESSION OF MYOCARDIAL CONTRACTILITY(MC) BY IRON(Fe) M.Artman, R.D.Olson, R.C.Boerth, R.J. Boucek, Jr.; Vanderbilt University, Dept. of Pediatrics, Nashville, TN

The current concept of shock produced by acute Fe poisoning proposes an Fe-induced venous dilation with decreased ventricular filling and a decline in cardiac output. However, Fe may also be cardiotoxic. Thus, we examined the effects of Fe on MC in isolated rabbit papillary muscles(PM; n=11)and left atrial strips(LA; n=8). The table below shows values ($\bar{X}$ ± SEM)for peak developed tension (DT;grams), maximum rate of tension development(dT/dt;grams/sec) and time to peak tension(msec) at various concentrations of Fe.

		Concentration of Iron (µg/ml) 0	10	30	100
DT	PM	1.14±.16	1.02±0.15*	0.95±.14*	0.86±0.12*
	LA	0.90±.06	0.78±0.07*	0.68±.07*	0.53±0.06*
dT/dt	PM	8.4 ±0.9	7.7 ± 0.9*	7.2 ±0.8*	6.5 ±0.7*
	LA	21±2	18±2*	15±1*	12±1*
Time to Peak Tension	PM	197±8	186±8	188±8	194±9
	LA	71±3	71±3	69±2	70±2

(*=different from control (0µg/ml) at $p < 0.01$)

Resting tension and the duration of contraction were not affected by Fe. However, Fe produced a dose-related depression of MC as evidenced by decreased DT and dT/dt. This effect was not reversible by washing the Fe from the bath. The direct depressant effect of Fe on MC may significantly contribute to the genesis of shock in acute Fe poisoning. Our findings suggest that further studies may be indicated to evaluate the use of inotropic agents in severe Fe poisoning.

● **252** PHARMACOKINETICS OF CHLORAMPHENICOL IN CYSTIC FIBROSIS PATIENTS. W. Banner, K. McCoy, S. Seidner, L. Taussig, T. Davis. Univ. of Az, Departments of Pediatrics and Pharmacology, Tucson (Spon. by J. Corrigan)

Chloramphenicol (C) is widely used in treatment of pulmonary infections in cystic fibrosis (CF). Since C is administered as a prodrug, chloramphenicol succinate (CS), lack of specific assay techniques and inadequate modeling have made characterization of C kinetics difficult. We studied 5 CF patients given a single intravenous dose of CS. By characterizing concentration-time data for C and CS along with urinary excretion of CS, sufficient data were obtained to allow modeling of the kinetics of both C and CS. The data for both C and CS were fitted simultaneously using SPSS non-linear regression. The model best describing these processes utilized 2 compartments for both C and CS, with CS as an input function to C. Utilizing this model the following data were calculated. $\bar{X}$ ± SEM

	For C	For CS
β	.226 ± .04	2.45 ± .64
Vd-β	.415 ± .18	.10 ± .03
Vss	.28 ± .20	.038 ± .02
Clearance	72.9 ± 28.9	193.8 ± 88
Cl (renal)		44.87 ± 18.2
Cl (non renal)		148.88 ± 79.5

Average % renally excreted as CS 24.4 ± 11%. Based on variability of clearances, it appears that even with adequate modeling and detailed kinetic analysis, pharmacokinetics of C in CF patients show wide variation and will require individual therapeutic drug monitoring to provide safe and efficacious therapy.

253 EXCRETION OF DIETARY CAFFEINE (C) IN HUMAN MILK (M) AND SALIVA (S). Cheston M. Berlin, Jr., H. Mark Denson, Catherine H. Daniel and Robert M. Ward (Spon by M. Jeffrey Maisels). Penn State Univ Coll of Med, M. S. Hershey Med Ctr, Dept of Peds, Hershey, PA.

Although C is in many dietary products, the dose of C available to a nursing infant from these sources has not been studied in detail. Simultaneous M and S samples were obtained from 10 lactating women (ages 25-32) nursing 2 wks-9 mos. After each woman drank her usual a.m. coffee or tea over 10-15 mins., samples of S and M were obtained at 0.25, 0.5, 0.75, 1, 2, 3, 5, 8 and 12 hrs. Urine was collected from infants 2-6 hrs after maternal C ingestion. Samples were assayed for C by HPLC using β-OH ethyltheophylline as internal standard with a lower limit of detection of 0.1 μg/ml. Two subjects ingesting 35 and 86 mg showed no C in either M or S. In 8 subjects C appeared by 0.5 hr in both M and S and peaked at 1 hr. In 7 of 8 patients after 2 hrs M levels of C were greater than S levels. In 4 of 8 patients M levels were always greater than S levels. Two subjects with significant chronic intake of C had the two longest $t_{\frac{1}{2}}$ for both M and S. Elimination phase $t_{\frac{1}{2}}$ (linear) ranged from 1.5-9.9 ($\bar{x}$=4.0±3.0, mean±SD) hrs for M and 1.3-5.7 ($\bar{x}$=2.32±1.54) hrs for S. Assuming each infant would ingest 90 ml M every 3 hrs for 24 hrs after maternal ingestion of C, the amount C available for infant absorption ranged from 0.09-1.6 mg or 0.06-1.0 % of maternal dose. C was not detected in any infant urine samples. The maternal ingestion of 85-336 mg dietary C in the form of a single cup of tea or coffee does not appear to present significant doses of C to the nursing infant.

254 PIPERACILLIN (PIP) PHARMACOKINETICS IN CYSTIC FIBROSIS (CF). Joseph S. Bertino, Jr., Michael D. Reed, Carolyn Meyers and Jeffrey L. Blumer (Spon. by W.T. Speck). Case Western Reserve University School of Medicine, Rainbow Babies and Childrens Hospital, Department of Pediatrics and Pharmacy Services, Cleveland, Ohio.

The first dose and steady-state pharmacokinetics of PIP were evaluated in 13 patients with CF aged 10 to 28 years. Subjects received a 75 mg/kg IV infusion over 30 min. every 4 hours for a total of 9 to 50 days. Serum samples obtained at 0, 0.25, 0.50, 0.75, 1, 2, 3 and 4 hours during the first and a later dosing interval were analyzed using a specific HPLC technique. Serum concentration data was fit to a one-compartment pharmacokinetic model (r=0.99). The analysis revealed: $t_{\frac{1}{2}}$=0.70±0.18 hr; V_D=20.9 ±8.4 L/1.73m^2; Cl_{TOT}=341.9±180.5 ml/min/1.73m^2 and Cpmax (30 min) =168.4±69.4 μg/ml. No significant difference was observed in pharmacokinetic parameters between first dose and steady-state. Compared to non-CF patients, our subjects had a significantly shorter $t_{\frac{1}{2}}$ ($p<0.001$) and a more rapid Cl_{TOT} ($P<0.05$). Under present dosing recommendations, serum PIP concentrations exceed the MIC_{90} for Pseudomonas for only 50% of a dosing interval. Moreover using an IV infusion = 25% of a total dose is eliminated during drug infusion. Based upon predicted steady-state serum concentrations, CF patients will require 2.3 times the dosage to attain a C_{SS} equivalent to that for non-CF patients. In addition, a rapid infusion may be required in order to avoid significant excretion during drug administration.

255 EFFECTS OF CYTOSOLIC FACTORS ON MATURATION OF HEPATIC DRUG METABOLISM IN THE RABBIT. Rama Bhat, Michael A. Evans, Dharmapuri Vidyasagar. Dept.'s of Pediatrics and Pharmacology, University of Illinois Hospital, Chicago.

Previous studies from this laboratory have indicated the existence of endogenous cytosolic factors in the neonatal rabbit liver which inhibit the oxidative metabolism of indomethacin. These studies were designed to further examine the kinetics and specificity of the cytosolic factors on hepatic drug metabolism. Hepatic tissue from 10 day postnatal rabbits and 3 month adult-male rabbits were used in the study. Initial studies demonstrated that hepatic cytosol from infant but not from adult rabbits significantly inhibited *in vitro* metabolism of 1 mM biphenyl by adult hepatic microsomes. Addition of an NADPH generating system to the incubation medium containing cytosol had no significant effect on rates of drug metabolism. Based on cytosolic protein concentration, a final concentration of 6 mg/ml of hepatic cytosolic protein from infant rabbits in the microsomes from adult rabbit significantly reduced the hydroxylation of biphenyl of 2-OH and 4-OH biphenyl by 50% and 24% respectively. A similar percent inhibition was observed with hepatic microsomes from infant rabbits. Kinetic studies demonstrated that the inhibition of 4-OH biphenyl was competitive and K_i was calculated at 5.3 mg/ml. No effect on microsomal biphenyl hydroxylation was observed with cytosol from adult rabbit liver. Microsomal glucuronication of p-nitrophenol was also significantly inhibited by addition of hepatic cytosol but no significant difference was observed between the values obtained with the hepatic cytosol from infant or adult rabbit. It is concluded that maturation of oxidative metabolism in the rabbit is limited in part by cytosolic factors which are specific and competitive for microsomal mixed function oxidase activity.

256 THE EFFECT OF THEOPHYLLINE ON URINARY EXCRETION OF BIOGENIC AMINE METABOLITES IN PRETERM INFANTS WITH APNEA by Abdul M. Bhat, John W. Scanlon, Bennett Lavenstein, L. Chuang, Farouk Karoum; Georgetown University Hospital, Department of Pediatrics, Washington, D.C. 20007.

12 hour urinary excretion of various biogenic amine metabolites (VMA, HVA and MHPG) were studied in 14 AGA preterm infants with apnea of prematurity, treated with theophylline. Their birth weight and gestational age was 0.95 ± 0.21 kg and 27.9 ± 2.2 weeks (Mean ± SD) respectively. 10 infants had urine collection before and after theophylline therapy but only 6 had paired samples. The mean serum theophylline level was 9.2 μgm/ml. The urinary concentration of VMA, HVA and MHPG expressed as μgm/kg body weight (BW) and μgm/mg of creatinine (C) are shown in the table (Mean ± SE).

Metabolites		Before Theophylline	After Theophylline	P Values
VMA	μgm/kg BW	35.9 ± 6.51	59.01 ± 12.79	NS
	μgm/mg C	10.7 ± 2.40	12.24 ± 2.70	NS
HVA	μgm/kg BW	54.5 ± 6.64	86.03 ± 13.10	0.05
	μgm/mg C	16.5 ± 2.97	16.02 ± 2.32	NS
MHPG	μgm/kg BW	117.7 ± 25.58	183.85 ± 49.55	NS
	μgm/mg C	33.12± 6.95	34.16 ± 8.04	NS

Although mean levels of various amines are higher after theophylline therapy, the difference is not statistically significant, except for HVA when expressed as μgm/kg BW, which is higher after theophylline therapy. We conclude that theophylline does not relieve apnea by increasing catecholamine output as measured by various catecholamine metabolites.

● **257** REGULATORY GENE PRODUCT OF THE *Ah* LOCUS: DEMONSTRATION OF THE CYTOSOLIC RECEPTOR IN HUMAN PLACENTA. Sanford W. Bigelow, Raul A. Lazarte, Howard J. Eisen, and Daniel W. Nebert, NICHD, NIH, Bethesda, MD 20205

The *Ah* locus regulates the induction of numerous drug-metabolizing enzyme activities by polycyclic aromatic compounds such as 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD). The major *Ah* regulatory gene product is a cytosolic receptor to which TCDD binds avidly (apparent K_d~0.5 nM). TCDD-binding moieties were examined in the placentas of several dozen patients who are cigarette smokers, passive smokers (*i.e.* who live with a smoker yet themselves do not smoke), and non-smokers. Three TCDD-binding peaks--similar to those reported with the use of gel permeation chromatography of mouse liver cytosol [Hannah *et al.*, *J. Biol. Chem.* 256:4584-4590 (1981)]--were found in human placenta: peak I, a large aggregate eluted in the void volume; peak II, an asymmetric protein (M_r~245,000) with high affinity for TCDD and saturability at TCDD concentrations greater than 10 nM; and peak III, a globular protein (M_r~40,000) not saturable with TCDD. Differences in *Ah* receptor levels (peak II) exist among the human population; the receptor concentrations are quite similar to those found in liver supernatant fractions among various inbred strains of *Ah*-responsive mice and rats. These data lend further support to the hypothesis that the *Ah* system is present in the human.

● **258** NEONATAL ADAPTATION IN NEONATES BORN TO BETA BLOCKER TREATED HYPERTENSIVE MOTHERS. M. J. Boutroy, P. Vert G. Bianchetti, P.L. Morselli. (Spon. by J.V. Aranda). Centre de Recherche en Biologie et Medicine du Developpement Humaine, Univ. de Nancy, and LERS Synthelabo, Paris, France.

Twenty-nine hypertensive mothers were given Acebutolol (A), a cardio selective beta blocker, 200 to 800 mg/d. A and its main active metabolite, N-acetyl acebutolol (N-AA) plasma concentrations were measured by HPLC. Clinical status, physiologic and biochemical data were collected in the 31 neonates (19 term, 12 preterm, 4 twins) for at least 72 hours. At birth, plasma A and N-AA concentration were found in the same range, in cord and in maternal vein plasma. In all neonates, but one, early or late hypertension was observed. A close correlation was found between blood pressure values and A ($r = 4.63$, $p<0.01$) on the first day. Continuous physiologic recording showed deceleration of basal heart rate below 120 bpm in 12 cases. In these infants, mean A plasma concentrations were 2-fold higher than in 19 newborns without bradycardia. One infant died from cardiogenic shock on day 3. Six newborns suffered from transient tachypnea associated with x-ray pattern of wet lungs and had mean (±SE) A plasma concentration higher than newborns without respiratory symptoms (260 ± 124 vs 87 ± 23 ng/ml, $p<0.05$) similar to the effect observed in newborn lambs treated with propranolol*. These data indicate an effective and hazardous beta blockade in infants born to A treated hypertensive mothers.

*Walters, R.V., Olver, R.E. : Pediatr Res 12:239-242, (1978).

259 PLACENTAL TRANSFER OF ACEBUTOLOL, A CARDIO SELECTIVE BETA BLOCKER. M.J. Boutroy, P. Vert, G. Bianchetti, P.L. Morselli, (Spon. by J.V. Aranda), Centre de Recherche en Biologie et Medicine du Developpement Humaine, Univ. de Nancy, and LERS Synthelabo, Paris, France.

The placental transfer of acebutolol (A) and its main active metabolite N-acetyl acebutolol (N-AA) was studied in 14 hypertensive mothers receiving a daily dose of 200 to 800 mg of A chronically and in their 14 newborns. The delay between last dosing and birth varied from 5.0 to 26.5 hours. A and N-AA plasma concentrations were measured in mothers' veins, umbilical vein and umbilical artery by HPLC. N-AA concentrations were always higher than those of A, both in mothers and in newborns. In one case, A was not detected (below 9 ng/ml) but N-AA was present. Mean (±SE) plasma concentrations were:

	ACEBUTOLOL (ng/ml)	N-AAA (ng/ml)
Maternal vein (n = 13)	157.2 ± 34.6	526.7 ± 97.8
Umbilical vein (n = 15)	93.0 ± 18.8	344.5 ± 92.6
Umbilical artery (n = 11)	78.6 ± 10.3	361.0 ±114.9

Ratios between umbilical/maternal vein concentrations ranged from 0.1 to 1.1 ($\bar{x}$ ±SE = 0.7 ± 0.3 for A) and 0.1 to 1.4 (0.6 ± 0.3 for N-AA). Ratios between umbilical artery and vein concentration ranged from 0.3 to 4.3 (0.8 ± 0.3)for A, 0.4 to 2.0 (0.7 ± 0.1) for N-AA. Data show a substantial placental transfer of A and N-AA and suggest a drug uptake by the fetus which might be both of physiological importance.

260 FOLLOW UP OF INFANTS <1500 GRAMS BIRTHWEIGHT WITH ANTENATAL ISOXSUPRINE (ISX) EXPOSURE. Jane E Brazy Carol Echerman, and Steven J Gross (Spon by Samuel Katz), Duke Univ Med Ctr, Dept of Ped & Duke Univ, Dept of Psychology, Durham, NC

Follow up at 24 months corrected age was performed on 20 preterm infants with ISX exposure within 24 hours of delivery, 20 gestational age and weight-matched controls, and 20 term infants matched for social and environmental factors, to ascertain possible sequellae to maternal beta-mimetic tocolytic therapy. ISX exposed infants were subdivided into high and low drug groups according to their cord drug concentration and drug-free interval before delivery. All groups had similar mean maternal age, parity, education, and racial distribution. Groups were assessed for growth, physical and neurologic abnormalities and development by the Bayley Mental and Motor Scales of Infant Development. Growth failure, microcephaly, and major neurologic abnormalities were seen only in preterm infants and did not differ between preterm groups.

	HIGH ISX (n=12)	LOW ISX (n=8)	PRETERM CONTROL	TERM
MENTAL INDEX (MDI) $\bar{x}$(SD)	79(16)	85.5(9)	85.6(17)	91.1(14)
PSYCHOMOTOR INDEX (PDI) $\bar{x}$(SD)	91.5(11)	99(7)	96.9(21)	109.8(14)

Preterm infants born after tocolytic failure but with low cord levels have outcomes comparable to preterm infants without tocolytic exposure. Further studies are needed to assess the possible risk of high drug levels at the time of birth to future development.

261 EFFECT OF 2 TREATMENT REGIMENS ON MANAGEMENT OF THE NEONATAL NARCOTIC WITHDRAWAL SYNDROME. Imelda Carin, Leonard Glass, Aruna Parekh, Nathan Solomon, Joseph Steigman, Depts. of Pediatrics and Radiology, Downstate Medical Center, Brooklyn, NY.

31 neonates exposed to methadone in-utero requiring treatment for withdrawal symptoms were randomly assigned to a paregoric (PG) or phenobarbital (P) treatment group. Maternal drug intake, birth weights, gestational ages and time of institution of therapy were similar in both groups. The following results (median values) were obtained on days 4, 7 and 14:

	Resp. rate			pH			PCO_2(mmHg)		
Day	4	7	14	4	7	14	4	7	14
PG	48	50	46	7.40	7.41	7.41	30	32	33
P	51	50	46	7.41	7.39	7.39	34	36	36

	Syst BP(mmHg)			T_4(ug/dl)			Platelets(mm^3)		
Day	4	7	14	4	7	14	4	7	14
PG	64	67	68	14.3	13.0	9.1	-	380,000	400,000
P	64	66	65	17.6	12.9	9.7	-	350,000	475,000

Rates of weight gain were similar for both groups. PG infants required treatment for a median duration of 22 days, as compared to 17 days for P patients ($p<0.01$). Infants in the former group became increasingly tolerant to therapy, and required progressively higher doses of PG to control symptoms. These data suggest that P may be more efficacious than PG in treatment of the neonatal narcotic withdrawal syndrome.

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● **262** BILIRUBIN DISPLACEMENT FROM ALBUMIN BY BETA-LACTAM ANTIBIOTICS. William J. Cashore, Masahisa Funato, Georges Peter, and William Oh. Brown University, Women and Infants Hospital, Dept. of Ped., Providence, RI.

Moxalactam (MOX) and Cefoperazone (CEF) are currently under evaluation for future clinical use. Since both drugs are bound to serum albumin (ALB), concerns have been raised over the potential of these drugs to displace bilirubin (BR) from albumin binding sites. Using horseradish peroxidase oxidation (specimen dilution 1:40) and estimation of reserve albumin (RA) by dialysis of ^{14}C-monoacetyl diamino diphenyl sulfone (MADDS) in undiluted samples, we found that both MOX and CEF displaced BR in vitro from its primary site on ALB; estimated K_D for MOX and CEF were $5X10^{3}M^{-1}$ and $9X10^{3}M^{-1}$, respectively, at the primary BR site. In vitro, 0.25 mmol MOX (141 µg/ml) decreased RA by 12% and 0.25 mmol CEF (167 µg/ml) decreased RA by 24%, respectively. To test for in vivo displacing effects of CEF on reserve albumin, we gave 50 mg/kg of CEF intravenously to 5 newborns and measured RA by the MADDS technique at 30 min. following administration of CEF. The data are shown below:

DRUG LEVEL, µg/ml Pre	DRUG LEVEL, µg/ml Post	RA, µmol/l Pre	RA, µmol/l Post	%ΔRA	p**
0	144±16*	67±10	47±8	-29.8±8	p<0.01

*Mean'S.D. **paired t-test

These data indicate that both MOX and CEF are potential BR displacers, and that further evaluation of this potential side effect is required prior to their clinical use in jaundiced newborns.

263 CEFOPERAZONE (C) PHARMACOKINETICS IN BACTERIAL MENINGITIS. Stephen A. Chartrand, Melvin I. Marks, Jimmie T. Johnston, Donald Frederick, James Dice. Univ. Oklahoma Health Sci. Center, Dept. Pediatrics, OKC, OK.

C is a third generation cephalosporin with excellent in vitro activity against H. influenzae (HIB), S. pneumoniae (Sp) and N. meningitidis (M). We administered C to 12 children receiving standard therapy for bacterial meningitis (10 HIB mean C MIC = .014 ug/ml; 2 Sp mean C MIC = .15 ug/ml). C was infused over 20 minutes on days 2 and 10 of illness. Two patients were studied after single doses; the remainder received 3 doses at 6 or 8 hour intervals. Serum was obtained at peak (end of infusion) and trough and at 15,30,60,90,120,180,240,300 and 480 minutes after infusion. Spinal fluid was obtained 1.5-2.0 hrs after the infusion. C concentrations were determined by HPLC and bioactivity confirmed by CSF killing assay. Pharmacokinetic data was analyzed by a NONLIN computer program.

Dose mg/kg	Serum C max ug/ml	CSF ug/ml 2	CSF ug/ml 10	$T_{\frac{1}{2}\beta}$ 2	$T_{\frac{1}{2}\beta}$ 10	V dArea 2	V dArea 10	Inhibitory Quotient 2	Inhibitory Quotient 10
50 q 6 hr	232	5.2	2.0	3.0	2.3	.453	.408	1:643	1:175
100 q 6 hr	431	6.9	2.5	2.4	1.1	.433	.203	1:28	1:28
100 q 8 hr	482	10.5	5.5	2.5	2.2	.326	.289	1:858	1:454
100 single	455	4.7	-	2.7	-	.447	-	1:756	-

The pharmacokinetics best fit a two compartment model although some patients exhibited one compartment characteristics. No adverse effects were seen. These data suggest that C may be effective in treating bacterial meningitis and should be further evaluated.

● **264** "T'S AND BLUES": EFFECTS ON THE NEONATE. Ira Chasnoff, William Burns, Roger Hatcher (Spon. by C. Hunt). Northwestern University Medical School, Northwestern Memorial Hospital, Dept. of Pediatrics, Chicago.

There is currently little information concerning the use of pentazocine during pregnancy and its effect on the neonate. Three groups of women enrolled in a comprehensive perinatal addiction program were studied: Group A (N=27) were drug-free controls, Group B (N=38) were low-dose methadone-maintained women, and Group C (N=10) were women addicted to pentazocine and pyribenzamine ("T's and Blue's") throughout pregnancy. No differences were seen in maternal age, gravidity, obstetrical complications, gestational age or neonatal Apgar scores. Significant differences were observed in the following physical parameters:

	A	B	C
Birth weight (gm)	3492	2836	2785
Birth length (cm)	51	48	47
Birth HC (cm)	34.6	32.6	33

An evaluation of neonatal status using the Brazelton Neonatal Behavioral Assessment Scale revealed that infants of mothers who used "T's and Blue's" were more irritable, less consolable and showed reduced orientation and motor maturity than control infants and greater impairment than the methadone-addicted infants in all these parameters. These data suggest that infants delivered to "T's and Blue's" addicted women are at as great a risk for neonatal difficulties as methadone-addicted newborns. Placing the pregnant pentazocine addict on low-dose methadone maintenance may improve the prognosis of the newborn.

265 POLYDRUG- AND METHADONE-ADDICTED NEWBORNS: A CONTINUUM OF IMPAIRMENT. Ira Chasnoff, Roger Hatcher, William Burns (Spon. by C. Hunt). Northwestern University Medical School, Northwestern Memorial Hospital, Department of Pediatrics, Chicago.

Two groups of infants born to drug-addicted mothers were evaluated in a prospective controlled study and compared to a third control group of normals. Group I infants (N=39) were delivered to mothers on well-controlled low-dose methadone maintenance, Group II infants (N=19) were delivered to polydrug-(nonnarcotic) abusing mothers and Group III infants (N=27) were delivered to control mothers who had no history or evidence of drug abuse. All three groups were similar in maternal age, gravidity and socioeconomic class and neonatal gestational age and Apgar scores. Significant differences in mean weight, length and head circumference at birth are detailed in the table. Neonatal behavior was evaluated using the Brazelton

GROUP	I (Methadone)	II (Polydrug)	III (Control)
Wt (gm)	2815	3172	3492
Lt (cm)	47.9	49.6	51.1
HC (cm)	32.5	33.8	34.6

Neonatal Assessment Scale. Group I infants showed more depression of interactive behaviors and state controls than Group II infants, who in turn were more depressed than Group III infants. The effects of nonnarcotic drugs on intrauterine growth and neonatal behavior appear to place the polydrug-addicted newborn in a gray zone between normal and opiate-addicted newborns.

266 AMPHETAMINE ABUSE DURING PREGNANCY. Ira J. Chasnoff and Sidney H. Schnoll (Spon. by Carl E. Hunt). Northwestern University Medical School, Northwestern Memorial Hospital, Depts. of Pediatrics and Psychiatry, Chicago.

There is limited information in the medical literature regarding the management of the pregnant woman addicted to amphetamines and her neonate. A 23-year-old, G_1P_0 woman who abused 800 mg of amphetamines per day throughout her pregnancy was admitted to the Chemical Dependence treatment unit of Northwestern Memorial Hospital at 7 months gestation. She was withdrawn by reducing the dose of amphetamines by 3% of her total initial dose per day. Ultrasound examinations of the fetus were performed weekly to evaluate his status. The woman was drug free for the 2½ weeks prior to spontaneous vaginal delivery at 37 weeks by ultrasound and exam. Neonatal Apgar scores were 5 and 9. Birth weight was 2820 gm, length 48 cm and HC 34 cm. The Brazelton Neonatal Assessment Scale was administered at 2 days of age. The infant demonstrated decreased reflex responsivity, tremulousness, low threshold to startle and a "hyper-alert" state with poor orientation. In follow-up there was evidence of long periods of apnea which was documented by an abnormal pneumogram. Blood and urine levels on the infant at birth, 2 weeks and 1 month of age were negative for amphetamines. Due to the history of high levels of amphetamine exposure in utero, α_1, α_2 and β receptor sites were evaluated in the placenta and on the peripheral blood platelets at birth and 1 month of age. The results of these findings and their significance in terms of the withdrawal patterns and apnea of the newborn will be discussed.

267 THE EFFECT OF PERITONEAL DIALYSIS (PD) ON SERUM CONCENTRATION OF THREE COMMONLY USED DRUGS. Elizabeth Chow-Tung, Alan H. Lau, Eunice John, Dharmapuri Vidyasagar. Department of Pharmacy Practice and Pediatrics, University of Illinois Medical Center, Chicago.

The effect of PD on serum concentrations (conc.) of Phenobarbital (Ph), Amikacin (Ak), Cefazolin (Cf) were studied in 2 pediatric patients. In patient 1 (5 days of age, 4.5 kg), intravenous (IV) Ph was administered (7.5-10 mg/kg/day) for seizure control. He received PD for management of hyperammonemia secondary to argininosuccinate deficiency. Ph clearance by PD was 6.36-8.22 ml/min/1.73m^2. In patient 2 (16M, 7.5 kg), Ak (10 mg IV q 24°) and Cf (45 mg IV q 8°) were administered for presumptive sepsis post A-V canal repairment and cardiac pacemaker implantation. PD was instituted because of progressive renal function deterioration of renal function post-operatively. PD clearance of Ak and Cf were 2.34-3.72 ml/min/1.73m^2 and 1.72-4.44 ml/min/1.73m^2 respectively. Serum concentrations (conc.) of all three drugs decreased substantially during PD. Additional amount of Ph was required to maintain therapeutic serum conc. to assure seizure control. PD clearance of Cf was found to correlate with cardiovascular function integrity. Our experiences demonstrated that substantial amount of the drugs can be removed during PD to result in sub-therapeutic serum conc. Serum drug conc. should therefore be obtained to determine the amount of drug necessary to maintain adequate therapy.

268 DEVELOPMENTAL PATTERN OF THE HEPATIC MICROSOMAL METABOLISM OF INDOMETHACIN (INDO) IN THE RAT. M. Clozel*, K. Beharry*, J.V. Aranda. McGill University-Montreal Children's Hospital Research Institute, Montreal, Quebec, CANADA

Plasma elimination of INDO in the newborn infant with patent ductus arteriosus is prolonged 2 to 10 times relative to the adult. We studied the in vitro oxidative metabolism of INDO to desmethylindo (DMI) by hepatic microsomal preparations in 1,8,14,30 and 60 (adult) day old rats. Microsomes were incubated for 15 minutes with 5 increasing concentrations of INDO ($5x10^{-5}$ to 10^{-3} M) and the formation of DMI was measured by HPLC after extraction. Michaelis-Menten constant (Km) and maximal velocity(Vm) were calculated and their development compared to the changes in enzymatic activity at a concentration of INDO of 2.5×10^{-4} M (V).

AGE (n)	1 (18)	8 (8)	14 (5)	30 (8)	60 (7)
V (nmol/mn/mg prot)	0.26±0.02	0.39±0.04	0.41±0.03	0.51±0.06	0.50±0.06
Km (nmol/dl)	2.31±0.65	2.90±0.65	2.39±0.83	1.09±0.18	0.73±0.17
Vm (nmol/mn/mg prot)	0.53±0.11	0.80±0.09	0.83±0.18	0.80±0.14	0.69±0.09

Results (Mean ±SEM; see Table) show that from 8 days of age on, the increase in V inversely correlated (r - 0.97) with Km, with no significant change in Vm. This suggests that the age-related increase in specific activity is due to progressive increase in affinity with no changes in total enzyme concentrations. We conclude that deficient INDO microsomal metabolism postnatally could be due to presence of enzymatic competitive inhibitors and/or low substrate-enzyme affinity.

269 INDUCTION OF INDOMETHACIN (INDO) METABOLISM IN THE NEWBORN RAT (NR). M. Clozel*, K. Beharry*, J.V. Aranda. McGill University-Montreal Children's Hospital Research Institute, Montreal, Quebec, CANADA.

The oxidative metabolism of Indo into desmethylindo (DMI) in the NR is decreased compared to adult. We studied the possibility of increasing this metabolism with two inducers. Zero-day-old rats were injected IP for 3 days with either phenobarbital (PB) in saline (40 mg/kg/d) or β naphthoflavone (NF) in corn oil (20 mg/kg/d) and compared to a control group receiving either saline or corn oil. At 3 days, hepatic microsomes were incubated for 15 min with 5 increasing concentrations of Indo ($5x10^{-5}$ to 10^{-3} M). Michaelis constant (Km), maximal velocity (Vm) and activity at an Indo concentration of $2.5x10^{-4}$ M (V) were calculated. Cytochrome P-450 (Cyt P-450) and NADPH cytochrome C reductase (Cyt C red) were measured spectrophotometrically. There was no difference in the control group between saline and corn oil.

GROUP (n)	V* (nmol/mn/mg prot)	Vm* (nmol/mn/mg prot	Km* (nmol/dl)
Control (9)	0.42 ± 0.03	0.71 ± 0.11	1.90 ± 0.74
NF (6)	0.47 ± 0.05	0.85 ± 0.12	1.48 ± 0.54
PB (9)	0.72 ± 0.05(a)	1.16 ± 0.08(b)	1.60 ± 0.28

* Mean ±SEM (a) $p<0.02$ (b) $p<0.05$

PB increased V and Vm without significant change in Km. Cyt P-450 was increased by both NF and PB (by 80% and 145%, respectively), as was Cyt C red (by 250% and 375%). The greater induction effect of PB relative to NF suggests involvement of Cyt P-450 rather than Cyt P-448 to catalyze Indo metabolism in the NR. Data also suggest possible interaction between PB and Indo in neonates treated with both drugs.

● **270** ECHOCARDIOGRAPHIC EFFECTS OF INTRAUTERINE RITODRINE EXPOSURE. C.S. Crawford, M.L. Hall, C. Otis. (spon. by A. Pongiovanni). Univ. of Penn., Sch. of Med., Penna. Hosp., Phila., Pa.

Infants exposed in-utero to Isoxsuprine (ISX), a B-sympathomimetic tocolytic agent have been reported to have increased birth weights and to have increased ventricular septal thickness when examined with echocardiography (ECHO). Ritodrine (RIT), a newly-approved B-sympathomimetic tocolytic agent is now being used for premature labor. Infants exposed in-utero to RIT had similarly increased birth weights and thickened septums. Studies were performed on 27 control infants, 23 ISX and 11 RIT infants. Normal septal thickness is 3-4 mm.

	Gestational Age (weeks)	Birth Wt. (grams)	Septal Thickness (mm)
Control	32.9±3.57	1577±493	3.8±0.4
RIT	34.0±4.56	2345±1097	4.83±.08
p	N.S.	< .05	<.0005
ISX	33.9±3.99	2094±825	5.5±1.3
RIT	34.0±4.56	2345±1097	4.83±0.08
p	N.S.	N.S.	N.S.

These results suggest that RIT and ISX exert similar effects on fetal somatic and septal growth.

271 EFFECTS OF ACETYLCHOLINE AND EPINEPHRINE ON FETAL CANINE HEARTS. Peter Danilo, Jr. & Ofer Binah (Spon. by W. Gersony) Columbia University, College of P&S, Department of Pharmacology, New York, N.Y. 10032

We studied the effects of acetylcholine HCl (ACH) and epinephrine bitartrate (Epi) on hearts from fetuses from early, middle, and late gestation. Hearts of canine fetuses delivered by hysterotomy were attached via the aorta to a cannula and perfused through their coronary vasculature with a physiologic salt solution. Intrinsic sino-atrial (SAR) rate and atrioventricular (A-V) conduction time varied linearly as a function of fetal development. For the least developed fetuses SAR was 226±8.5/min and A-V conduction time was 62.3±3.7 msec. For near-term fetuses, SAR was 141±14/min and A-V conduction time was 81.4 msec. ACH, 1.82 pg/l to 1.82 mg/l or Epi, 3.33 pg/l to 18.2 mg/l was added to the perfusing solution. Concentrations of ACH < 18.2 ng/l had no significant effect on SAR of fetal hearts at any stage of development. For the least developed fetuses, the threshold concentration for decreasing SAR was 18.2 ng/l. Complete atrial quiescence occurred at ACH 18.2 mg/l. For near-term fetuses, the threshold concentration was 182 ng/l; atrial quiescence occurred at 18.2 mg/l. These effects were significantly attenuated by atropine sulfate, 70 ng/l. Epi induced increases in SAR which were statistically equivalent amongst all stages of fetal development. Threshold concentration was 1.82 ng/l and maximal increases in rate were observed at Epi 182 ng/l. The effects of Epi were attenuated by propranolol, HCl, 29.6 ng/l. These data suggest that the response of the fetal heart to cholinergic stimulation is a function of on-going development whereas the response to adrenergic stimulation changes little over the range of fetal development studied.

272 GENTAMICIN DOSING IN THE NEWBORN: USE OF A ONE-COMPARTMENT OPEN PHARMACOKINETIC MODEL TO INDIVIDUALIZE DOSING Bruce Edgren, Padmani Karna, David Sciamanna, Eugene A. Dolanski, Department of Pediatrics and Human Development, Michigan State University, East Lansing, and Departments of Neonatal/Perinatal Medicine and Pharmacology, E. W. Sparrow Hospital, Lansing, Michigan (Sponsored by Michael Netzloff).

Gentamicin pharmacokinetics in the neonate has been described by a two compartment open model in recent literature. Proper characterization of the beta phase of this model is clinically infeasible on an individual basis. We chose to characterize the pharmacokinetics of our patients using a one compartment open model on the first dose to individualize gentamicin (G) therapy in sixty neonates (term and preterm). A dose of 2.5mg/kg was given intravenously over 20 minutes and serum gentamicin concentrations (SGCs) were determined at 1, 7 and 11 hours post infusion. Linear regression analysis on these SGCs was used to determine half-life and volume of distribution. From this data a new regimen and a predicted peak (P) and trough (T) SGC was determined for each neonate. The predicted P and T were compared to a measured P or T drawn at least 48 hours later. Criteria for successful dosing was based on attaining peaks of 4-8mcg/ml and troughs of ≤ 2mcg/ml.

	n	Predicted	Measured	Criteria Met
P	30	6.1±0.4	6.4±1.4	93%
T	30	1.2±0.4	1.5±0.6	83%

Gentamicin dosing of the newborn based on one compartment open pharmacokinetic model is a useful clinical tool in predicting P and T SGCs, thereby preventing nephrotoxicity due to Gentamicin.

273 EFFECT OF FORMULA ON CARRAGEENAN TOXICITY IN NEWBORN RATS. D.I. Eneanya and P.D. Walson, Dept. of Pediatrics/Pharmacology, Columbus Children's Hospital and The Ohio State University, Columbus, Ohio 43205

Carrageenan (C) is a sulfated polygalactose food additive used in infant formulas. C in water causes more toxicity in newborn than adult rats. Studies were conducted to test the effect of two infant formulas on this toxicity. Newborn (<12 hours after birth) Sprague-Dawley rats were gavage fed with 1% C in either water, Nutramigen(R) (N) or Enfamil(R) (E). Untreated controls were handled only. The survival at the end of 5 days was:

		Survival (alive/treated)				
Volume (ml x #/day)	Untreated litter mates	1% C in water	E	1% C in E	N	1% C in N
.1ml x 2	20/20	21/31	11/12	13/15	12/12	11/14
.2ml x 2	25/25	17/30	10/13	14/14	13/14	12/14
.2ml x 3	24/24	18/35	13/14	14/15	12/14	11/15

Both formulas decreased the incidence of C induced toxicity. The mechanism of this protection and the possibility that the amount of protection is formula specific are under investigation.

274 DETOXIFICATION OF NEONATES UNDERGOING ABSTINENCE, Loretta P. Finnegan, Shobhana Desai, Betty Leifer Thomas Jefferson University, Department of Pediatrics, Philadelphia, Pa.

Pharmacologic agents recommended for detoxification of infants of drug abusing mothers undergoing abstinence have included phenobarbital, paregoric and diazepam. In clinical studies, these agents have been shown to be beneficial in alleviating symptomatology. The purpose of this study was to further evaluate the efficacy of these drugs by clinical measures. Infants were assessed and managed using the neonatal abstinence scoring system (Ped. Res. 58:1978). Procedure dictates that the infants receive varying dosages of a specific drug dependent on abstinence severity. Prenatal drug exposure in the majority of infants was to opiates, however most of the women had utilized more than one agent. Of 171 infants born to psychoactive drug abusing women,59 did not require treatment. Of 112 requiring treatment, random assignment of either phenobarbital, paregoric or diazepam occurred. Each drug was escalated to the highest dosage prescribed by the scoring procedure. Abstinence not controlled at the highest dosage of a specific drug demanded a second agent. Results were as follows:

INITIAL DRUG		PERCENT REQUIRING ADDITIONAL DRUG
Paregoric	N=28	21% (N=6)
Phenobarbital	N=68	41% (N=28)
Diazepam	N=16	62% (N=10)

These results suggest that paregoric treated infants require a econd drug infrequently in comparison to phenobarbital or diazeam treated infants. The above data should also alert the clinian to the possible necessity of utilizing more than one pharmaologic agent in the detoxification procedure.

275 DRUG EVOKED POTENTIALS (DEP): A NON-INVASIVE METHOD OF DRUG IDENTIFICATION IN THE NEWBORN INFANT. Liane M. Gilbert, S. Thomas Westerman, I. Mark Hiatt, Thomas Hegyi, (sponsored by L. Stanley James). Department of Pediatrics, CMDNJ-Rutgers Medical School, New Brunswick, NJ, Department of Pediatrics,Monmouth Medical Center, Long Branch, NJ and Department of Otolaryngology, Hahnemann Medical College, Philadelphia PA.

Drug specific waveforms (ref), termed drug evoked potentials, were identified by an electronystagnometer (ENG) in a group of newborn infants exposed to the following medications: caffeine, (N=12) theophylline (N=12), dopamine, (N=1) meperidine (N=7), phenobarbital, (N=2)diazepam, (N=1) and fluphenazine (N=1). Electrodes were applied to the outer canthus of the eyes and to forehead of each infant and potentials were recorded in four head positions (straight, right, left, and neck arched). Group I consisted of 20 control infants with no drug exposure in whom no discernible DEP pattern was noted. Group II consisted of 35 newborns exposed to drugs by direct administration (n=27), passive placental transfer (N=7) and passive breast milk transfer (N=1).

Specific and reproducible DEP waveforms were obtained in each group of infants exposed to the same drug. Results of these observations reveal that these drugs can be identified by evaluation of the frequency, amplitude, and slope of the DEP waveform. This rapid non-invasive procedure provides an accurate alternative method to blood and urine analysis for immediate identification and continuous monitoring of a large variety of therapeutic agents.

Reference: Westerman and Gilbert, Laryngoscope 91:1536, 1981.

276 PHARMACOKINETIC PROPERTIES OF THIOPENTAL IN THE ASPHYXIATED NEONATE. Ronald N. Goldberg, Dyal Garg, Donald J. Weidler, Diane DeBogory, Pedro Moscoso, Eduardo Bancalari, Departments of Pediatrics and Pharmacology, University of Miami, Miami, Florida.

Thiopental (T) may be clinically useful in protecting the neonate against asphyxial brain damage. As yet there are no pharmacokinetic data for this age group. We studied T properties in 4 asphyxiated neonates ($\bar{x}$ ± SE; BW=3345±360 gm; GA=40.3±0.25 wks) as part of a randomized trial. T was begun by 2 hours of age in all and was given as a constant IV infusion in the following sequential dosages: 1)10 mg/kg over 30 min; 2)5 mg/kg over 30 min; 3)5 mg/kg/hr x 3; 4)3 mg/kg/hr x 8; 5)1.5 mg/kg/hr x 6 and 6)0.75 mg/kg/hr x 6. This regimen was modified to ensure sedation and seizure control. T levels were obtained just prior to the next dose, before any modification in dosage and for 4-6 days after the infusion was stopped. The steady state (10 to 18 µg/ml) was obtained within 1 hour of starting the infusion, was maintained during the infusion and for about 48 hrs after the infusion was stopped. Mean elimination half-life, plasma clearance and volume of distribution for T were 45 hrs (range 26-70); 60 ml/(hr x kg) (range 43-74); and 3.7 L/kg (range 2.4 to 5.9), respectively. The variation in $t_{\frac{1}{2}}$ was probably secondary to variability in the volume of distribution. No adverse effects were noted other than a drop in mean arterial blood pressure of 7 mmHg (range 4-11). We conclude from these preliminary data that it is feasible to give T at these infusion rates and that its pharmacokinetic properties are significantly different from those of the adult. Supported by NIH Grant 1R01 HD/NS 14940 -01.

277 AMINOGLYCOSIDE LEVELS ARE UNNECESSARY IN CHILDREN WITH NORMAL RENAL FUNCTION. T.P. Green, B.L. Mirkin, Div. Clin. Pharmacol., Univ. of Minn., Minneapolis.

Several strategies for achieving desired serum tobramycin concentrations (STC) were compared in 18 patients (age>2y) with normal renal function who received 26 treatment courses of tobramycin. All subjects had a 3 point kinetic study and subsequent daily monitoring of STC. Each STC was compared with the predicted STC derived from data used in the following drug monitoring strategies: I, individual patient kinetic study; II, 2 peak STC's; III, no STC monitoring (assuming that the patient conforms to mean population kinetics). Mean first order kinetic constants for the group were: Vd, .30±.16 L/kg; $t_{\frac{1}{2}}$, .98±.45 h. All strategies were similar in accuracy: STC's were slightly higher than those predicted by each of the three strategies, presumably reflecting the well described deep compartment accumulation of aminoglycosides. However, the precision of methods I and II was not better than III and they actually tended to be less precise (See Table).

RATIO OF ACTUAL STC: PREDICTED STC(%)

STRATEGY	MEAN	± 1 SD	RANGE
I. Kinetics	114	81-160	50-233
II. 2 peak STC's	107	78-147	48-237
III. no STC	111	100-123	96-138

Random intraindividual variation among daily STC's (1SD=78-129% of mean) was greater than the interindividual variation of the mean data (1SD=90-110%). The true variation in the disposition of tobramycin in this population is small relative to other factors contributing to the variation of STC's. Routine STC monitoring in this population cannot be recommended.

278 FUROSEMIDE ADMINISTRATION AND PROSTAGLANDIN (PG) LEVELS. Cathy Hammerman and William Zaia (Spon. by Kwang-sun Lee). University of Chicago, Pritzker School of Medicine, Department of Pediatrics, Chicago, IL.

Plasma and urine PGE_2 and $PGF_{2\alpha}$ levels were measured in 10 rats to determine whether changes in urinary excretion of prostaglandins are reflected by alterations in plasma prostaglandin levels. Five rats received 8 mg/kg/day of furosemide IP x 3 days; 5 control rats were administered normal saline. Urine PGE_2 excretion decreased in response to furosemide with no change in plasma PGE_2 levels. However, urine $PGF_{2\alpha}$ excretion increased nearly four-fold following furosemide administration and plasma $PGF_{2\alpha}$ levels decreased by more than 50%.

	Plasma PGE_2 (pg/ml)	Urine PGE_2 (ng/24 hr)	Plasma $PGF_{2\alpha}$ (pg/ml)	Urine $PGF_{2\alpha}$ (ng/24 hr)
Controls	#298.4+71.9	30.5+4.5	622.2+154.1	22.5+ 4.4
Furosemide	257.2±34.2	19.1±2.2*	290.0± 75.5*	79.9±25.0*

#Mean ± S.E.M. *p <0.05

Administration of high dose furosemide has been correlated with an increased incidence of clinically significant patent ductus arteriosus (PDA) in the premature. This has been postulated to be secondary to the effect of furosemide on renal PGE_2 excretion and/or synthesis. These data suggest that an increase in the plasma dilator (PGE_2) to constrictor ($PGF_{2\alpha}$) prostaglandin ratio secondary to increased renal excretion of $PGF_{2\alpha}$ may contribute to ductal dilatation although absolute PGE_2 levels are essentially unchanged.

279 ETHANOL PHARMACOKINETICS IN MATERNAL, FETAL, AND NEONATAL MONKEYS. Donald E. Hill, William Slikker, Jr., John R. Bailey, Phillip T. Goad, Andrew G. Hendrickx. Dept. of Pediatrics, University of Arkansas for Medical Sciences, Little Rock, Ar; Div. of Teratogenesis Res., National Center for Toxicological Research, Jefferson, Arkansas and University of California, Primate Res. Center, Davis, Ca.

Ethanol is a teratogen in experimental animals and humans and the effects are variable but correlate best with maternal blood ethanol concentration(BEC). The purpose of this study was to measure BEC in mother, fetus and newborn monkeys to define the pharmacokinetics at different gestational ages and doses. Rhesus and cynomolgus monkeys from 106-156 days gestation were prepared with indwelling catheters in both maternal and fetal arteries. Dilute ethanol was infused in a maternal vein for 30 min. at doses of 1.5,1.0 or 0.8 g/kg. Simultaneous blood samples were drawn from mother and fetus and for 4-6 hours after the infusion. Three neonates were sampled for 120 min. after delivery to obtain elimination kinetics. Maternal and fetal BE elimination rates(ER) were nearly identical during the four hours following infusion. Maternal and fetal BEC correlated highly (r=0.98) during the elimination phase. After delivery of the fetus, the maternal ER of 14.9±1.6 mg%/hr was 4 times that of the neonatal ER (3.6±0.2 mg%/hr). We conclude that the maternal BEC in monkeys is highly predictive of the fetal BEC. The capacity of the neonate to eliminate ethanol is limited, probably due to a low level of alcohol dehydrogenase in the newborn. Therefore, fetal exposure to this teratogenic agent is determined primarily by maternal elimination capacity.

280 ALTERATION IN AMINOGLYCOSIDE CLEARANCE AS A FUNCTION OF HYDRATION IN CHILDREN. Karen M. Kumor (Spon. by Warren Dodge) University of Texas HSC, Houston, Department of Pediatrics and Pathology and Laboratory Medicine.

The simultaneous clearances of amikacin (ACl) and inulin (ICl) were studied in 9 hospitalized children with normal renal function aged 5-18 yrs. The children were hydrated for 5-6 hrs prior to study with 100cc/M^2/hr of ¼ Nl saline. During the study the rate was increased to 125cc/M^2/hr. ACl was calculated as D/AUC from 10 serum levels of amikacin obtained throughout 4 hours time. The AUC was estimated beyond 4 hours. Urine flow rates were calulated from spontaneously voided timed urine specimens obtained during the same period. A linear relationship was demonstrated between ACl and urine flow as ml/min/M^2 (p<.001; r=.81) ICl was obtained using a loading dose followed by a constant infusion of inulin. ICl calculated as D/AUC had a linear relationship to urine flow (p<.001; r=.79). Both ICl and ACl calculated using UV/P correlated well with the results obtained using D/AUC indicating urine loss was not a problem. Two children not receiving amikacin were hydrated for 1½-3 hrs with ¼ Nl saline at a rate of 62cc/M^2/hr and had fractional sodium excretion rate FE_{Na} and ICl measured. The IV rate was then increased to 125cc/M^2/hr for 2-4 hrs and the studies repeated. In one child the GFR (D/AUC) changed from 92 ml/min to 136 ml/min while the FE_{Na} changed from 0.36% to 1.11%. In the other the GFR changed from 132 ml/min to 207 ml/min while the FE_{Na} was 1.3% and 1.15% respectively. These data suggest a responsiveness of GFR and drug clearance to alterations in the hydration rate in children who have a normal sodium balance.

281 THE CAFFEINE BREATH TEST (CBT) IN MAN. George H. Lambert, Alvin N. Kotake, Dale Schoeller, David Schaffer, Hanna Josephs. Pritzker Sch. of Med., U. of Chgo., Michael Reese Hosp., Dept. of Ped., and Comm. Clin. Pharmacol., Dept. Pharmacol. & Physiol. Sci., U. of Chgo. (Spon. by: John B. Paton).

The aim of this study was to develop a noninvasive, safe, sensitive clinical test capable of detecting xenobiotic-induced alteration of the cytochrome P_1450-dependent mixed function oxidase system in the adult and pediatric patient. Cigarette smoking, known to induce both cytochrome P_1450 system and caffeine (Caf) clearance, was the experimental variable. Labeled Caf with ^{13}C or ^{14}C in the (1,3,7) methyl groups (TRI-Caf) or specifically labeled at the 1-, 3-, or 7- methyl group were studied as substrates for the CBT. TRI-Caf, 1, 3, or 5 mg/kg was orally administered to 5 smokers and 4 nonsmokers and the exhaled labeled CO_2 was monitored for 8 or 24 hr. The absolute rate of labeled CO_2 exhaled was dose-dependent at 1 and 3 mg/kg but demonstrated saturation kinetics at 5 mg/kg. The rate of labeled CO_2 excretion averaged 2-fold greater in the smokers. The 2-hr cumulative labeled CO_2 excretion correlated highly with the apparent oral metabolic clearance rate of Caf (r=0.90) during the 3 mg/kg dose study. To determine the contribution of labeled CO_2 in the breath from demethylation of the 1,3, or 7 methyl groups, Caf specifically labeled at the 1,3, or 7 position was administered on 3 separate days to a smoker and a nonsmoker. The majority (95 and 79%, respectively) of the labeled CO_2 exhaled in the first 2 hr of the TRI-Caf CBT was derived from the 3 position while at 6-8 hrs equal amounts were derived from the 3 and 7 positions. The optimal substrate for the CBT was (^{13}C-3 methyl) Caf, at a dose of 3 mg/kg. The 2-hr cumulative excretion of labeled CO_2 was the most sensitive CBT measure of Caf N-demethylation induction.

282 MEGADOSES OF VITAMIN E (E) IN THE PREMATURE. George H. Lambert, Louis A. Papp. Pritzker Sch. of Med., U. of Chicago, Michael Reese Hosp., Dept. Ped. (Spon. by: John B. Paton).

The aim of this study was to determine if megadoses of E administered to the O_2-dependent premature could raise the total plasma tocopherol to pharmacologic levels above the normal adult range (1.1 mg/dl ± 0.5). All subjects were <1500 gm, AGA, <48 hr old and required an $F_iO_2 \geq 0.4$ for at least the first 24 hr of life. E, dl-α-tocopherol acetate in a dose of 50, 100, or 200 mg/kg/day was administered for 7 days via nasogastric tube. Seven infants who continued to be O_2-dependent after 7 days were continued on E at 100 or 200 mg/kg/day until weaned to room air at a mean age ± 1 SD of 26± 16 days. Total plasma tocopherol was determined just prior to the next dose of E at 24, 48, 168 hr, and at weekly intervals (Table). For each dosage group, the mean gestational age, birth weight, Apgar score, and F_iO_2 were similar.

E (mg/kg/day)	# Patients	Total plasma tocopherol (mg/dl) 24 hr	48 hr	7 days
50	7	0.7 ± 0.4[a]	0.8 ± 0.1	1.0 ± 0.4
100	6	0.6 ± 0.3	0.9 ± 0.2	2.2 ± 0.5[b]
200	9	0.8 ± 0.4	1.0 ± 0.4	2.0 ± 0.9[b]

[a]±1 SD; [b]Student's t test vs. 50 mg/kg/day dosage group, P < 0.05.

The oral administration of E at 100 and 200 mg/kg/day produced similar total plasma tocopherol levels and only on day 7 were the levels above the normal adult range. In the 7 newborns O_2 dependent beyond 7 days, the plasma tocopherol level on the last day of O_2 supplementation was 1.5±0.8 mg/dl. Thus, the continued administration of E beyond 7 days at 100 or 200 mg/kg/day in the O_2-dependent premature did not further increase the E level above the normal adult range.

283 GENTAMICIN (G) PHARMACOKINETICS (Pk) IN PREMATURE INFANTS. Susan Landers, Phillip Berry, Sheldon Kaplan, Gregory Kearns, Arnold J. Rudolph, Department of Pediatrics, Baylor College of Medicine, Houston, and Section on Clinical Pharmacology, LSU College of Medicine, Shreveport.

The steady state pharmacokinetics of G were characterized in 22 infants (700-1470 gms, 25-33 wks gestation) following IV administration of 2.4 mg/kg at 12 or 18 hr dosing intervals. ESTRIP analysis of G disposition in infants at steady state revealed a biexponential function from which Pk parameters ($\bar{m} \pm$ SEM) were calculated: K (elimination rate constant)= 0.08 ± 0.01 hr^{-1}, $t_{1/2\beta}$ = 9.8 ± 0.86 hr, Cl_p^{ss} (plasma clearance)=0.64 ± 0.06 ml/kg/min, and V_{dss} (volume of distribution)= 0.50 ± 0.03 l/kg. None of these values was different in infants greater than or less than 1000 gms. The apparent distribution phase was unexpectedly prolonged (3.5 ± 0.48 hrs). Serum creatinine (S_{cr}) correlated with kinetic parameters:

S cr vs.	y= a + bx	r	p
$Cl_p ss$	y= 1.17 - 0.411x	.76	< .01
$t_{1/2\beta}$	y= 2.37 + 5.76x	.71	< .01
K	y= 0.126 - 0.037x	.59	< .05

Elevated trough G levels correlated with higher S_{cr} on day 3 but not on day 7. Similar trough levels were found in 12 and 18 hr dosing interval groups. G levels measured in 5 infants from 2-140 hrs after their last dose had an apparent $t_{1/2}$= 14.6 ± 1.4 hrs. Multiexponential G disposition during routine dosing precludes accurate assessment of $t_{1/2}$ from peak and trough levels alone. G therapy can be individualized, based on Pk parameters.

284 GENETIC DIFFERENCES IN THEOPHYLLINE (THEO) TOXICITY ASSOCIATED WITH THE Ah LOCUS: EFFECTS OF CIMETIDINE IN VITRO AND IN VIVO. Raul A. Lazarte, Daniel W. Nebert, and Roy C. Levitt, Developmental Pharmacology Branch, NICHD, NIH, Bethesda, MD 20205

The Ah locus controls the induction of more than two dozen drug-metabolizing enzyme "activities" by polycyclic aromatic compounds such as 3-methylcholanthrene (MC). About a 15-fold difference in the induction response between C57BL/6N (B6)("responsive," Ah^b) and DBA/2N (D2)("nonresponsive," Ah^d) inbred mouse strains reflects differences in the cytosolic Ah receptor. The B6D2F1 (Ah^b/Ah^d) is phenotypically like the B6, indicating the Ah-responsiveness trait is dominant. Cytochrome P-450 induction by THEO is not correlated with the Ah locus. THEO toxicity resulting in cardiac arrhythmias, seizures, and death clinically are not uncommon; similar toxicity can be produced in mice. The dose required to kill 50% of mice (LD_{50}) is twice as high in MC-treated Ah^b/Ah^b and Ah^b/Ah^d, as compared with MC-treated Ah^d/Ah^d. THEO-treated B6 and D2, and control B6 and D2 mice. Cimetidine in vitro inhibits THEO metabolism by mouse liver microsomes. Cimetidine (80, 160, or 240 mg/kg given 2 h before THEO) in vivo does not change, however, the LD_{50} values for THEO toxicity. We conclude that induction of P-450-mediated monooxygenases by MC but not by THEO protects against THEO toxicity presumably by enhancing detoxication.

285 NEONATAL ABSTINENCE: AN ABBREVIATED SCORING SYSTEM, Betty Leifer, Herman Michael, Loretta P. Finnegan, Thomas Jefferson Univ., Dept. of Peds., Phila., Pa.

The abstinence scoring system (Ped.Res.58:1978)is an adjunct in the assessment and treatment of infants undergoing abstinence and is comprised of 21 symptoms in varying degrees of severity including central nervous,metabolic,vasomotor,respiratory,and gastrointestinal disturbances. A factor analysis was performed on a sample of 100 random scores to determine which symptoms are primary indicators in order to simplify the scoring system and increase efficiency of care. The individual symptoms were then ranked according to their respective weights. The 7 variables with highest weights (LF>.02) were: tremors (disturbed), increased muscle tone,fever,excoriation,nasal stuffiness,high pitched cry, and hyperactive Moro reflex. Using these symptoms,and their degrees of severity,as a revised system,125 random matched scores were obtained and a comparison made. Correlation between the two systems was r=.85(p<.0001). A regression was calculated to establish a critical point on the revised system with the results that a 5 on the new system corresponds to an 8 on the current one (an 8 being the point at which treatment is initiated). The matched pairs of scores were then divided according to these critical points with the result that 112 pairs corresponded exactly for treatment/non-treatment status. Of the 13 scores which did not "match",8 infants would have been treated earlier on the revised system than on the current one, while 4 had local peaks and therefore would not have been treated on either system. This abbreviated scoring system, consisting of 7 pertinent symptoms of neonatal abstinence, may be a more efficient tool in the management of these infants.

286 POTENTIATION OF $MgSO_4$ INDUCED LETHALITY BY TOBRAMYCIN (TOB) AND AMIKACIN (AMK). C.S. L'Hommedieu, D. Armes, L.K. Pickering. Dept's of Anesthesia and Pediatrics University of Texas Medical School at Houston, Houston, Texas.

Aminoglycoside antibiotics potentiate muscle weakness in patients with presynaptic (botulism) or post synaptic (myasthenia, competitive blockade) neuromuscular transmission defects. Because two patients whose clinical course of muscle weakness due to hypermagnesemia worsened after aminoglycosides, and the similarity of action of Mg^{++} ion to botulinal toxin on the neuromuscular junction, we investigated the ability of tob and amk to potentiate $MgSO_4$ induced lethality in Swiss-Webster mice. Six week old male mice were given $MgSO_4$ in saline, or $MgSO_4$ was given after tob or amk so that peak levels of each drug (aminoglycosides and $MgSO_4$) would coincide. $MgSO_4$ alone produced death in 4 of 30 mice (13%). $MgSO_4$ plus three concentrations of tob (90 mice in each group) resulted in a significantly ($p< 0.001$) greater number of deaths when compared to matched groups given $MgSO_4$ alone ($MgSO_4$ + tob 25 mg/kg - 63% deaths, $MgSO_4$ + tob 50 mg/kg - 57% deaths, $MgSO_4$ + tob 100 mg/kg - 70% deaths). $MgSO_4$ plus three doses of amk also resulted in a significantly ($p< 0.001$) greater number of deaths, when compared to matched groups given $MgSO_4$ alone. ($MgSO_4$ + amk 50 mg/kg - 50%, $MgSO_4$ + amk 100 mg/kg - 70%, $MgSO_4$ + amk 200 mg/kg - 80%). Tob or amk alone did not generate symptoms associated with neuromuscular blockade or death. Aminoglycoside antibiotics potentiate neuromuscular block by further decreasing acetylcholine release.

287 PULMONARY DILATION FROM AMRINONE IN UNSEDATED LAMBS Mark Mammel, Stanley Einzig, Thomas J. Kulik, Theodore Thompson, James E. Lock. (Spon. by R. Lucas) Dept. of Pediatrics, Univ. of Minnesota Hosps, Minneapolis, MN

Amrinone(AM) is a non-glycoside cardiotonic agent currently used in adult heart failure. Although its neonatal myocardial effects are under study, its effects on systemic(SVR) and pulmonary resistance(PVR) are unknown. We placed flow probes around the R and L pulmonary arteries(PA) of 10 4-20 day old lambs and implanted LA lines. Lambs were studied in normoxia(N) and hypoxia(H) 5-9 days later, after catheter placement in the aorta(Ao) and just distal to RPA or LPA probe. Bolus doses of AM were delivered at 0.1, 0.3, 1.0, and 3mg/kg into R or LPA. Cardiac output(CO), LA, Ao, and PA pressures were measured continuously. SVR, PVR, the proportion of CO directed to the injected lung(Q_{inj}/Q_T), and the resistance in the injected lung over SVR(R_{inj}/SVR) were derived before and 10-120sec after injection. Seven lambs were studied in N and H; 5 were studied (1 mg/kg only) before and after propranolol (1 mg/kg IV).

	Q_{inj}/Q_T		CO(L/min)		Ao(mmHg)		PA(mmHg)		R_{inj}/SVR	
	N	H	N	H	N	H	N	H	N	H
Control	0.38	0.37	1.68	1.78	86	83	18	21	0.59	0.72
AM(0.3mg/kg)	0.43*	0.39*	1.67	1.87*	85	83	18	20	0.52	0.66*

AM is a direct PA dilator, lowering Q_{inj}/Q_T (threshold=0.3mg/kg). At higher doses, AM is a systemic dilator, lowering SVR*(1 mg/kg) and Ao pressure(3mg/kg). At every dose, AM lowers R_{inj}/SVR; the decrease is significant* in H at 0.3 and 1 mg/kg. AM did not change LA pressures; propranolol did not alter PA or Ao vasodilation.

AM directly dilates neonatal pulmonary vessels, and increases CO. In H, PVR is lowered more than is SVR. As such, AM may be useful in treating neonatal PA hypertension. (*p< 0.05)

288 HUMAN CYTOCHROME P-450:RESPONSE TO MATERNAL SMOKING IN PLACENTAS FROM MALFORMED NEONATES. David K. Manchester, (Spon. R. Gotlin) Univ. of Colorado School of Medicine, Departments of Pediatrics and Pharmacology, Denver.

Human cytochrome P-450 monooxygenase can be induced by polycyclic aromatic hydrocarbons (PAH). Enhanced activity is implicated in certain solid tissue cancers; nonresponse has been associated with leukemia. Placenta contains a P-450 system whose activity increases in response to smoking, presumably due to PAH exposure. This system can be identified by activity toward benzo(a)pyrene (BP) and 7-ethoxyresorufin (ER) and is specifically inhibited in vitro by 7,8-benzoflavone (BF). We measured BP and/or ER activity in placentas obtained at the delivery of 29 malformed neonates. Abnormalities included:neural tube defects(12), GI and GU anomalies (5), cleft lip and palate (4), congenital heart disease (3), amniotic band syndrome (2), and multiple malformations (3). Eighteen mothers smoked as determined by postpartum interview and cord blood thiocyanate levels. Placentas from 8 of these cases failed to respond to smoking (5 anencephaly, 1 cleft, 1 GI, 1 multiple anomalies). Applying these same criteria to concurrently determined placental activities from 54 normal pregnancies in smokers identified 3 nonresponses ($p<0.01$, Fisher's exact test). Inhibition of ER activity by BF indicates the expected cytochrome P-450 is probably present in nonresponsive placentas, but does not increase to anticipated levels. Although decreased estrogen in anencephaly could influence response to smoking, nonresponse was not limited to this defect and the findings may indicate increased risk for malformation in association with lack of response to PAH exposure.

● **289** THEOPHYLLINE INDUCED CEREBRAL ACIDOSIS DURING HYPERVENTILATION IN THE NEWBORN PIGLET. Francois Marchal, Pierre Monin, Paul Vert (spon. by Hakan Sundell). Centre de Recherche en Médecine et Biologie due Développement Humain. Université de Nancy I, France.

This study was designed to test whether the Theophylline (Th) induced decrease in cerebral bloodflow demonstrated in adult humans and animals affects cerebral tissue pH (C_tpH). The effect of Th on cerebral tissue-arterial H^+ concentration gradient (ΔH^+) was studied in 3 anesthetized newborn piglets (1) during hyperventilation (HV) (2) after a 10 mg/kg i.v. injection of Th and (3) during HV after Th therapy. C_tpH was continuously measured with a tissue pH electrode (Roche Bioelectronics) implanted in the cererbral cortex. Arterial blood pH was measured intermittently. Baseline C_tpH was lower than arterial blood pH (7.07-7.18* vs 7.39-7.42*). After HV, there was a slight decrease in ΔH^+ (- 10%, - 17%, - 20% respectively). Th did not affect baseline ΔH^+. However, in Th pretreated animals, HV was associated with a dramatic increase in ΔH^+ (+ 48%, + 77%, + 126% respectively). Indeed, after Th, HV resulted in a transient increase in C_tpH followed by a decrease from pre HV values (6.98-7.24*) to (6.96-7.10*), although blood pH remained in the range of 7.6 to 7.8. This phenomenon was never observed during HV before Th. It is suggested that the decrease of cerebral blood flow induced by HV in Th pretreated animals results in an impaired tissue oxygen supply and in subsequent tissue acidosis. It is concluded that Th induces cerebral acidosis during HV.
*RANGE.

292 PHARMACOKINETICS OF MOXALACTAM EPIMERS IN PEDIATRIC PATIENTS. Milap C. Nahata, William J. Barson, (spon. by Milo D. Hilty), Ohio State University Colleges of Pharmacy and Medicine, Children's Hospital Department of Pediatrics, Columbus, Ohio.

Moxalactam, a new 1-oxa-beta lactam is a mixture of R and S epimers. Although R moxalactam has been shown to be twice as active as S moxalactam against many microorganisms, their pharmacokinetics have not been reported. We studied the pharmacokinetics of R and S moxalactam in 12 patients (age 8-45 mo). Nine patients had periorbital cellulitis, 2 had epiglottitis and 1 had facial cellulitis. Patients received a single dose of moxalactam, 50 mg/kg intravenously over 20 min. Blood samples were obtained just prior to the infusion and at 0.5,1,2,4,6 and 8 hr after stopping the infusion. An HPLC method was used to measure the serum concentrations of R and S moxalactam. Total body clearance of R, S and R + S moxalactam ranged from 29.01 to 183.7, 19.00 to 79.95 and 23.34 to 113.6 ml/min/m^2, respectively. The respective apparent volumes of distribution of R, S and R+S moxalactam ranged from 6.68 to 25.3, 4.06 to 10.8 and 5.14 to 14.7 L/m^2. Total body clearance and apparent volume of distribution of R moxalactam were higher than S moxalactam ($p < 0.004$). Mean elimination half-lives of R, S and R + S moxalactam were 2.04, 2.26 and 2.24 hr, respectively. A five-fold interpatient variation and difference in clearance of the epimers may indicate the need for monitoring serum or CSF moxalactam concentration in patients with severe unresponsive CNS infections.

● **290** PHENOBARBITAL (PB) CHANGES IN BRAIN DURING RESPIRATORY ALKALOSIS IN NEWBORN PIGLETS. Pierre Monin, Paul Vert, Yves Badonnel, Paolo Morselli. (Spon. by William Oh). Centre de Recherche en Biologie du Développement Humain. Université de Nancy. LERS Synthelabo - Paris, FRANCE.

PB dissociation and distribution are related to pH, and tissue release is observed with alkalosis. To study brain PB release 9 anesthesized piglets (<10 days, 1060-2900 g) were studied 12 to 24 hrs after an intra peritoneal injection of 10 mg.kg^{-1} of PB. Arterial blood pH, arterial and venous PB levels and brain PB content were measured before and during respiratory alkalosis (pH range : 7.55 to 7.65). Brain tissue was sampled from the left hemisphere before and during alkalosis ; samples were obtained either before 10 minutes or after 10 minutes of hyperventilation.

Brain PB content changes show a biphasic pattern : early (10mn) after the onset of respiratory alkalosis, brain PB rises unexpectedly (+24±14%*) and decreases later on (-16±18%*). A negative correlation between ΔPB (%) and alkalosis duration at sampling was observed ($r=-0.8$, $p<0.01$). Arterial blood levels of PB increase early after the onset of alkalosis (+20.6±14%*) while venous levels were not significantly modified (-1.8±15.6%*). These data show 1) Brain PB changes significantly with pH. 2) Changes are dependent on the duration of alkalosis and PB release only occur after 10 mn. 3) The early rise of brain PB might be related to the rise in arterial PB; PB distribution changes might differ with organs and further studies are needed to explore these multicompartimental changes.
* mean + 1 SD.

293 BIOAVAILABILITY AND PHARMACOKINETICS OF CHLORAMPHENICOL (C) AFTER INTRAVENOUS (IV) CHLORAMPHENICOL SUCCINATE (CS) IN PREMATURE INFANTS. Milap C. Nahata, Dwight A. Powell, (spon. by Milo D. Hilty), Colleges of Pharmacy and Medicine, Department of Pediatrics, Children's Hospital, Columbus, Ohio.

Disposition of the prodrug, CS, affects the bioavailability and kinetics of C. An incomplete bioavailability of C has been reported in fullterm infants and children, no data are available for premature infants. We studied the bioavailability and kinetics of C in 5 patients with CNS infections (gestational age: 28 wk-37 wk; chronologic age: 5 wk-13 wk; weight: 1.8-2.6 kg). CS,12-28 mg/kg was given IV every 12 h over 0.5-1.0 h. At steady state, blood samples were obtained at 0, 0.5,1,2,4,6,8 and 13 h after starting infusion. Total timed urine output was collected over the same dosing interval. Both C and CS were analyzed by HPLC. Peak serum conc. of C and CS ranged from 10.11-59.86 and 2.62-40.98 µg/ml, respectively. Bioavailability of C ranged from 0.79-0.99 and total, renal, and nonrenal clearance from 0.88-3.17, 0.15-0.84 and 0.66-2.33 ml/kg/min; the respective clearances of CS ranged from 4.39-15.2, 0.17-2.7, 4.15-15.19 ml/kg/min. Urinary recovery of C was 10.1%-29.4% and that of CS was 0.5%-20.8%. Mean apparent volumes of distribution were 1.55 L/kg for C and 0.79 L/kg for CS and elimination half-lives were 10.1 and 0.9 hr, respectively. Incomplete bioavailability of C and 4-fold variability in clearance of both C and CS explain the need for individualizing doses to achieve therapeutic effect and minimize toxicity.

● **291** ADENOSINE 3'5'-MONOPHOSPHATE (cAMP) BINDING PROTEIN AND cAMP DEPENDENT PROTEIN KINASE (cAMP-PK) IN HUMAN PLACENTA. John J. Moore, Jennifer Pollinger, Jeffrey A. Whitsett, Children's Hospital Medical Center, Cincinnati

β-Adrenergic stimulation of placenta suppresses placental lactogen secretion and increases glycogenolysis, estrogen synthesis and HCG secretion. In this laboratory, β_1 adrenergic receptors coupled to catecholamine-stimulated adenylate cyclase have been previously demonstrated in human placenta. cAMP generated by adenylate cyclase presumably exerts its major intracellular effect by binding with cAMP-PK which in turn phosphorylates cell proteins. cAMP binding and cAMP-PK have not been previously identified in placenta. [^{3}H]cAMP binding to crude cytosol fractions of term placenta was rapid, saturable and reversible. Scatchard analysis was linear suggesting a single class of cAMP binding sites, $K_D=1.13\pm0.11\times10^{-8}$M, n=5, with a binding capacity of 1.27±0.18 pmoles/mg protein. Competition for the [^{3}H]cAMP binding site showed the potency order cAMP>>cGMP>> $N^{6}O^{2}$ dibutyryl cAMP, analagous to cAMP binding to cAMP-PK in other tissues. ADP, ATP and adenosine did not compete for the binding. cAMP-PK activity was demonstrated in the same crude fractions of placental cytosol by its ability to incorporate ^{32}P from [γ^{32}P]ATP into added histone protein (1.80±.15 fold stimulation, $p<.05$). Phosphorylation of endogenous placental proteins in both crude membrane and cytosol was also stimulated by cAMP ($p<.05$). DEAE-cellulose column chromatography performed to identify placental cAMP-PK isoenzymes showed two peaks of [^{3}H] cAMP binding and coincident cAMP-PK activity coresponding to classical Type I (31%) and Type II (69%) cAMP-PK. Regulation of placental function by catecholamines and other hormones known to mediate cAMP levels may be accomplished through phosphorylation of cell proteins by these cAMP dependent protein kinases.

294 CHLORAMPHENICOL SUCCINATE (CS) KINETICS CHANGE WITH TIME. Milap C. Nahata, Dwight A. Powell, (Spon. by Milo D. Hilty). Colleges of Pharmacy and Medicine, Ohio State University, Children's Hospital, Department of Pediatrics, Columbus, Ohio.

Bioavailability and kinetics of chloramphenicol (C) depend on the disposition of its prodrug, CS. Although an incomplete hydrolysis of CS to C has been shown, little is known about the change in CS kinetics during hospitalization. We studied CS kinetics on two occasions at steady state in 10 patients (age 4.5mo-17 yr). The kinetic studies were separated by 2-17d (7.3 ± 4.3d). Doses of CS were, 19.7-26 mg/kg q 6 hr and 19-25.4 mg/kg q 6 hr IV over 0.5-1.0 hr, respectively. Blood samples were obtained at 0,0.5,1,2,4 and 6 hr after starting infusion and analyzed by HPLC. Peak serum concentration ranges of CS after first and second studies were 22.9-181.6 and 18.7-57.9 µg/ml, while that of C were 16.9-46.3 and 12.5-37.6 µg/ml, respectively. Trough serum concentration ranges of C also decreased with time from 1.77-27.0 to 0.88-6.10 µg/ml. Total body clearance of CS after the first study, 9.32 ± 3.64 increased to 19.36 ± 7.32 ml/kg/min after the second study ($p < 0.005$). Apparent volume of distribution and elimination half-life of CS did not change considerably with time. An increase in CS clearance and decrease in C concentration may be due to an autoinduction of CS and C metabolism and/or increased renal elimination of unhydrolyzed CS with time. Serum concentration of C should be monitored frequently to detect changes in its formation from CS, particularly in children receiving CS for longer than 5 days.

295 RENAL CLEARANCE OF FUROSEMIDE IN PRETERM INFANTS ON MULTIPLE DOSE THERAPY. Z.D. Najak, D. Ellwanger, and A. Pruitt, Emory University School of Medicine, Atlanta Georgia.

Serum and urine concentrations of furosemide(F)were measured using gas chromatography in 2 groups of preterm infants. One group(S.D.)received a single bolus I.V.,dose of F(1mgm/kgm/day); the second group(M.D.)received 4 bolus I.V. doses of F(1mgm/kgm/6hrs.).Both groups were treated with F because of their persistent lung disease and the treatment period in both groups lasted 4 to 7 days.The mean gestational age of S.D. group was 29 weeks, and mean birth weight was 1013grams.For the M.D.group mean gestational age was 30 weeks and mean birth weight 1097grams. Postnatal age was similar for the 2 groups:6-17 days.At 6 hours after a dose, serum F concentrations(Se F),urine F clearance(R Cl)and diuresis during the 6 hour period(output)were calculated on initial(D1)and final(D4)treatment days:

	Se F (µgm/ml)		6Hr.R Cl(ml/min/kgm)		6Hr.Urine Ouput(ml)	
Groups	D1	D4	D1	D4	D1	D4
S.D.	(a) 4.68	(b) 6.57	0.04	0.04	29	29
M.D.	(c) 6.28	(d) 21.08	0.08	0.14	39	37

a vs. b, p = NS a vs. c, p = NS
c vs. d, p = 0.0001 b vs. d, p < .001

With multiple doses of F there is significant drug accumulation in serum.Despite increased exposure to the drug renal F clearance is minimal and does not equal total body clearance. The diuresis is proportional to the increased renal excretion of F.

● **296** POSTNATAL DEVELOPMENT OF α_1-ADRENERGIC RECEPTOR(α_1AR) IN MAMMALIAN LIVER. A.Noguchi (Spon. by Wm. J.Keenan) Dept. Peds, St.Louis Univ, Sch. of Med, St. Louis.

Catecholamine stimulated liver glycogenolysis and gluconeogenesis are vital mechanisms for glucose homeostasis, and are mediated by α_1AR in adult rat. However development of liver α_1AR is unclear. We studied postnatal ontogeny and thyroid regulation of α_1AR with specific α_1-adrenergic radioligand ^{3}H-prazosin on purified rat liver plasma membrane(LM) obtained from euthyroid control and PTU treated(17 day of 22 day gestation onwards) newborn rats.^{3}H-Prazosin binding to LM was rapid, saturable and reversible. Its competition with various non-labelled adrenergic agonists and antagonists for α_1AR sites showed stereoselectivity and potency order of inhibition:Prazosin=WB4101>Epi=Norepi>yohimbine>Isop, characteristic of α_1AR. The LM from all the rats had 7-8 fold enrichment of plasma membrane marker enzyme 5'-nucleotidase from crude homogenates. Postnatal changes of α_1AR were as follows:

	1d	5d	28-34d	Adult
Euthyroid	ND	145±11	1052±147*	873±76
(n)	(4)	(5)	(4)	(3)
Hypothyroid	ND	157±21	381±31*	-------
(n)	(4)	(4)	(4)	

M±SE fmoles/mg. prot., ND: not detected, * P< 0.01 t-test
Affinity (K_D) did not change with age or with PTU treatment and was approximately 0.1nM. Thus we conclude that liver α_1ARs develop postnatally, reaching adult level by 4 weeks normally and is regulated by thyroid hormone. The results support the hypothesis that cathecholamine stimulated glycogenolysis is not mediated by α_1AR in the early newborn period.

297 THE EFFECTS OF OBSTETRIC MEDICATION ON A SAMPLE OF IRISH INFANTS AND MOTHERS: A ONE YEAR FOLLOW UP. J. Kevin Nugent (Spon. by T. Berry Brazelton). In a sample of 47 normal middle class infants, we compared 24 infants whose mothers received no medication with 23 infants whose mothers received a single intramuscular injection (50 mg) of pethedine (the most widely used analgesic in Europe). They were assessed on the Brazelton scale on day 1 and 3, while the attitudes of mothers to pregnancy, labor and delivery and child rearing, and the extent of social support, were coded from interviews on day 3. At 1 month the Broussard Neonatal Perception Inventory and the Bates Infant Questionnaire were administered. At 12 months the Bayley Scales, Carey Temperament Scale, and Cohler Maternal Attitude Scale were administered. We found no differences in infant behavior due to drugs on the 7 clusters of the Brazelton scale but medication was related to maternal perception of infant behavior and temperament at 1 month, as measured by the Broussard and the Bates. The findings at 1 year suggest that the combination of obstetric and sociocultural variables explains more of infant behavior at 1 year than do the single effects of either class of variables alone. The influence of obstetric factors and neonatal behavior on later developmental outcome may be potentiated or attenuated by sociocultural (maternal perception, social support systems, child rearing practices, etc.) dimensions.

298 PROTEIN CARBOXYMETHYLTRANSFERASE (PCM) IN C-1300 MURINE NEUROBLASTOMA (MNB) CELLS. Maura C. O'Leary, Bernard L. Mirkin, and Robert F. O'Dea. Div. of Clin. Pharmacol. and Ped. Oncol., Depts. Peds and Pharmacol., Univ. of Minn., Minneapolis, MN 55455.

PCM has been identified in a variety of tissues derived from neural crest anlage including in vivo MNB (Mirkin and O'Dea, 1981). These observations have stimulated inquiries regarding the role of PCM in tumor growth and differentiation. A tissue culture line derived from MNB has been used to characterize the subcellular distribution and kinetic behavior of PCM.

The activity of PCM was determined in subcellular fractions of MNB cells after differential centrifugation. In the presence of exogenous substrate (+ gelatin), 51% of the PCM activity was present in the 100,000 x g supernatant and 28.8% in the 800 x g particulate fraction. Endogenous (- gelatin) activity, which reflects the relative amount of PCM and its methyl acceptor proteins, was low amounting to less than 2.6% and 0.5% of the total PCM activity present in the 800 x g particulate and 100,000 x g soluble fractions, respectively. The enzyme has an apparent Km of 13.9×10^{-6}M and a Vmax of 33 pmols/min/mg prot. Cytoplasmic PCM was competitively inhibited by adenosyl homocysteine (Ki=2.6µM), sinefungin (Ki=1.5µM) and A9145C (Ki=0.2µM).

These data demonstrate that the PCM activity of cultured MNB cells is located primarily in the soluble fraction similar to in vivo MNB and non-malignant neural tissues. Cultured MNB, however, exhibits lower endogenous PCM activity and a higher Km and Vmax than PCM derived from in vivo MNB. (Supported by USPHS Grant NS-17194 and the Minnesota Medical Foundation.)

299 ALTERATIONS IN FETOPLACENTAL DRUG METABOLISM AS A CONSEQUENCE OF CHRONIC MATERNAL ADDICTION: I. PLACENTAL CHANGES. Enrique M. Ostrea, Jr., James E. Balun, James N. Wardell. Wayne State University School of Medicine, Hutzel Hospital, Department of Pediatrics, Detroit.

The placenta is not just an inert barrier to the transfer of drugs between the maternal and fetal bloodstream but is actively involved in drug detoxification or biotransformation. It is important to determine whether alterations in placental drug metabolism is induced by chronic maternal addiction since the effects on the fetus could be far-reaching. We therefore studied 3 aspects of drug metabolism in the placentas of 4 drug dependent (heroin/methadone or alcohol) women and in 3 normal controls, namely: (1) reduction (neoprontosil), (2) conjugation (bilirubin) and (3) oxidation, type II (aniline).

RESULTS: There was no significant increase in the reduction (0.75±0.18 vs 0.72±0.06 µM/mg protein/h) nor conjugation (0.123±0.058 vs 0.109±0.058 µg/mg protein/h) ability of the drug dependent (DD) vs control placentas. However, there was a significant ($p<0.02$) increase in oxidation ability of the DD placentas (0.762±0.179 µM/mg protein/h) as compared to control (0.388±0.088).

IMPLICATIONS: Except by oxidation, the placenta of the drug dependent woman is unable to help the fetus in the metabolism of excess drugs by conjugation or reduction. Whether the increase in oxidation capability of the placenta affects the metabolism of both xenobiotic and endogenous (ex. steroids) compounds needs to be determined.

300 FREE VALPROIC ACID: STEADY STATE PHARMACOKINETICS IN CHILDREN WITH SEIZURES. N. Otten, K. Hall, J. Irvine-Meek, M. Verma, M. Leroux, D. Budnik, S. Seshia (Spon. by J. C. Haworth), Health Sciences Centre and University of Manitoba, Winnipeg, Manitoba, Canada.

Since VPA is extensively bound to plasma proteins, determination of free drug pharmacokinetic variables may be of therapeutic importance. In view of the paucity of such information, we present the following data from 6 children.

Subject	Age (Yrs)	$t_{1/2}$ (total) hours	$t_{1/2}$ (free) hours	V_D (total) (L/kg)	V_D (free) (L/kg)	Cl (total) ml/min/kg	Cl (free) ml/min/kg
1	6	8.4	4.1	0.214	1.25	0.29	3.5
2	21	7.6	3.2	0.185	0.84	0.28	4.0
3	5.5	4.6	5.5	0.166	3.45	0.4	7.3
4	15	7.4	4.8	0.171	1.46	0.27	6.1
5	11	7.4	7.5	0.147	0.89	0.23	3.3
6	16.5	9.4	4.7	0.251	1.34	0.41	5.3
Mean		7.5	5.0	0.189	1.51	0.30	5.6
±		±	±	±	±	±	±
S.D.		1.6	1.5	0.038	0.98	0.09	2.0

Regression analysis of % free VPA vs. total VPA demonstrated the following relationship:% free = $\frac{\text{total VPA} - 13.9}{5.39}$ (r = 0.836)

These results show that 1)%free drug concentration may vary fourfold over the total serum concentration range of 40-120 mcg/ml thus emphasizing the need for the establishment of a therapeutic range for free drug 2) the clearance of VPA is restrictive and therefore independent of liver blood flow but dependent on changes in the free fraction of the drug. This study was sponsored by the White Cross Guild, MMSFI and CHRF.

● 301 THE INFLUENCE OF AGE ON THE RENAL EFFECTS OF DOPAMINE

Juan C. Pelayo & Pedro A. Jose. Univ. Calif. San Diego Dept. of Medicine, San Diego and Georgetown Univ. Med. Ctr., Dept. of Peds., Washington, D.C.

The ability of dopamine (DA) to induce renal vasodilation is presumed to be one of its beneficial effects in the treatment of shock. However, the renal effects of DA in the newborn has not been evaluated. Thus we studied the renal effects of intrarenal infusion of DA in the puppy.(Group I=16.4±1.2 days,Group II=29.6± 1.6 days, Group III=49.8±2.5 days). Renal blood flow (RBF), glomerular filtration rate (GFR), urine flow(V) and fractional sodium excretion (FENa) were monitored. The results M± SEM are:

Group	Dose[a]	RBF(ml/min)	GFR(ml/min/gm)	V(ul/min)	FENa%
I	C	29.90±6.10	0.34±0.06	21.82±3.90	.16±.09
	0.5	34.91±6.22	0.32±0.05	20.22±3.78	.22±.10
	1.0	33.29±6.58	0.40±0.60	24.87±4.79	.60±.50
	5.0	30.76±5.78	0.26±0.04	12.23±1.90	.15±.07
II	C	46.98±2.78	0.69±0.14	38.30±10.42	.22±.05
	0.5	49.04±5.30	0.99±0.22	51.32±12.73	.46±.21
	1.0	46.30±4.00	*1.08±0.19	*70.20±13.50	*.80±.52
	5.0	50.60±4.94	0.56±0.07	41.43±9.75	.75±.44
III	C	48.80±1.96	0.61±0.08	135.29±60.37	1.35±.73
	0.5	51.96±2.01	*0.92±0.15	128.54±43.48	1.03±.60
	1.0	*56.92±3.47	*0.83±0.05	111.16±38.86	.91±.46
	5.0	54.51±5.68	0.82±0.06	87.49±23.20	.72±.31

a=ug/kg body wt/min C=control *p<0.05 paired t-test

These studies demonstrate the influence of age on neonatal response to dopamine. These findings coupled with our report of increasing glomerular DA receptors with age suggest a role of DA in maturation of neonatal renal function.

302 THEOPHYLLINE PHARMACOKINETICS IN INFANTS WITH BRONCHIOLITIS.

Dwight A. Powell, Milap C. Nahata, Thomas G. Franko, (Spon. by Milo D. Hilty) Colleges of Medicine and Pharmacy, Ohio State University, Children's Hospital Dept. of Pediatrics, Columbus, Ohio.

Although many infants with bronchiolitis receive theophylline (T), little is known about T pharmacokinetics in this age group. We studied T kinetics in 12 patients (age 3 weeks-6.5 mo) with normal liver, renal and cardiac function. Nine of the 12 patients received a single dose of aminophylline (5.0-8.5 mg/kg) whereas the remainder were at steady-state receiving multiple doses (2.5-5.0 mg/kg) of aminophylline. The dose was administered IV over 0.5-1.0 hr. Blood samples were obtained at 0,0.5,1,2, 4 and 6 hr after the start of drug infusion. In 6 patients, urine output was collected over the same dosing interval. Peak serum concentrations of T measured by HPLC ranged from 8.48-21.6 µg/ml. Total, renal and nonrenal clearance of T ranged from 4.66-19.3, 1.07-5.76 and 3.59-16.8 ml/min/m^2, respectively; renal clearance accounted for 15-50% of total clearance. Apparent volume of distribution and elimination half-life of T varied from 7.04-12.0 L/m^2 and 5.77-29.0 hr. Although no significant correlation was observed between age and theophylline kinetic parameters, clearance appeared to increase and half-life tended to decrease with age. Our patients had a substantially lower clearance and longer half-life as compared to published data in children > 1 yr of age. A five-fold variation in T clearance demonstrates the need for monitoring T serum concentration to individualize therapy.

303 KINETICS OF ACETAMINOPHEN (Ac) FOLLOWING SINGLE STRENGTH (SS-Ac) VS DOUBLE STRENGTH (DS-Ac) ADMINISTRATION TO FEBRILE CHILDREN.

Dwight A. Powell, Milap C. Nahata, (Spon. by Milo D. Hilty). Ohio State University Colleges of Medicine and Pharmacy, Children's Hospital, Dept. of Pediatrics, Columbus, Ohio.

Although Ac is one of the most widely used pediatric drugs, data are lacking to define optimal doses for fever control in young children. As part of a study comparing the efficacy and safety of SS-Ac (12-15mg/kg q 4hr) vs DS-Ac (24-30mg/kg q 8hr), kinetics of Ac were studied in 9 children ages 6 mo-6 yr randomly assigned to one of these regimens for a maximum of 3 days. Blood samples were obtained at 0,0.5,1,2,4,6 and 8 hr after the first and last dose. No other antipyretics were given for 6 hr prior to or during the study period. Serum conc. of Ac were measured by HPLC. All calculations were made assuming complete Ac bioavailability. Based on peak and trough Ac conc. after the first and last dose, no drug accumulation was noted over the study period. Respective peak Ac conc. (mcg/ml) after first and last dose were: SS-Ac (N=5) 15.57 ± 2.87 vs 18.10 ± 7.43; DS-Ac (N=4) 23.94 ± 12.42 vs 24.14 ± 12.28. Trough Ac conc. (mcg/ml) after first and last dose were: SS-Ac (at 4 hr) 5.22 ± 3.44 vs 6.34 ± 5.89; DS-Ac (at 8 hr) 5.76 ± 3.20 vs 4.87 ± 3.54. Ac kinetic values for the 9 pts after first and last dose were: clearance (ml/kg/min) 5.51 ± 2.81 vs 5.12 ± 3.28; Vd (L/kg) 0.97 ± 0.35 vs 0.74 ± 0.33; t ½ (hr) 2.13 ± 1.01 vs 2.26 ± 1.00. Liver enzymes remained normal up to 72 hr after the study. Without evidence of drug accumulation, we suggest a comparitive efficacy trial of fever control is safe to conduct.

304 OPTIMIZING CHLORAMPHENICOL THERAPY IN NEONATES

P.Rajchgot,C.Prober,S.Soldin,J.Chabot,F.Good, E.Harding and S.Macleod (Spon by D.Biggar), Hospital for Sick Children,Toronto.

Because of dose related toxicity, chloramphenicol (C) is used with caution in neonatal care. We have recently altered our approach to C use in an attempt to improve safety. The present study compares our early experience (period A) with more recent results (period B). During A drug vials containing C at a standard C concentration [C] of 100mg/ml were used. During B a 25mg/ml [C] was used instead and a drug monitoring team of research nurse biochemist, and pharmacologist assessed and reported serum [C]. Neonates in A (n=18) and B (n=17) were similar in gestational age birth weight and postnatal age. The same dosing regimen was used for both. Duration of therapy was 8.9±6.3d(m±SD) in A and 4.3±1.9 d in B. Three infants in each period had documented infection. All pre and post dose [C] were compared in A vs B. (units: mcg/ml

	A			B		
	Sample size	mean	SD	Sample size	mean	SD
Pre [C]	n=62	13.4	10.2	n=24	9.4	5.3
Post [C]	n=62	17.8	11.6	n=25	16.6	7.6

Though mean [C] was not significantly different between groups, the variance of [C] was significantly greater in A vs B ($p<.01$). The number of patients with [C]>40mcg/ml was 6 in A and none in B. Sequential [C]'s suggested administration errors in A,possibly related to high vial [C] and excess syringe dead space. We conclude that more dilute drug concentration, more rapid reporting and a team approach permitting close communication with ward staff can reduce the hazards associated with use of C.

305 PROLONGED HYPOGLYCEMIA IN AN INFANT OF A DIABETIC TREATED WITH CHLORPROPAMIDE.

Robert Rapaport, Minerva Castillo, Shyan C. Sun, Anne Koons, (Spon. by Franklin C. Behrle), CMDNJ-New Jersey Medical School, Department of Pediatrics, Newark, New Jersey.

A 2.9kg boy was born at 34 weeks of gestation to a 28 yr old non insulin dependent primigravida. Severely allergic to insulin the mother's diabetes had been well controlled during pregnancy with 200mg of chlorpropamide daily. Apgar scores were 4 & 5 at 1 & 5 min. He developed respiratory distress, lethargy but no convulsions. The blood glucose (BG) at 4 hrs of age was 9mg/dl. The baby required continuous infusions of glucose (CIG) of up to 20mg/kg/min to maintain euglycemia. He required two exchange transfusions (ET) at the ages of 5 & 6 days because of hyperbilirubinemia. He had no evidence of renal or hepatic dysfunction. His glucose requirement fell to below 10mg/kg/min only at 14 days of age. Cord and maternal serum chlorpropamide levels (SCL) were 51µg/ml and 40µg/ml respectively - normal therapeutic adult levels.

Age (days)	2	4	5 pre ET	5 post ET	6 pre ET	6 post ET	9
SCL µg/ml	51	38	47	21	27	13	5
CIG mg/kg/min	17	20	20	20	20	20	15
BG mg/dl	70	50	45	90	45	60	80
Insulin uU/ml	24						8

The persistence of elevated SCL in this baby indicates a prolonged and delayed metabolism and excretion of chlorpropamide in neonates compared with adults.

306 EFFECT OF THEOPHYLLINE ON BEHAVIORAL STATE DEVELOPMENT IN THE NEWBORN RABBIT.

John R. Raye, Louis P. Zeidner, Evelyn B. Thoman, Paul A. Kramer, Jonelle C. Rowe, Anthony F. Philipps, and Victor H. Denenberg. University of Connecticut Health Center, Departments of Pediatrics, Biobehavioral Sciences and Pharmacy, Farmington.

Theophylline (T) is widely used for treatment of apnea of prematurity. T is a central nervous system stiumlant with central effects in addition to those on the respiratory center. Clinically T is used during a period of rapid brain organization and maturation. For this reason we have investigated the effect of T on the pattern of state behavior maturation in the newborn rabbit. We have previously developed methods in the rabbit for quantifying state behavior and have characterized its developmental course which is remarkably similar to that of the human premature infant. Following a single dose of T (10 mg/kg) on the first day of life, state behavior of treated and control rabbits was measured blindly on days 2, 3, 5, 7, 15, 20, 30 and 40. T treatment significantly reduced the % of active sleep from day 2 through day 20 ($p<.01$). There was a concomitant significant increase in % wake seen on day 2 which persisted until day 30. An inhibition of the development of quiet sleep persisted until day 30. Both quiet and active components of wake were increased until day 30 ($p<.01$). Thus a single dose of T on the first day of life disrupted the pattern of state behavior maturation for 30 days thereafter. This alteration of early behavioral organizational events was not reversibly related to serum drug levels and raises serious questions of potential long term behavioral effects of this widely used drug.

● **307** THE PHARMACOKINETICS (PK) OF MOXALACTAM (M) IN PEDIATRIC PATIENTS. Michael D. Reed, Joseph S. Bertino, Carolyn Meyers, Marcia Husak, Jeffrey L. Blumer (Spon. by W.T.Speck). Case Western Reserve University School of Medicine, Rainbow Babies and Childrens Hospital, Department of Pediatrics and Pharmacology, Cleveland, Ohio.

The PK of M were assessed following the 1st dose and again during steady-state (ss) conditions in 18 children (0.1-26 years). All patients received 150 mg/kg/day IV in 3 divided doses. Multiple serum samples obtained during the 8 hour dosage interval were analyzed using a sensitive specific HPLC technique. First dose one-compartment PK analysis revealed $\bar{x}(\pm SD)$ $t_{1/2}$-1.6 hr (0.4), Vd-12.19 L/1.73m^2(6.4), Cl_{ToT}107.8 ml/min/1.73m^2 (36), and Cpmax 146.5 mg/L (48.5). No differences in these parameters were observed when compared to ss values. Two-compartment PK analysis could be performed in 9 of 18 patients; no significant differences existed between 1 and 2 compartment PK analysis. Statistically significant correlates ($p<0.05$) were observed between age and both $t_{1/2}$ and Cl_{ToT}. Comparison of these parameters to those obtained in adults revealed a shorter $t_{1/2}$ ($p<0.001$) and smaller Vd ($p<0.001$). In children <10 years of age, the $t_{1/2}$ was decreased ($p<0.05$) and Cl increased ($p<0.05$) from values obtained in older children. In addition, a significant ($p<0.05$) inverse relationship existed between $t_{1/2}$ and age for the children between the ages of 0.2-10 years. These data suggest that for most pediatric infections, 3 if not 4 divided daily doses is necessary to maintain adequate M serum concentrations. Moreover, as children develop, their elimination of M increases and plateaus just prior to adolescence.

308 INDUCTION OF PARALDEHYDE METABOLISM IN THE DOG BY PHENOBARBITAL. George C. Rodgers, Jr. (Spon. by Billy F. Andrews), University of Louisville School of Medicine, Department of Pediatrics, Louisville, Kentucky

Paraldehyde is a drug often used to treat refractory seizures in children. It is commonly used in patients who have previously received other anticonvalsants, some of which are known to alter hepatic drug metabolism. As paraldehyde is thought to be primarily cleared by the liver, the present study was undertaken to assess the effect of phenobarbital pretreatment on the rate of paraldehyde elimination.

Three male mongrel dogs were given paraldehyde, 0.25ml of a 4% solution/kg by intravenous infusion over 15 minutes. Multiple serum samples were obtained over a 8 hour period and analyzed for paraldehyde. Animals were then dosed for seven days with phenobarbital (5mg/kg/d). Following a two day drug free rest period the paraldehyde kinetic study was repeated. The serum half-life of paraldehyde was 2.1 hours (S.D=0.7) prior to phenobarbital treatment and 0.4 hours (S.D=0.24) post treatment ($p<0.05$). No significant differences in V_D were observed. Two dogs showed a small secondary peak at 4-6 hours after the dose, suggestive of enterohepatic recycling. We conclude that the clearance of paraldehyde is significantly increased by pretreatment with phenobarbital, a known hepatic enzyme inducer. Patients who have received prior treatment with enzyme inducing drugs may require higher doses of paraldehyde than patients who have not received such drugs.

● **309** IN UTERO METHADONE EXPOSURE - THREE YEAR FOLLOW-UP Tove S. Rosen and Helen L. Johnson, Spon. by L.S. James

This report presents findings from an ongoing follow-up study of children born to methadone-maintained mothers(M) and a matched comparison group(C) at three years of age (N_M=28,N_C=15). A physical evaluation and review of clinical course, a neurological assessment, and behavioral evaluation including the Merrill-Palmer Scale of Mental Tests(MP), were performed on all subjects. There was no significant difference between groups on height, weight or rate of infections. However, there were significantly more head circumferences(HC) below the 3%ile in M vs. C ($p<.01$). Suspect or abnormal neurological findings, including eye findings and abnormalities in tone, coordination and language, were also more frequent in M vs. C ($p<.05$). The eye findings, which were strabismus and/or nystagmus, occurred in 34% of M, but in none of C. Although the groups did not differ in overall performance on the MP ($\bar{X}_M$=51.67±27.27; $\bar{X}_C$=56.73±22.61), low scores were significantly more frequent in M (31%) than C(7%) ($p<.003$). While MP scores were not correlated with eye findings or neurological assessments, they were significantly related to HC at birth ($r=.40$, $p<.02$) and at 36 months of age ($r=.52$, $p<.01$). Our studies show that a positive correlation between HC at birth and neurobehavioral outcome in infancy persists through early childhood. The data presented here indicate that maternal methadone maintenance is associated with impaired development; specifically, smaller HC, eye findings, developmental delays and lower IQ scores.

310 EFFECTS OF $CaNa_2EDTA$ ON LEAD (Pb) AND TRACE METAL METABOLISM IN BONE ORGAN CULTURE. John F. Rosen, Hobart Kraner, Keith Jones. Albert Einstein Coll. Med., Montefiore Hosp., Dept. Pediatrics, New York City; Brookhaven National Laboratory, Dept. of Physics, New York.

Little is known concerning interactions between Pb, trace metals and bone, the primary site of Pb storage and the major source of chelatable Pb. To understand further the metabolism of Pb and essential metals, these elements were studied within the strictly defined chemical conditions of bone organ culture. Fetal rat bones, dissected free from cartilage, were cultured for 120H in plain BGJ medium (control = C) or BGJ + $CaNa_2EDTA$ (treated bones = T). At 120H, bones were ashed, solubilized in HNO_3, and 25 µl were mounted on a mylar target. Elemental characteristic x-rays, excited by a 2.5 Mev proton beam, were observed with a Si(Li) spectrometer. X-rays for the metals analyzed from blanks, standards, and solubilized control and treated bones were measured by computer analysis of the spectra. The results (*$p<.01$, **$p<.001$ for T vs C bones), in µg/100 mg bone ash (mean ± SE), at $CaNa_2EDTA$ medium levels of .001 and .05 mM, respectively, were: Pb: 31±1*, 25±1**, Zn: 38±2*, 18±1**; Cu: 3±0.5, 2±0.5; Cr: 11±1*, 3±0.5**; Fe: 18±2, 9±1**, Mn: 3±0.5**, undetectable**. Complementary studies examined effects of Zn medium levels on bone resorption: at Zn concentrations $<10^{-5}$M, the release of previously incorporated ^{45}Ca and ^{210}Pb was enhanced from bone explants to the medium. Conclusions: 1) Bone losses of essential metals accompany Pb chelation in vitro; this may occur in vivo as well; 2) A reduction in medium (ECF) Zn enhances bone resorption thereby increasing Pb efflux.

311 EFFECT OF β RECEPTOR BLOCKADE (PROPRANOLOL) ON BRAIN AND HEART MITOCHONDRIAL ACTIVITY OF HYPOXIC GUINEA PIGS. Linda M. Sacks, David W. Herbert, Joseph W. Starnes, Ellen O. Fuller and Maria Delivoria-Papadopoulos. Univ. of PA. School of Med., Depts. of Physiology and Pediatrics, Phila., PA.

Mitochondria adapt to hypoxia in-vivo by increasing state 3 respiratory rate (RR). Epinephrine administration in-vivo and perfusion of isolated organs with cyclic AMP produce a similar rise in mitochondrial RR. The present study investigates the role of β receptor stimulation as a mediator of mitochondrial adaptation to hypoxia. 10 guinea pigs, of which 6 received .5 mg/kg/IV propranolol, breathed 8% O_2. 3 guinea pigs received propranolol while breathing room air. Brain and heart subsarcolemmal mitochondria were isolated and state 3, state 4 RR (nmol O_2 min^{-1} $nmol^{-1}$ cytochrome oxidase ± SEM) assayed. Heart mitochondria of propranolol-treated normoxic animals had 23% higher state 3 than controls (342 ±23 vs. 419±12, $p<.05$). Hypoxia produced an 8% increase in heart state 3 RR in propranolol-treated animals. Hypoxia without β blockade produced a 29% increase in heart state 3 (342±21 to 442±59, $p<.05$). Brain mitochondria of normoxic propranolol-treated animals had 28% lower state 3 RR than controls. However, brain mitochondria in propranolol-treated animals responded to hypoxia by increasing state 3 RR 29% (465±42 to 600±19, $p<.01$). Propranolol has been shown to decrease O_2 requirements in rat brain and in ischemic myocardium. In the present study during hypoxia, in-vivo β blockade did not prevent increased mitochondrial state 3 RR in the brain, and only partially blunted the increase in heart mitochondrial RR. These data suggest that mitochondrial adaptation to hypoxia may be independent of β receptor stimulation.

312 6β-HYDROXYCORTISOL (6βOHF) AS INDEX OF MICROSOMAL INHIBITION IN LEAD BURDENED CHILDREN. P. Saenger, M.E. Markowitz, J.F. Rosen, Dept. Ped. & CRC, A. Einstein Coll. Med., Bronx, N.Y.

6βOHF is a normally occurring polar urinary metabolite of cortisol formed by the cytochrome P-450 dependent mixed function oxidase (MFO) system in the liver. Lead (Pb) ion inhibits hepatic microsomal activity in animals. We therefore evaluated the usefulness of 6βOHF excretion as an index of inhibition of microsomal function in 20 children (age 1-9 yrs) with mild to moderate increases in Pb burden (blood Pb 30-69µg/dl) and normal renal function. Since the $CaNa_2EDTA$ provocative test provides the most accurate "chemical biopsy" of chelatable Pb stores we examined the correlation between 6βOHF and urinary Pb excretion (Pb_u) after $CaNa_2EDTA$ provocation. We observed a highly significant correlation between 6βOHF and Pb_u ($r=-.60$, $p<.001$), but none between blood Pb and 6βOHF ($r=-.08$). Closer examination of 12 children with positive $CaNa_2EDTA$ provocative tests (Pb>500µg/24h) showed that 6βOHF was markedly reduced to 180±17 vs 280±30mg/m^2/24h in normal age matched controls ($p<.01$). Urinary free cortisol (FF) was normal in Pb burdened children (39±4 vs 40±2µg/m^2/24h in nl controls). There was no correlation between FF and blood Pb or Pb_u ($r=.05$ and .03 respectively). This suggests that adrenal function is not suppressed in this group of Pb burdened children.

Conclusions: Pb may inhibit MFO in children. An inverse correlation exists between 6βOHF and Pb_u but not blood Pb. In particular those with positive provocation tests have markedly reduced 6βOHF excretion. Thus measurement of 6βOHF appears to be a clinically useful, non-invasive probe in the evaluation of soft tissue lead burden in children.

313 DISTRIBUTION AND METABOLISM OF 125 I EXOGENOUS INACTIVE BIG RENIN IN THE NEWBORN PUPPY. Sharon R. Siegel and Terry Parkhill, Department of Pediatrics, UCLA, Los Angeles, Calif.

Human plasma has approximately two-thirds of its renin activity in the form of inactive renin, which could be secondary to a slower clearance rate than active renin. Active renin has a half-life of 12-20 min in the newborn piglet. The distribution and metabolism of exogenous 125 I inactive human plasma big renin, M.W. 56,000, was studied in 5 newborn puppies. The animals were sacrificed and the organs removed and studied chromatographically along with periodic blood samples during the 120 min study, for evidence of conversion of high-molecular-weight renin to low-molecular-weight renin. The decay curve had an initial rapid phase of 10 + 1.5 min followed by a slower elimination half-life of 40 + 4.6 min. 125 I inactive big renin was taken up by the red blood cell and released slowly. The liver, kidneys, and lungs had the highest percentage of 125 I inactive big renin at the termination of the study; and there was no evidence of a change in molecular weight. Conclusion: In the newborn puppy: 1) inactive big renin has a slower clearance half-life than active renin in the newborn piglet, 2) blood cells could form one compartment and act as a reservoir for inactive renin, and 3) there is no evidence of conversion of high-molecular-weight renin to low-molecular-weight renin in the blood or tissues.

314 DIFFERENCES IN CLINICAL RESPONSE TO AMINOPHYLLINE AMONG PRETERM INFANTS WITH APNEA. Maureen E. Sims, Gloria Yau, and Paul Y.K. Wu. Univ. of So. Calif. Sch. of Med., LAC-USC Med. Ctr., Dept. of Peds., Los Angeles, CA.

Aminophylline (A) is widely used to treat apnea in preterm infants. In order to determine the relationship of gestational age (GA) and birth weight (BW) to the efficacy of A, we conducted a randomized, controlled study of 31 preterm infants with apnea of prematurity. Their mean GA=31+2.3 wks. and BW=1309+331 g. Infants in the study had a minimum of 3 apneic episodes ≥ 20 sec. in an 8 hr, period or 6 in a 24 hr. period. The infants were divided into two groups. Group A (17 infants) received a 7 day course of A with a loading dose of 6.8mg/kg and a maintainence dose of 2.0 mg/kg q8h. Mean serum level of A was 7.1+2.2 mg% on the 2nd to 3rd day of therapy. Group B (14 infants) were controls, and did not receive any A. Results: In Group A, 5 infants had increased apnea and developed respiratory failure requiring assisted ventilation. In 1 infant the apneic spells remained unchanged on A. The GA and BW for these 6 infants were 26-30 wks, and 690-1130g respectively. Two of these infants died. In Group B, 5 infants developed respiratory failure. The GA and BW for these infants were 27-29 wks, and 820-1040 g respectively. There were 2 deaths in this group. For the non-respirator infants the decline in apnea in Group A was 3-4 times greater than in Group B. The data indicate that in preterm infants with apnea: 1) A was effective in reducing the frequency of apnea in infants whose GA> 30 wks and BW>1130 g, but ineffective in those with lower GA and BW.2) A did not decrease the need for assisted ventilation 3) A did not alter mortality.

● **315** PHENYTOIN TERATOGENIC INJURY IN A MOUSE ANIMAL MODEL-POSSIBLE ROLE OF A REACTIVE METABOLITE. Wayne R. Snodgrass. (Sponsored by: Michael D. Bailie)

To test the hypothesis that the fetal hydantoin syndrome is due to metabolic activation of phenytoin to a toxic metabolite, pregnant mice were given phenytoin with or without pretreatment by an inducer, phenobarbital (Pb), or an inhibitor, piperonyl butoxide (Pip) of drug metabolism. Phenytoin treatment alone produced a 42% incidence of teratogenic injury (cleft palate and resorptions); controls had a 3.0% incidence. Pb pretreatment increased the incidence of teratogenic injury to 100%. Pip pretreatment decreased the incidence of teratogenic injury to 36%. In another group of experiments young adult male mice were given phenytoin in a single i.p. dose. Liver glutathione (GSH) was determined 4 hours after the dose. Pretreatment with Pb lowered liver GSH content from 82% of control non-pretreated to 53% of control. Pretreatment with Pip entirely prevented the decrease in liver GSH by phenytoin. Pretreatment with butylated hydroxytoluene (BHT), an inducer of epoxide hydrolase, prevented phenytoin-induced GSH depletion.

These data demonstrate that: 1. phenytoin teratogenic injury in this mouse animal model is increased or decreased by inducers and inhibitors of drug metabolism, respectively; 2. phenytoin produces liver GSH depletion; 3. this GSH depletion is increased or decreased by inducers and inhibitors of drug metabolism, respectively. The conclusions from these data are: 1. phenytoin teratogenic injury may occur via a reactive metabolite; 2. this reactive metabolite possibly may be an epoxide.

● **316** PHENYTOIN EXPOSURE IN UTERO PRODUCES INFERTILITY IN FEMALE OFFSPRING. B.R. Sonawane, M. Kobylkevich, M. DeRosa and S.J.Yaffe, Dept. of Peds., Uni. of Penn. and Children's Hospital of Philadelphia, Phila., PA 19104

Drug exposure during pregnancy may result in permanent reproductive dysfunctions in progeny. We have previously demonstrated in the rat that prenatal phenobarbital exposure results in reproductive disorders in the offspring (Science 208:508,1980). Therefore, we examined the possibility of whether phenytoin (P), a known teratogen and a structurally related anticonvulsant, is also capable of causing reproductive dysfunctions. Timed-pregnant rats (CD strain) were injected (SC) with a single daily dose of Na phenytoin (75mg/kg body wt) dissolved in 0.1N NaOH on 17 thru 20 days of gestation. Control mothers were given vehicle. Pregnancy was uneventful and P treated mothers delivered litters which appeared normal, except for body weight which was significantly decreased. P treated offspring (16 wk old), when mated with normal adult stud males, had a higher incidence of infertility, despite the presence of sperm in the vagina (P-30% vs C-16.7%). In addition, the mean number of implantation sites per animal was markedly reduced (P-11.0 vs C-15.8). The mean rate of resorption was higher (38.2%) in P offspring than in control (6.1%). As a consequence, P offspring had a fewer number of live fetuses (P-8.0 + 1.8 vs C-15.0 + 1.2). These findings suggest that prenatal phenytoin exposure during the period of neuroendocrine differentiation adversely affects the fertility of offspring. The basic mechanisms by which phenytoin contributes to these manifestations are unclear. (Supported in part by NIH-HD10063).

● **317** INCREASED ACETAMINOPHEN TOXICITY IN LYMPHOCYTES HETEROZYGOUS FOR GLUTATHIONE SYNTHETASE DEFICIENCY: FAILURE OF N-ACETYLCYSTEINE PROTECTION. Stephen P. Spielberg, Hospital for Sick Children, Div. Clin. Pharm., Toronto

Glutathione(GSH) serves as a major cell defense against toxicity from metabolites of drugs such as acetaminophen(APAP). Patients heterozygous for GSH synthetase deficiency(GSH-SH) are phenotypically normal in the absence of drug-induced stress, and have normal baseline intracellular GSH content. We have studied the response of GSH-SH lymphocytes to APAP metabolites generated by a murine hepatic microsomal system. Cells were incubated with microsomes and APAP for 2 hrs, collected by centrifugation, suspended in drug and microsome-free medium for 16 hrs, and toxicity assessed by trypan blue dye exclusion. GSH-SH cells had normal baseline viability. However, the cells showed significant damage at low APAP concentrations which were non-toxic for normal cells, and had an increased percent of dead cells at high concentrations (normal:18.3+0.5% dead cells at 1.5mg/ml APAP; patients:29.9+0.5% and 29.7+1.5%). N-Acetylcysteine added to the medium after the 2 hr drug challenge decreased toxicity in normal cells(3.9+0.5%), but did not alter GSH-SH cell toxicity. GSH-SH cell GSH content did not recover as much as in normal cells when incubated with N-acetylcysteine after APAP exposure. N-Acetylcysteine may protect cells in part by providing cysteine for synthesis of GSH which, in turn, may be involved in cell repair processes after APAP-induced damage. GSH-SH patients(prevalence approx. 10^{-4}) may be at increased risk for APAP toxicity, and may not be protected by N-acetylcysteine because of decreased ability to regenerate GSH after APAP challenge secondary to their ½ normal enzyme activity.

● **318** ANTICONVULSANT-INDUCED APLASTIC ANEMIA: INCREASED SUSCEPTIBILITY TO TOXIC DRUG METABOLITES IN VITRO. S.P. Spielberg, W.T. Gerson, D.G. Fine, Johns Hopkins Schl. Med., Depts. of Pediat. and Pharmacol., Baltimore, and Hospital for Sick Children, Div. Clin. Pharm., Toronto.

A patient sequentially developed aplastic anemia from phenytoin and carbamazepine. Both compounds undergo metabolism to potentially toxic arene oxide metabolites(AOM). We tested the hypothesis that the patient's adverse reactions were due to decreased ability to detoxify AOM by challenging his peripheral lymphocytes with metabolites generated by a murine hepatic microsomal system. The patient's cell viability was normal in the absence of drugs. Phenytoin metabolites produced dose-dependent(31-125uM) toxicity from 10.6 to 22.6% dead cells; normal cells from 20 control subjects showed no toxicity above baseline(approx. 5%). Carbamazepine metabolites also produced greater toxicity to patient cells than to controls. Toxicity was dependent on microsomes and NADPH, was enhanced in normal cells by inhibiting epoxide hydrolase, and was blocked by adding purified epoxide hydrolase to the medium. Cells from another patient with phenytoin toxicity who tolerated carbamazepine without sequelae showed increased toxicity from phenytoin but not from carbamazepine metabolites. While no relatives of the first patient were available for study, the defect in detoxification in the second patient was expressed in relatives' cells as an autosomal recessive trait. The results provide the first evidence for the role of AOM in the pathogenesis of aplastic anemia in humans. Individual differences in cell response to potentially toxic AOM may be due to genetically heterogeneous defects in detoxification of these metabolites.

319 PLASMA GLUCOSE CHANGES DURING THEOPHYLLINE THERAPY. G. Srinivasan, J. Singh, R.S. Pildes, T.F. Yeh, Cook County Hospital, Depart. of Pediat. Chicago, Ill.

Changes in daily plasma glucose after oral theophylline (T) therapy were studied in 13 apneic or respirator dependent preterm infants. Glucose was measured 1-2 hrs after each morning dose of T. All infants were on nasogastric drip feedings and/or intravenous fluids. Serum T levels ranged from 6-9µg/ml. Gestational age (mean±SEM) was 31±0.67 wks and postnatal age at the time of study was 14.7±10.4 days. Total duration of treatment was 8.8±0.8 days.

		Glucose(mg%)	Cal/Kg/Day	Glucose(I.V.) mg/kg/hr
-24 hrs	(13)	73.4 ± 4.6	73.9 ± 8.6	262 ± 53
Day 0	(13)	73.0 ± 5.1	73.5 ± 8.5	279 ± 49
Day 1	(12)	95.0 ± 5.8**	74.8 ± 8.7	280 ± 56
Day 2	(11)	91.5 ± 3.7**	89.1 ± 8.2**	250 ± 57
Day 3	(11)	90.0 ± 6.0*	98.2 ± 8.4**	215 ± 61
Day 4-6	(9)	90.2 ± 3.35*	99.8 ± 8.4**	185 ± 64**
Day ≥ 7	(9)	87.4 ± 4.3	116.7 ± 14.2**	
Post Rx	(10)	80.3 ± 2.8	121.6 ± 13.1***	

***p<0.01 (two tail), **p<0.05 (two tail), *p<0.05 (one tail)

There was a significant increase in plasma glucose during Day 1 through 6; the values then decreased and glucose values were not different from those at base line after 7 days of T and after therapy was discontinued. The increase in plasma glucose could not be attributed to caloric intake or I.V. glucose and was probably mediated through cyclic AMP. Hyperglycemia (plasma glucose >150mg%)was not noted during the study period.

320 PHARMACOKINETIC EVALUATION OF CIMETIDINE IN INFANTS. Ina Stile, Robert Simon, I. Mark Hiatt, Thomas Hegyi,(sponsored by L. Stanley James)Department of Pediatrics, CMDNJ-Rutgers Medical School, St. Peter's Medical Center,New Brunswick, NJ and Department of Pediatrics, Monmouth Medical Center, Long Branch, NJ.

Cimetidine, an H_2 receptor antagonist, blocks histamine induced acid secretion. Cimetidine has been successfully used in the management of reflux esophagitis in newborns, although little is known about the pharmacokinetic characteristics of this drug. We administered cimetidine 10 mg/Kg intravenously to one term infant with a gastrointestinal bleed and orally to a second infant with reflux esophagitis. Venous blood samples were drawn at 0.5, 1,2,4 and 8 hours after the initial dose. Concentration of drug in plasma was assayed by high pressure liquid chromatography.

After I.V. administration the serum half life was 1.8 hours and the clearance rate was 730 ml/kg/hr. The half-life and clearance rate was 2.2 hours and 500 ml/Kg/hr respectively after oral administration. Maximum serum levels observed were 5.0ug/ml (IV) and 4.2 ug/mL (PO) at 30 minutes, and minimum levels of 0.3ug/ml (IV)and 0.6ug/mL (PO) at 8 hours. A serum level of 0.5ug/mL is necessary to achieve 80% suppression of gastric acid secretion. The higher level attained after oral administration may be due to delayed absorption of cimetidine. Our preliminary results indicate that the elimination of cimetidine in infants is similar to that in adults. Oral and intravenous administration appears to result in equivalent elimination patterns. Current dosing guidelines suggesting the administration of 5-10 mg/kg of cimetidine every twelve hours may not be applicable to infants. Our data implies that a lower dose and decreased dosing interval may be necessary in order to avoid potential adverse CNS, renal, and hepatic reactions.

321 THE EFFECT OF AMINOPHYLLINE ON BRAIN BLOOD FLOW IN THE PIGLET WITH CONTROLLED VENTILATION. Barbara S. Stonestreet, Philip T. Nowicki, Nancy B. Hansen, and William Oh,, Brown Univ., Women & Infants Hosp., Dept. of Ped., Providence, RI

Aminophylline (A) constricts the cerebral vasculature and reduces brain blood flow (BBF) in the adult because of hyperventilation induced hypocapnea and/or direct pharmacologic effects of the drug on the cerebral blood vessels. To examine the direct pharmacologic effects of A upon the newborn cerebral vasculature, BBF (by microsphere technique) and brain O_2 consumption (BVO_2, by Fick's principle) were determined in 14 piglets (age 1-6 days) with controlled ventilation before and after intravenous administration of 6mg/kg of A (n=9) or placebo (n=5). Arterial hematocrits, pH, pCO_2, and pO_2 remained unchanged throughout the studies.

	Minutes Post Aminophylline			
	0	15	45	85
Total BBF	109±38 M±SD	100±27	112±54	114±43
Cerebrum (ml/min/100gm)	109±36	103±29	116±59	118±49
Cerebellum	122±41	108±31	118±50	114±45
Brain Stem	125±62	111±36	123±73	129±52
BVO_2 (µM/min/100g)	285±90	259±38	274±65	297±74
(A) Plasma Conc. (mg/dl)	0	7±2	7±2	6±1

Piglets receiving placebo showed no changes in the above parameters. The data indicate that A does not have a direct pharmacologic effect on BBF and BVO_2 in the piglet with controlled ventilation. Hypocapnea-mediated cerebral vasoconstriction by A in spontaneously breathing piglets is currently being studied in our laboratory.

● **322** IV MORPHINE FOR YOUNG CHILDREN BASED ON TOTAL BODY CLEARANCE. H. Vandenberghe, H.Chinyanga,L.Endrenyi, S.MacLeod,S.Soldin, Spon. S. Spielberg, Research Institute, The Hospital for Sick Children, Toronto, Canada.

The use of intravenous (IV) morphine in combination with muscle relaxants, nitrous oxide and oxygen in balanced anaesthesia is of growing importance in children, but optimal dosage and rate of morphine administration is controversial due to limited available pharmacokinetic information. We have studied 12 children from birth to 5 yr of age receiving IV morphine as part of balanced anaesthesia regimens at varied dosages including bolus injections of 11 and 50 µg/kg and maintenance infusions of 1 and 2 µg/kg/min. In order to determine morphine serum concentrations we developed a sensitive and specific assay by reverse phase paired-ion high performance liquid chromatography with electrochemical detection. Only 100 µl serum or plasma is required for analysis permitting quantitation at multiple points. Total body clearance (TBC) of morphine was 21.1 ± 2.4 ml/kg/min ($\bar{X}$ ± SD, n= 11), a value significantly greater than the TBC of 6.2 ml/kg/min reported by Dahlström et al. (Clin. Pharmacol. Ther. 26:354-365, 1979) for children aged 1-7 yr after a single dose. From our data it appears that a loading dose of 50 µg/kg over 5 min followed by a maintenance infusion of 2 µg/kg/min will provide a steady state serum morphine concentration between 80 and 100 µg/L. The minimum serum concentration for analgesia during surgery in children approximates 65 µg/L according to Dahlström (see above). Calculation of parenteral morphine dosage for children must take into account a TBC three times greater than previously realized if subanalgesic serum concentrations are to be avoided.

● **323** CONCENTRATION-RELATED LOWERING OF PULMONARY VASCULAR RESISTANCE (PVR) RELATIVE TO SYSTEMIC VASCULAR RESISTANCE (SVR) BY TOLAZOLINE (TZ). RM Ward, CH Daniel, and SR Willis (Spon by MJ Maisels). Penn State Univ Coll of Med, M. S. Hershey Med Ctr, Dept of Peds, Hershey, PA.

TZ has been administered to newborns to lower PVR since the first description of persistent fetal circulation (PFC). Right to left cardiovascular shunts in PFC prevent accurate measurement of vascular resistances in newborns. Cardiovascular effects of TZ have not been reported in animals without anesthesia or surgery on the day of study, nor correlated with plasma TZ concentrations ([TZ]).

A chemically specific micro-assay for TZ was developed and used to determine pharmacokinetic parameters for TZ in lambs in order to achieve steady state [TZ] (coefficient of variation <15%) rapidly. Lambs were prepared for study by peripheral insertion of catheters 16+ hours before study. After a control period, a series of increasing [TZ] (similar to those observed in neonates) were achieved (2-5/experiment) and confirmed by chemical analyses. Cardiovascular resistances and heart rate were determined 3-5 times at each concentration, averaged and compared to control. The relationship between cardiovascular parameters and log [TZ] from 0.30 to 11.71 mcg/ml (N=24) were analyzed. Increasing [TZ] produced a concentration-related increase in cardiac index ($p<0.05$), decrease in SVR ($p<0.01$, slope = -15.8), and decrease in PVR ($p<0.001$, slope = -28.2). Thus, increasing [TZ] decreases PVR twice as rapidly as SVR.

● **324** VITAMIN E INHIBITION OF HYPEROXIA EFFECTS IN THE NEWBORN RABBIT LUNG. Jill A. Ward and Robert J. Roberts, Depts. Pediatrics and Pharmacology, University of Iowa College of Medicine, Iowa City, IA 52242.

Rabbit pups delivered via Caesarian-section at 31 days gestation (term) were housed in temperature, humidity and bacterially controlled chambers and exposed to 95+% oxygen or air for 48 hours. 100 mg/kg vitamin E or placebo was administered S.Q. at 1 and 24 hours of life. On sacrifice, the pups' tracheas were cannulated for pressure-volume determinations and lavage collection, or for glutaraldehyde fixation and morphometric analysis. Oxygen exposure resulted in 25% less total lavage phospholipid content, smaller relative concentration of lavage phosphatidylglycerol (2.3 vs 3.6% total phospholipid), smaller maximum lung volumes and a higher pressure to inflate the lungs to 30% maximum volume (19.2 vs 15.5 cm H_2O). Additionally, reduced air: tissue ratios were determined from lung sections in oxygen-exposed pups as compared to air-treated littermates. Treatment with vitamin E was shown to completely abolish all these effects of hyperoxia, with values for oxygen-exposed +vitamin E-treated pups unchanged from those for air-exposed controls. Vitamin E treated air-exposed animals were found to be the same as placebo-treated, air-exposed littermates. These data indicate that hyperoxia exposure in the newborn rabbit affects the lung biochemically, functionally, and morphologically. Vitamin E treatment restores these changes to control values without exerting any additional effect of its own in the control, air-exposed situation. Thus, vitamin E treatment may act as a protectant in the lung challenged with hyperoxia, possibly through its action as an antioxidant. Supported by NIH predoctoral Traineeship #GM07069.

325 TISSUE DISTRIBUTION OF GENTAMICIN IN LAMBS: EFFECT OF POSTNATAL AGE AND ACUTE HYPOXEMIA. Douglas Weismann, James Herrig and Oliva McWeeny (Spon. by Jean Robillard), Univ. of Iowa Col. of Med., Dept. of Ped., Iowa City.

Gentamicin tissue distribution and uptake were studied in chronically-catheterized lambs (n=28) in relation to their possible role in postnatal age- and hypoxemia-related effects on serum gentamicin concentration (S_{Gent}). Gentamicin was administered intravenously in a dosage of 2.5 mg/kgBW(n=18) or 10 mg/kgBW(n=10). Lambs were grouped as young (less than 1 week of age, n=13) and older (2-5 weeks of age, n=15) and were studied during normoxemia or hypoxemia (mean pO_2 36±7 torr). Tissue blood flow (TBF) to liver, spleen, ileum, jejunum, skeletal muscle, heart, adrenal and kidney was determined by radiolabelled microspheres. Gentamicin delivery to these organ tissues (D_{Gent}, calculated as product of TBF and S_{Gent}), tissue gentamicin content (T_{Gent}) and S_{Gent} (determined by radioimmunoassay) were dose-dependent. S_{Gent} (µgm/ml) per unit (mg per kgBW) dose was significantly higher ($p<0.05$) in older (2.40±0.58) relative to younger (1.16±0.43) normoxemic lambs. Hypoxemic lambs had significantly higher S_{Gent} than normoxemic lambs in both young (2.44±0.48 to 1.16±0.43) and older (3.48±0.79 to 2.40±0.58) groups. D_{Gent} (µgm/min·gm) per unit dose was also significantly higher in hypoxemic relative to normoxemic lambs to liver (0.79±0.41 to 0.19±0.22), heart (16.89±7.47 to 6.12±3.08) and adrenal (15.48±9.13 to 4.62±3.13) tissues. T_{Gent} (µg/gm) responded similarly: liver (0.44±0.2 to 0.27±0.09), heart (0.34±0.41 to 0.15±0.09) and adrenal (0.66±0.44 to 0.24±0.14). Hypoxemia- and age-related effects on S_{Gent} were not explained by differences in T_{Gent} in these lambs.

326 UNTOGENY OF α- AND β-ADRENERGIC RECEPTORS IN RAT LUNG. Jeffrey A. Whitsett, Jeffrey A. Burdsall, Akihiko Noguchi, Children's Hospital Medical Center, Cincinnati

Catecholamines mediate lung function by interacting with α- and β-adrenergic receptors (α-AR, β-AR). α Adrenergic stimulation of the lung results in pulmonary vascular and bronchiolar constriction contrasting with the smooth muscle relaxant effects of β-adrenergic agonists. Because of the possible role in the regulation of pulmonary blood flow and airway resistance during development, the ontogeny of lung α_1- and β-AR's were compared. The binding of the α_1-adrenergic ligand [^{3}H]prazosin was demonstrated in membranes of rat lung from day 18 of gestation to adulthood. Specific binding was present at all ages, was reversible and inhibition by agonists followed the order: (-)epi=(-)norepi>>(-)iso>(+)norepi; antagonist potencies were: prazosin>WB4101, >>yohimbine. Binding capacity increased progressively during the neonatal period from 52±9 on day 18 of gestation to 105±4 fmoles·mg^{-1} protein (mean±SE) by postnatal day 15 then decreased reaching adult levels by 28 days of age, 62±3 fmoles·mg^{-1}. The pattern of α_1-AR's contrasted with that of β-AR's assessed with [^{3}H]dihydroalprenolol ([^{3}H] DHA). [^{3}H]DHA binding increased during this same time period from 46±4 on day 18 of gestation to 496±44 fmoles·mg^{-1} in the adult lung. Affinity for [^{3}H]prazosin and [^{3}H]DHA did not change with age. α-AR density is high in the neonatal period, decreasing thereafter. The timing of the changes in α_1-AR's correlates with the timing of increased sympathetic innervation of the developing rat lung and is distinct from that of β-AR's sites.

327 RESPONSE TO INDOMETHACIN IN PREMATURE INFANTS <1000 GMS WITH PATENT DUCTUS ARTERIOSUS (PDA). T.F. Yeh, I. Carr, D. Raval, J. Luken, A. Thalji, R.S. Pildes. Cook County Hospital, Dept. of Ped., Univ. of Ill. and Chicago Medical School, Chicago, Ill.

There are conflicting reports on the effect of Indomethacin (I) therapy on PDA in tiny premature infants. To determine possible factors associated with this variable response, an analysis of clinical, biochemical and pharmacokinetic data of 17 premature infants with symptomatic PDA (echo LA/Ao >1.3) was undertaken. 0.3mg/kg,IV I was given q 24 hrs, for a maximum of 3 doses if needed. The infants were divided into two groups: Gr I: 7 infants with BW <1000gms (mean±SD 837±105gms, GA 29.5±2.1wks); Gr II: 10 infants >1000gms (1391±190gms, GA 32.1±1.3wks). There was no difference between Gr I and Gr II before study in postn. age (11.4±9.1 vs 9.9±3.5 days), postconcept. age (31.1±3.1 vs 33.3±1.4wks) or in cardiopulmonary status. "Successful response" required clinical and echo improvement and disappearance of murmur.

	Gr I (7)	Gr II (10)
AVD (L/kg)	0.47±0.28	0.25±0.07*
Half life (hrs)	26.2±11.7	10.1±5.7
Clearance (ml/kg/hr)	16.5±13.5	9.7±3.7
Peak Concentration (µg/ml)	1.04±0.31	1.35±0.27*
Responders (1 dose)	1	7*
Responders (2-3 doses)	5	3
Non-responders	1	0

*p<.05 **p<.01

This study indicates that both groups of infants responded to I therapy but tiny prematures may need more doses than larger infants possibly due to larger AVD and lower peak I concentration.

328 DECREASED PLASMA GLUCOSE (G) FOLLOWING INTRAVENOUS INDOMETHACIN (I) THERAPY IN PREMATURE INFANTS WITH PDA. T.F. Yeh, D. Raval, L.D. Lilien, G. Srinivasan, R.S. Pildes. Cook County Hosp. Dept. of Ped., Univ. of Ill. and Chicago Medical School, Chicago, Ill.

In a double-blind study of I therapy in premature infants with symptomatic PDA, G was measured in 47 infants (22 control, C; 25 I) before and at 24, 48, 72 hrs after medication. All infants had failed to respond to 24 hrs fluid restriction and furosemide. 0.3mg/kg I or saline placebo was given q 24 hrs for a maximum of 3 doses, as needed. Plasma I was measured in 15 infants of the I group by gas chromatography. Prior to the study, the C and I groups were comparable in BW (mean±SD 1130±420 vs 1350±401gms), GA (30.5±2.2 vs 31.4±2.3wks), postn age (8.9±4.8 vs 9.0±5.4dys). Total fluid and caloric intake were similar.

	Plasma glucose (mgs%) C	Plasma glucose (mgs%) I	IV gluc.(mg/kg/min) C	IV gluc.(mg/kg/min) I
Before med.	83.9±30.3	94.3±48.2	3.2±3.7	3.8±2.5
After med. (24hrs)	94.2±35.9	70.8±19.6**	2.7±2.2	3.8±2.9
(48hrs)	90.4±19.0	70.9±29.5*	2.6±2.2	3.6±2.6
(72hrs)	80.4±13.3	70.5±18.3	2.7±2.0	3.2±1.8

While there was no sign. difference between the groups in IV glucose intake, infants in I group had a sign. lower (*p<.05; **p<.01) glucose than that of the control group at 24 and 48 hrs after medication. A sign. neg. correlation was seen between G and I concentration ($p<.05$) and between G and corresponding I concentration-time integral ($p<.01$). This study suggests that I therapy decreases G and that endogenous PGs may play a role in glucose homeostasis in premature infants.

329 A DOSE RESPONSE CURVE IN CHILDHOOD ASTHMA FOR FENOTEROL. J. Yahav, C. Mindorff, P. Reilly, G. Worsley and H. Levison. The Hospital for Sick Children, Department of Pediatrics, Toronto, Ontario, Canada.

Inhaled beta$_2$ adrenergic agonists are the most effective inhaled bronchodilators used for the management of bronchial asthma. In adult patients, fenoterol, a specific B_2 bronchodilator produces maximal bronchodilation in the dose range of 0.8 - 1.3 mg. There are no dose response curves in children for this class of bronchodilators. The object of the present study, was to define a safe bronchodilator dose in childhood asthma. The study was carried out as a 4 way crossover, doubleblind, randomized study. 20 children took part in the study, 8 of whom were 5-9 years of age and 12 were 10-14 years of age. Each group had a separate randomization of treatment using the following doses: 1) placebo, 2) 100 mcg, 3) 300 mcg, 4) 1,000 mcg. The 4 medications were given on 4 separate days. Pulmonary function was measured at 0, 15, 30, 60, 120 and 180 minutes after the inhalation. The results showed that maximum bronchial dilatation occurred after 30 minutes and reached a plateau at 60 minutes. After 3 hours, there was still significant bronchodilatation when compared to the placebo. There was no statistical difference between a 100 mcg Vs. 300 mcg, but a comparison of the area under the curve between the high and low dose showed a significant increase for 1,000 mcg $p < .03$. We conclude that inhaled fenoterol is a very adequate bronchodilator in asthmatic children and the dose required to produce maximum bronchodilation is in the range of 100 - 300 mcg.

ENDOCRINOLOGY

330 CONCORDANCE OF INITIAL AND FINAL DRUG INDICATION IN NEONATAL THERAPY. J.V. Aranda, J.M. Collinge, E.W. Outerbridge. McGill University-Montreal Children's Hospital Research Institute, Montreal, Quebec, Canada.

To assess the accuracy of initial drug use in neonatal pharmacotherapy, the degree of indication at onset of therapy was compared to that at discharge or completion of therapy. Nine indications (see Table)were assigned to 6616 drug regimens given for the first time to 495 neonates in an intensive care unit in 1977-78. 135 drugs were used and indications were based on arbitrarily set criteria:1)evidence for definite existence of disease process, based on laboratory and clinical criteria, 2)evidence for efficacy and appropriateness of a drug for the disease process based on available pharmacologic data.Results show a good concordance of the initial and the final degree of indication except for the non-inidcated drugs and those given on a presumptive basis.

INDICATION: DRUG REGIMEN-	#INITIAL	#FINAL	(% CONCORDANCE)	Δ%
Definite	2039	2127	(95.8%)	+ 4.3
Presumptive	783	580	(74.0%)	-25.9
Emperical	1046	920	(87.9%)	-12.0
Procedure related	665	665	(100%)	0
Prophylactic	1080	1065	(98.6%)	- 1.9
Resuscitation	183	182	(99.4%)	- 0.5
Palliative	132	131	(99.2%)	- 0.7
Not indicated	27	313	(0.8%)	+1059.2
Not classified	645	606	(93.9%)	- 6.0
Inadequate data	16	27	(59.2%)	-68.7

Data suggest justifiable use of most drugs in neonatal therapy except with antibiotics and diuretics.

331 PITUITARY FUNCTION IN CHILDREN WITH EMPTY SELLA SYNDROME-Silva Arslanian and James Gutai (Spon. by Jean F. Kenny) U. of Pgh, Children's Hospital of Pgh; Dept. of Peds; Pittsburgh and East Carolina University Dept. of Peds, Greenville, NC.

Hypothalamic pituitary function in the primary empty sella syndrome (ESS) has been studied extensively in the adult population, but few pediatric patients have been evaluated. We report on the pituitary function in 5 female children-1 black, 4 white-with ESS having a mean age at the time of diagnosis of 8 8/12 yrs. and a range of 2 9/12 - 12 8/12 yrs. The diagnosis of empty sella was established by CT scan with and without metrizamide cisternography. Pituitary TSH, ACTH, GH and prolactin reserve were assessed in response to provocative stimulation.

RESULTS: One patient had documented isolated growth hormone deficiency while none had TSH deficiency. One patient had pituitary dependent hypercortisolism. FSH/LH abnormalities were found in one patient only, having XO/XX mosacism. Prolactin levels were normal in 3 patients tested. Two patients had normal pituitary function tests; however, one of them had been on thyroid replacement therapy since the age of 2½ months for congenital hypothyroidism.

CONCLUSION: In children there appears to be a female predilection for ESS; however, unlike the adult population, there is no black predominance. Three of our five children with ESS had disturbed pituitary function at the time of diagnosis. This high incidence of endocrine abnormalities, though the study is small, stresses the importance of complete evaluation of pituitary function in children with ESS.

● **332** OXYTOCIN SECRETION IN LACTATING EWES. J. Ayramlooi, A-R Fuchs, A. Rasmussen, L. Sumulong. The Long Island Jewish Hospital, New Hyde Park, NY and Cornell University Medical College, New York City, Department of Obstetrics and Gynecology. (Spon. by Peter A. M. Auld)

Oxytocin (OT) is essential for milk removal in most animals but in sheep and goats normal milk yields have been obtained during hand milking without measurable release of oxytocin using bioassay techniques. To examine the influence of normal suckling on plasma OT, we have measured plasma OT by RIA in 4 sheep on days 1 to 15 of lactation. Each ewe nursed one lamb 2 to 3 times daily. Samples were taken through an indwelling catheter before the lamb was brought near the ewe, and before contact was allowed with the lamb, at active suckling, and at 1, 5, 10, 15, 30, and 60 min after suckling began. Basal OT was 10±4.5 pg/ml, rising significantly to 21.8±5.7 pg/ml after the lamb was returned but before tactile contact was established. A further rise occurred in all instances during suckling, maximum levels varying from 14 to 210 pg/ml. Mean plasma OT was raised over basal levels throughout the suckling periods which lasted 2.9±0.38 min on average. After suckling stopped, OT levels remained elevated in most instances for considerable lengths of time, returning to baseline in about 60 min. Thus, during each suckling episode, the lamb induced secretion of oxytocin in the ewe. Moreover, the reflex becomes conditioned very rapidly as indicated by the rise in maternal plasma OT at the sight of the lamb from day 2 onwards.

333 Testosterone Response to a Simplified Human Chorionic Gonadotropin (HCG) Stimulation Test in Boys. Laura K. Bachrach, Chris T. Cowell, F. John Holland (Spon by Ron Gold) Hosp. Sick Child., Dept. Peds., Toronto.

The measurement of serum testosterone concentration [T] after multiple HCG injections has been recommended for assessment of testicular function in prepubertal boys with cryptorchidism and other testicular anomalies. We determined the [T] before and 72 hours after a single HCG injection (1500 IU/m^2) in 28 boys aged .02 to 15.2 years. The groups included 17 with cryptorchidism, 3 with isolated micropenis, 1 with delayed puberty, 4 with Prader-Willi Synd., 2 with small testes and 1 with anorchia. Twenty-five of the 28 patients (89%) demonstrated a >3 fold increase in [T] over baseline and/or a peak [T] >100 ng/dl. Statistical analyses of the [T] response of these patients by paired t test are shown.

Age (yrs)	No.	Baseline [T] x ± SE	[T] post HCG x ± SE	Significance of change
<0.6	5	61 ± 28	234 ± 94	p <.2
0.7-5.0	9	12 ± 2	141 ± 21	p <.01
5.1-9	4	21 ± 4	112 ± 29	p <.05
9.1-11	2	26 (1 patient)	148 ± 89	----
11.1-14	4	19 ± 5	194 ± 22	p <.05

In infants <0.6 years, basal and peak [T] were higher than in other groups, and there was greater variability in response. The 4 patients with negligible increases in [T] following HCG included 2 boys with Prader-Willi, 1 with hypothalamic hypopituitarism and 1 with anorchia. We conclude that a single HCG injection can be used to screen for leydig cell activity in children.

● **334** LEVELS OF INSULIN-LIKE GROWTH FACTOR I AND II IN CORD BLOOD OF TERM INFANTS. Ann Bennett, Darrell M. Wilson, Frances Liu, Raymond J. Nagashima, Ron C. Rosenfeld, Raymond L. Hintz, Stanford School of Medicine, Department of Pediatrics, Stanford, CA.

Levels of insulin-like growth factor (IGF) I and II and somatomedin peptide content (SMPC) were measured in cord blood from 37 normal term infants. Following chromatography in 0.25M formic acid to remove somatomedin binding protein, samples were assayed for SMPC by radioreceptor assay using placental membrane. IGF-I was measured by radioimmunoassay using antibody provided by the NIH. 125-I IGF-I was used as radioligand in both assays. IGF-II was measured by radioimmunoassay using rabbit antibody generated against the C peptide region of IGF-II. 125-I tyrosylated C peptide of IGF-II was used as radioligand.

SMPC levels in cord blood averaged 0.49 ± 0.13 (SD) unit/ml (normal adult males 1.30 ± 0.25). IGF-I levels averaged 113 ± 35 ng/ml, significantly lower than normal adult levels (184 ± 32). IGF-II levels averaged 282 ± 84 ng/ml, also significantly lower than normal adult values (687 ± 169). IGF-II levels showed a strong correlation with birth weight ($p < 0.005$), while IGF-I levels correlated weakly with birth weight ($p = 0.05$).

Thus, IGF-II levels are relatively low in cord blood like SMPC and IGF-I. However, the correlations with birth weight suggest a role for SM/IGF peptides in fetal growth.

335 DOES SKIN CLEANSING WITH PVP-IODINE AFFECT PREMATURE NEWBORN (PN) THYROID FUNCTION? A CONTROLLED STUDY R.S. Brown, S.Bloomfield, F.Bednarek,L.E.Kertiles,and L.E. Braverman (spon. by P.L.Townes) U.Mass. Med.School,Worcester, MA.

Transient iodine-induced hypothyroidism in PNs has been reported to be secondary to the skin application of excessive amounts of PVP-Iodine (PVP-I) which results in an elevation of plasma and urinary iodine. In order to determine whether the routine use of PVP I in PNs causes abnormal thyroid function, a prospective study was carried out comparing the skin application of 1% PVP-I or the non I-containing antiseptic, Hibiclens (H). Skin was cleansed only on the first day of life. PVP-I and H groups were matched in terms of gestational age (32.1 vs 32.5 wk), # skin exposures (1-4),weight, and severity of illness. Blood filter paper T_4 (mcg/dl;mean±SD) before and after skin cleansing were:

	Baseline	Day 1	Day 2	Day 5
PVP-I (n=9)	6.3±1.9	6.7±1.5	7.5±5.1	6.1±1.3
H (n=9)	6.0±1.8	6.1±1.5	4.6±2.1	5.9±1.4

TSH was <20 mcU/ml in all babies. Another 37 PNs were evaluated of whom 24 received PVP-I (1-7 exposures)and 13 received H.Values were not obtained at all time points. There was no difference in mean T_4 and TSH concentrations between groups. Blood T_4 concentration fell by >50% in 6 very ill PNs who received PVP-I.TSH remained <20 mcU/ml in five, and rose slightly in one,strongly suggesting that iodine-induced hypothyroidism was not present and that the low T_4 was secondary to severe systemic illness.

Conclusions: Exposure of PNs to a maximum of 7 skin applications of PVP-I on the first day of life does not result in transient iodine-induced hypothyroidism.

336 THE EFFECT OF SEX ON THE CONCENTRATIONS OF MAGNESIUM (Mg) AND CALCIUM (Ca) IN BONE OF WEANLING RATS FED Mg-SUFFICIENT OR Mg-DEFICIENT DIETS. Joan L. Caddell and Linda T. Pilla. (Spon. by Thomas Aceto, Jr.), St. Louis Univ. Sch of Medicine, Dept. Pediatr/Adol. Med., St. Louis, MO.

If bone is to be used as a diagnostic tissue for postmortem evaluation of Mg and Ca in infants, one must know if sex differences exist. In adult mammalian bone, estrogen accelerates the rate of accretion of Mg (Goldsmith et al., Lancet 2: 567, 1967) and of Ca (Ranney, Endocrinology 65: 594, 1959). We studied male and female weanling rats fed 150 mg of added Mg to a purified diet (150-Mg) or no added Mg (0-Mg) for 7 days. We analyzed plasma and combined R and L femurs for Mg and Ca, using an atomic absorption spectrophotometer. We found no sex differences in the plasma, but higher values for Mg and Ca in bone from females.

DIETARY Mg	MALE (M)		FEMALE (F)		P VALUE
Magnesium in mg/kg dry bone					
150-Mg	3,561±72	(8)*	3,786±136	(5)	0.05**
0-Mg	1,257±28	(15)	1,330± 26	(14)	0.025
Calcium in mg/kg dry bone					
150-Mg	120,690±2,880	(8)	131,660±4,480	(5)	0.05
0-Mg	133,640±1,030	(15)	146,620±2,820	(14)	0.001

* Mean + SEM (Number in sample); ** two-tailed Student's t test.

We conclude that analytical work concerning Mg and Ca concentrations in infant bone as well as adult bone should be matched for sex. In view of the unexplained higher morbidity and mortality in the male neonate, other sex differences should be sought.(Support: Life Seekers, the Gus L. Connellys, the Citizens & Southern Bank).

337 LIMITED JOINT MOBILITY (LJM) IN INSULIN DEPENDENT DIABETES MELLITUS (IDDM): RELATION TO GLUCOSE CONTROL AND ZINC NUTRITURE. Wesley K. Canfield, H. Peter Chase, K. Michael Hambidge, Univ. Co. Health Sci. Ctr., Denver, and LuAnn K. Johnson, USDA-ARS-HN, Grand Forks.

Limited joint mobility (LJM) as described by Rosenbloom (NEJM 305: 191, 1981) defines Stage I as "mild" and Stage II as "moderate-severe" involvement. Amongst 111 subjects (57 males, 54 females) with IDDM from the greater Denver area, Stage I involvement was found in 14 (12%) and Stage II in 24 patients (22%). The age range was 3 to 25 yrs. (mean = 12.5). After correction for duration of IDDM using analysis of variance, the presence of LJM (either stage) correlated with higher $HgbA_{1C}$ ($p<.0001$), fasting glucose ($p<.0001$), triglyceride ($p<.0007$) and 24 hr. urine glucose ($p<.0467$) levels.

Those with Stage II involvement were significantly shorter than those with Stage I ($p<.0274$) or no involvement ($p<.049$). $HgbA_{1C}$, fasting glucose and triglyceride levels in subjects with Stage II were also significantly higher than for those with Stage I or no involvement. Fasting plasma zinc levels (µg/dl ± SEM) were significantly higher ($p<.0047$) in subjects without LJM (101 ± 1.4), than in those with Stage II involvement (92 ± 2.6), using least square mean analysis, correcting for duration of DM. Mean plasma zinc in control subjects was 91 ± 4.1. Hair and urinary zinc levels were similar in all groups.

This is the first study to suggest LJM may be related to glucose control in IDDM. Plasma zinc was inversely correlated with the severity of LJM, indicating an associated abnormality in zinc nutriture.

338 INSULIN EXCRETION (IE) BY CHILDREN AND YOUNG ADULTS WITH AND WITHOUT DIABETES MELLITUS (DM): RELATIONSHIP TO URINARY ZINC (UZ). Wesley K. Canfield, K. Michael Hambidge, Rhonda Wells, U. of Colorado Health Sciences Center, Dept. of Pediatrics, Denver, and LuAnn K. Johnson, USDA-ARS-HN, Grand Forks.

Twenty four hour urine collections from 43 subjects (21 males, 22 females) with DM and 29 controls (C) (19 males, 10 females) were analyzed for zinc, insulin and glucose. Mean age ± SD (range) in DM and C: 12.4 ± 3.6 (5.5 - 19.6) and 11.5 ± 3.9 (4.8 - 22.3) years. Age was the best single predictor of IE in C ($p<.002$, $r^2 = .30$) with urine volume (UV) the best in DM ($p<.0001$, $r^2 = .41$), even after correction for age. UZ and IE were significantly higher in DM, but were significantly correlated only in C ($p<.0309$, $r^2 = .40$). UV and IE were not correlated in C, but were in DM ($p<.0001$, $r^2 = .41$). The best model for IE in DM was: 47025 (insulin/kg) + 24 (UV ml) - 26530, ($p<0.0005$, $r^2 = 0.57$). As demonstrated by others, IE was significantly correlated with urinary glucose in DM ($p<.0007$, $r^2 = .34$). Differences between the means for IE and UZ:

	C M ± SEM	DM M ± SEM	p
UZ	344 ± 61 µg/day	790 ± 49 µg/day	<.0001
IE	19472 ± 1953 µU/day	46020 ± 3390 µU/day	<.0001

We conclude that hyperinsulinuria in DM is related to insulin dose, control as measured by glucose excretion, and urine volume. The hyperzincuria in DM is not secondary to hyperinsulinuria, although zinc and insulin excretion in normal children appear to be related.

● **339** SERUM IMMUNOREACTIVE PROCOLLAGEN (IRPC) LEVELS IN GROWTH HORMONE DEFICIENCY (GHD) AND HYPOTHYROIDISM(HT) Dennis E. Carey, Burton Goldberg, Susan K. Ratzan, Karen Rubin, and David W. Rowe. University of Connecticut Health Center, Department of Pediatrics, Farmington and New York University, Department of Pathology, New York.

A sensitive radioimmunoassay has previously been used to determine the level of procollagen in normal adult sera (range 2-14µg/dl). The assay measures the C-terminal extension propeptide of type I procollagen and is a reflection of collagen synthesis in a manner analagous to levels of C-peptide and insulin synthesis. Because collagen synthesis is a prerequisite for normal growth, we evaluated serum IRPC levels in 14 GHD children and in 2 children with growth failure resulting from primary HT before and during therapy with Human Growth Hormone (0.1 IU/kg IM, 3x/wk) and L-thyroxine, respectively. The response to Growth Hormone was:

	0	1 wk.	1 mo.	2 mos.	3 mos.	6 mos.	12 mos.
$\bar{X}$	11.9	16.5	25.1	23.1	22	20.4	23.5
SE±	2.0	2.2	4.3	3	3.2	2.2	2.0

The mean serum IRPC level was maintained significantly greater ($p<.005$) than the basal level from one month to 12 months.

Serum IRPC in the HT subjects increased from 5.9 and 11.2µg/dl to 42µg/dl (at 5 mos) and 40.5µg/dl (at 4 mos) during treatment.

The data demonstrates that basal serum levels of IRPC in hormone deficient children are significantly lower than the levels measured during appropriate hormone replacement. We conclude that the serum IRPC level is a measure of the rate of collagen synthesis, and may have clinical usefulness as a biochemical marker of the biologic response to growth stimuli.

● **340** THE RATE OF DE NOVO SYNTHESIS OF CHOLESTEROL IN HUMAN FETAL TISSUES. Bruce R. Carr and Evan R. Simpson (Spon. by Charles R. Rosenfeld). University of Texas Health Science Center, Cecil H. and Ida Green Ctr.for Reprod. Biol. Sci., and the Depts. of Ob-Gyn and Biochem., Dallas, Texas.

The fetus is believed to be the principal source of cholesterol utilized by the fetal adrenal gland. Thus, accurate measurements of cholesterol formed de novo in various fetal tissues are of signal importance in understanding the regulation of cholesterol metabolism in the fetus and more specifically in the fetal adrenal gland. We determined the rates of cholesterol formed de novo in short term in vitro incubations of various fetal tissues, obtained from human abortuses at gestational ages from 8-22 weeks by measuring the rate of incorporation of tritium from [^{3}H]water into cholesterol. The highest rates of cholesterol synthesis were found in adrenal and liver tissues (47±2 and 32±2 ng atoms tritium incorporated x mg^{-1} protein x h^{-1}, respectively; mean±SE), whereas intermediate rates were observed in testicular tissue (21±3 ng atoms x mg protein x h^{-1}) and lower rates (<6 ng atoms x mg^{-1} x h^{-1}) in all other tissues studied. Modest variations in rates of cholesterol synthesis were observed with respect to gestational age in liver and adrenal tissues. In testicular tissue, peak rates of cholesterol synthesis were noted at 14 weeks gestation, and declining values thereafter. Considering the rapid growth of the fetal liver and the high rate of cholesterol synthesis in this organ, it appears that cholesterol utilized for steroidogenesis by the fetal adrenal gland could be derived primarily by de novo synthesis in the fetal liver and adrenal gland.

341 ULNAR GROWTH DECELERATION IN CHILDREN WITH IDIOPATHIC PRECOCIOUS PUBERTY (IPP) TREATED WITH AN LHRH ANALOG. F.G. Cassorla, F. Comite, M. Skerda, I.M. Valk, G.B. Cutler, and D.L. Loriaux (Spon. by J. Sidbury). DEB, NICHD, NIH, Bethesda, MD and Catholic University of Nijmegen, The Netherlands.

We have shown that pituitary desensitization with the long acting LHRH analog D-Trp^6-Pro^9-NEt-LHRH ($LHRH_a$) produces a significant reduction in the concentrations of serum gonadotropins and gonadal sex steroids in children with IPP. We have now investigated the effects of $LHRH_a$ treatment on ulnar growth in patients with this condition. Ulnar growth is a sensitive index of short term growth in children and correlates well with linear growth. Seven girls and one boy (ages 4 to 8 years), with Tanner II-IV development, advanced bone age, and pubertal levels of gonadotropins and gonadal sex steroids, were studied. Three week ulnar growth rates (TUG) were measured 2 months before, and for several months after institution of treatment with 4 µg/kg/day of $LHRH_a$.

TUG (mm/3wk)	Basal (n=8)	1-2 mo (n=8)	3-4 mo (n=8)	5-6 mo (n=5)	7-8 mo (n=4)	9-10 mo (n=4)
Mean	1.00	0.86	0.83	0.73	0.60	0.33
SE	0.12	0.08	0.10	0.10	0.08	0.02
Significance	← p<0.05 →					

Mean TUG decreased during $LHRH_a$ therapy, with the mean TUG after 5 months of therapy being significantly less than before therapy ($p<0.05$). The ratio between bone age and chronologic age advancement remained at or below 1 during treatment with $LHRH_a$. We conclude that $LHRH_a$ produced a significant decrease in ulnar growth rate suggesting that it may be effective in reducing the accelerated growth of children with precocious puberty.

342 EFFECTS OF BI-DAILY INSULIN INJECTIONS ON ADOLESCENT DIABETICS: BIOCHEMICAL STUDIES. S. Castells, M. Noval and H. Copur, Dept. of Ped., Downstate Med Ctr State University of New York, Bklyn., New York

The biochemical effects of administering insulin once a day were compared to bi-daily injections in 19 diabetics. M-value, serum Hb A_{1C}, T_4, free T_4, T_3, cholesterol, triglycerides, HDL, and a TRH stimulation test were obtained on once a day insulin therapy and 3 months later on bi-daily; 14 normal adolescents had the same tests. There was a significant improvement in M-value, (mean ± SE) from 108.4±20.0 to 37.5±4.2, $p<0.01$ and Hb A_{1C} 12.1%± 0.6 to 9.2%±0.6, $p<0.01$. Serum T_4, free T_4 and HDL concentrations in diabetics in both therapies were not different from normal adolescent controls. Serum T_3 and T_3/T_4 ratio in insulin once a day were lower than normals (T_3=115±10.8 for diabetics and 182±8.9 for controls $p<0.03$; T_3/T_4 ratio=0.004±0.001 for diabetics and 0.029±0.002 for controls, $p<0.003$), and returned to the normal range of controls after 3 months of bi-daily injections. TRH produced a similar increase in serum TSH and prolactin concentrations at 30 m. in controls, diabetics on daily injections and on bi-daily. Serum cholesterol was elevated in diabetics on once a day insulin 189.3±18 mg/dl, and decreased with bi-daily injections to 159±13.9 (controls 156.5±8.1). Serum triglycerides on once a day insulin were elevated to 137.5± 30 mg/dl and on bi-daily became normal 99.9±14.3 (controls 98.3±14.8). Bi-daily insulin therapy appears to normalize serum levels of T_3, cholesterol and triglycerides in adolescent diabetics. The thyroid and TRH data suggests that hyperglycemia affects conversion of T_4 to T_3 but does not affect the pituitary-thyroid axis. Supported by NIH Grant RR-00-318.

343 EFFECTS OF BI-DAILY INSULIN INJECTIONS ON ADOLESCENT DIABETICS: CLINICAL STUDIES. S. Castells, M. Noval, and H. Copur, Dept. of Ped., Downstate Med. Ctr, State University of New York, Brooklyn, N.Y.

Adolescent diabetics are difficult to control with insulin injections due to the physiological changes associated with sexual maturation. We compared the effects of insulin once a day to bi-daily insulin in 19 adolescent diabetics, by admitting them to the Hospital on once a day insulin and re-evaluating them three months later on bi-daily injections; 23 normal adolescents were studied as controls. Maximum insulin dose tolerated without hypoglycemia was 0.9±0.1 unit/Kg/day on once a day and 1.5±0.1 on bi-daily. Systolic blood pressure and resting pulse rates were elevated as compared to controls (B.P. 121.5±2.5 and 105.1±1.6 $p<0.03$ and P.R.: 78.6±3.6 and 70.9±2.9, $p<0.05$) and decreased to normal after three months of bi-daily insulin. Eight of 10 diabetic females had amenorrhea or oligomenorrhea on one injection a day but the menses became regular after 3 months of bi-daily injections. Two quantitative indexes of diabetic control M-value and serum Hb A_{1C} significantly improved on bi-daily injections. M-value decreased from 108.4±20 in 1 injection to 37.5±4.2 on bi-daily, $p<0.01$ and Hb A_{1C} from 12.1%±0.6 to 9.2%±0.6, $p<0.01$. These results suggest that insulin administered bi-daily to adolescent diabetics normalizes B.P., P.R., menses and improves biochemical parameters of diabetic control. The most serious problem with bi-daily injections was compliance; three patients withdrew from using bi-daily injections on the 1st month and 4 found to have elevated serum Hb A_{1C} did not comply with bi-daily injections. Supported by NIH Grant RR-00-318.

344 ZINC METABOLISM IN TESTICULAR FEMINIZATION SYNDROME CULTURED FIBROBLASTS. Wai-Yee Chan, LeAnn Tease, James M. Bates, Jr., and Owen M. Rennert. University of Oklahoma Health Sciences Center, Department of Pediatrics, Oklahoma City, Oklahoma.

Testicular function is influenced by zinc (Zn) through its interaction with steroidogenesis. Recent report of testis specific Zn deficiency in the testicular feminization syndrome (Tfm) rats indicates the importance of studying Zn metabolism in this syndrome. Cultured genital skin fibroblasts of patients exhibited the androgen insensitive phenotype. We have studied Zn metabolism in Tfm patient cultured fibroblasts obtained from the Human Genetic Mutant Cell Repository. Intracellular Zn level of genital skin cultures was 136.6±23.5 ng/mg protein which was not significantly different from that of non-genital skin cultures (166.8±37.4 ng/mg protein). Kinetic studies showed the following results (n=3 for both type of cultures):

Uptake: (means ± S.D.; Zn-65 cpm/mg protein)

Time (Hour)	1	2	4	6	8	10
Genital skin	444 ±53	621 ±68	1081 ±131	1541 ±133	1775 ±178	1666 ±395
Non-genital skin	459 +93	681 +67	1046 +343	1349 +316	1375 +259	1669 +283

Efflux: (means ±S.D.; % of Zn-65 cpm/mg protein of start of chase.

Time of Chase (Hour)	2	4	6	8
Genital skin	65.5±11.3	50.9±17.2	31.9±0.9	28.5±5.7
Non-genital skin	52.0±6.3	43.5±2.8	33.9±1.5	26.5±4.2

These results showed that Zn metabolism in human Tfm genital skin cultured fibroblast is not abnormal.

● **345** AN IMPROVED METHOD FOR EVALUATING TESTOSTERONE BIOSYNTHETIC DEFECTS. Fred I. Chasalow, Sandra L. Blethen, and Frank S. French. Wash Univ, Dept of Peds, St. Louis Child Hosp, St. Louis, and Univ of North Carolina, Dept of Peds, Chapel Hill. (Spon. by R. Hillman)

We report a new technique for evaluating defects in the conversion of progesterone (P) to testosterone (T) and its application to the diagnosis of the cause of incomplete virilization in three children with XY sex chromatin, posterior labial fusion, clitoromegaly, and hypospadias. The T response to hCG (5000 u/m^2 x 4) was normal in Case 1 and deficient in Cases 2 and 3. Gonadectomy was performed 24-48 hours after the last dose of hCG. Testicular microsomes were isolated by differential centrifugation from about 1 gm of tissue (histochemistry on the remainder showed normal testicular tissue). The microsomes were incubated with (^{3}H) P and (^{14}C) 17-hydroxyprogesterone. At 0, 2, 5, 10, and 20 min aliquots were removed, mixed with methanol, extracted with ethyl acetate, and chromatographed on a Sephadex LH-20 column. In Case 1, T synthesis was confirmed by isolation of doubly labeled T. In Case 2, no T was detected but a large amount of androstenedione labeled from both precursors was present, indicating a deficiency in 17-hydroxysteroid dehydrogenase. In Case 3, neither androstenedione nor T was present in significant amounts. The isolated 17-hydroxyprogesterone contained (^{14}C) and (^{3}H) but the relative activity suggested that in addition to a lyase deficiency there was a substantial decrease in 17-hydroxylase activity. Thus, this method evaluated defects in the P → T pathway with a single incubation and a simple, rapid chromatographic system.

● **346** EFFECT OF HYPOTHYROIDISM ON GROWTH HORMONE (GH) SECRETION, BASAL SOMATOMEDIN-C (SM-C) CONCENTRATIONS, AND SM-C RESPONSES TO EXOGENOUS GH Steven D. Chernausek, Louis E. Underwood, Robert D. Utiger, Judson J. Van Wyk. University of North Carolina, North Carolina Memorial Hospital, Dept of Ped & Med, Chapel Hill

GH and thyroid hormone appear to act in concert to cause skeletal growth. To determine the mechanism for this, we assessed plasma Sm-C, GH release, and Sm-C responses to exogenous GH in 8 children and adults with primary hypothyroidism. Basal Sm-C concentrations were below age and sex related norms in all subjects, and rose an average of 3-fold after thyroid hormone replacement. Of 6 subjects tested, 3 had normal GH release to provocative stimuli, whereas 3 had subnormal responses (< 7 ng/ml). Sm-C increased in all 6 in response to a single injection of GH (0.1 U/kg) and rose to >4 times the basal level after 0.8 U/kg. GH secretion did not correlate with basal or GH-stimulated Sm-C.

In a companion study, the mean Sm-C in thyroidectomized (Tx) male rats was 0.71 ± 0.25 U/ml (controls=2.16 ± 0.38). Treatment with T4 or hGH raised the Sm-C to 1.55 ± 0.41 and 1.44 ± 0.27 U/ml, respectively. Binding of ^{125}I-hGH to "somatogenic" sites in crude membrane-rich homogenates from livers of Tx and GH-treated Tx rats was nearly twice that in euthyroid rats, and was due to increased binding capacity. Conclusion: Hypothyroidism is associated with low circulating Sm-C which is not due to an obvious decrease in GH secretion or responsiveness. It is possible that the growth failure of hypothyroidism is related to the lowered Sm-C.

347 EFFECT OF CAFFEINE(C) ON THYROID AND PITUITARY FUNCTION IN THE NEWBORN RAT(NR). M. Clozel*, C. Branchaud, G. Tannenbaum*, J.H.Dussault and J.V. Aranda. McGill University-Montreal Children's Hosp. Res. Inst. Montreal, Quebec

The possibility that C, often used in neonatal apnea, may produce acute or chronic changes in thyroxine(T_4), thyrotropin (TSH) and growth hormone(GH) was studied in the NR. Five day old rats were randomly divided into 3 groups(n=50/grp). Control group received saline; low-dose caffeine(LDC) group, received 5 mg/kg IP and high-dose caffeine(HDC) group, received 50 mg/kg IP. In each group, rats were sacrificed 2,4 or 24 h after a single injection (acute effects) or 24 h after 10 days of daily injection (chronic effects). GH, T_4 and TSH were measured by RIA, C by HPLC. After acute C, GH significantly increased 2h after HDC (mean ±SEM) (75.4 ±15.5 vs 27.7±6.3 ng/ml, $p<.05$); 24h after LDC (97.1±11.3 vs 40.9± 7.0, $p<.05$) and HDC (169.8±36.2 vs 40.9±7.0 ng/ml, $p<.001$). After chronic C the increase in GH was small suggesting depletion of pituitary reserve. After acute HDC, T_4 response was biphasic with an increase at 4h (3.8±0.1 vs 3.3±0.2 µg/dl, $p<.05$) and decrease at 24h (4.1±0.2 vs 4.8±0.2 µg/dl, $p<.001$). Thyrotropin-releasing hormone (TRH)-stimulated TSH at 24h was not influenced by C. Chronic C increased T_4 and TSH, but decreased TRH stimulated TSH, suggesting blunted TSH response after chronic C.

C Dose (mg/kg/dx10d)	0 (CONTROL)	5 (LDC)	50 (HDC)
T_4 (µg/dl)	4.1± 0.3	5.1± 0.3 ($p<.001$)	6.0± 0.2 ($p<.001$)
TSH (µg/dl)	10.6± 1.4	17.9± 2.6 ($p<.05$)	25.1± 6.9 ($p<.05$)
TRH-induced TSH	216.8±45.5	101.9±19.5 ($p<.05$)	153.6±31.7 ($p<.05$)

We conclude that doses of C currently used for neonatal apnea may produce acute and chronic changes in hormonal status in the NR. Hormonal effects of C in newborn infants require further studies.

348 SPECTRUM OF THE EMPTY SELLA SYNDROME(ESS) IN CHILDREN D.C.Costigan, D.Daneman, F.J.Holland and R.M.Ehrlich. University of Toronto, Hosp. for Sick Children, Toronto, Canada.

The ESS is typically described in endocrinologically normal adults, accounting for 35-46% of enlarged sellas. Only 4 children with ESS are recorded in the literature. We report a further 4 cases in whom the diagnosis has been made by either metrizamide cisternography (MC) or air encephalography (AEG). Clinical features at presentation and responses to insulin, LHRH and TRH testing are recorded in the table.

Case	Age(yr)	Sex	Presentation	Endocrine Evaluation
1	14.7	M	Minor head trauma	Normal
2	12.5	M	Pseudotumor cerebri	Normal
3	10.8	M	Precocious puberty	Adult LHRH response
4	15.0	F	2° Amenorrhea	Hyperprolactinemia

Case 3 had no mass on MC, but high levels of LHRH by RIA in his CSF (140pg/ml; controls-undetectable), implicating a suprasellar mechanism in the etiology of his precocity. Case 4 had an eroded sella and presumed prolactinoma (amenorrhea, galactorrhea, hyperprolactinemia). After 1 yr therapy with bromocriptine, transsphenoidal exploration revealed ESS confirmed by AEG, suggesting that tumor regression may predispose to arachnoid herniation. We conclude that in children (a) the spectrum of ESS is heterogeneous with both primary and secondary causes, and (b) endocrine abnormalities may be more common than in adults with the syndrome. The role of elevated CSF hormone levels in patients with abnormal CSF circulation warrants further investigation.

● **349** NORMAL VITAMIN D METABOLISM IN RENAL NON-RESPONSIVE, BONE-RESPONSIVE PSEUDOHYPOPARATHYROIDISM (PHP) MANIFESTING WITH RICKETS, Shermine Dabbagh, Russell Chesney, Leonard Langer, Hector DeLuca, Enid Gilbert, Univ. of Wisconsin, Departments of Pediatrics, Radiology, Biochemistry and Pathology, Madison, Wisconsin.

PHP is a very heterogeneous disorder. Some patients manifest typical hyperparathyroid bone changes, suggesting renal non-responsiveness but bone responsiveness to PTH. However, PHP presenting as rickets is not generally recognized.

We report a 13-year-old healthy white female who presented with bilateral bowing of the legs and varus deformities typical of rickets. She was appropriate for age by height, weight and intelligence and had no brachydactyly. Both parents and 6 siblings were normal. Radiology showed advanced subperiosteal resorption in the fingers, slipped capital femoral epiphyses bilaterally and rachitic changes in all the epiphyses. Lab data:

	SCa	SPO_4	AlkP	PTH	Total 25(OH)D	24,25-$(OH)_2$D	1,25-$(OH)_2$D
Pt	7.7	6.2	327	3530	23.3	2.4	39
HP	5.6	6.6	231	7440	30.6	1.24	16
N	9.4-10.2 mg%	3.5-5.0 mg%	75-250 IU/L	430-1860 pg/ml	30.5±9.7 ng/ml	1.7±0.47 ng/ml	43±12 pg/ml

The TMP/GFR was 7.2 mg% (Nl=4.97±0.61). There was no aminoaciduria, proteinuria or glucosuria, and renal function was normal. Iliac bone biopsy revealed changes compatible with hyperparathyroidism. After treatment with 1 µg 1,25(OH)2D daily, there was symptomatic relief and improvement in her serum chemistries. In conclusion, rickets could be a manifestation of renal non-responsive, bone-responsive PHP with normal vitamin D metabolism.

● **350** ROLE OF B-ADRENERGIC SYSTEM ON VASOPRESSIN (VP) RELEASE AND PLASMA RENIN ACTIVITY (PRA) IN THE HYPOXIC FETUS. Salha S. Daniel, Raymond I. Stark, Alan B. Zubrow, M. Kazim Husain and L. Stanley James. Columbia Univ., Coll. of P & S, Div. Perin. Med., Depts. Ped., Anes., Med., NY.

The role of the B-adrenergic system in fetal response to hypoxia was studied in 7 chronically instrumented fetal lambs given 1 mg/kg propranolol IV (Exp.) and 7 control (C). Hypoxia (H) was induced by administration of 10% O_2 to the ewe for 30 minutes. Propranolol alone caused a 20bpm fall in fetal HR but no change in blood composition. The change in BP, HR and acid-base indices following H were similar in both groups; however, during 30 minutes of recovery (R), no tachycardia was observed in (Exp.) and PHa fell significantly. The changes from pre-hypoxia in blood hormonal levels during H & R were:

	ΔVP(pg/ml)	ΔE(pg/ml)	ΔNE(pg/ml)	ΔPRA(ng/ml.hr)
H_C	45.1±4.71	256±115.7	1329±585.4	3.91±1.23
$H_{Exp.}$	31.7±11.30	530±224.5	2004±538.6*	0.90±1.38*
R_C	1.60±0.60	5±9.5	103±94.0	3.25±1.91
$R_{Exp.}$	4.6±1.57*	150±72.7*	1509±368.0*	0.09±0.86*

*P<0.05 Exp. compared to C

Thus during moderate hypoxia, B-adrenergic blockade caused an exaggerated increase in catecholamines, moderate decrease in VP and complete suppression in renin release. B-adrenergic system appears to be important during the recovery presumably by enabling the fetus to increase its HR and hence cardiac output.

● **351** BIOACTIVE LH INCREASES IN THE NEONATE FOLLOWING MATERNAL LHRH ADMINISTRATION DURING DELIVERY. Marco Danon, Inese Z. Beitins, Gustavo Gomez, Teofila Ostrea and John D. Crawford. Depts. of Ped. and Gyn., Mass. Gen. Hosp., Harvard Med. Sch., Boston, and Facultad de Medicina, Universidad del Valle, Cali, Colombia.

The study was designed to determine whether LHRH administered to the mother during labor resulted in increased bioactive (B)LH concentrations in the neonates. With their informed consent, 7 women with uncomplicated (39 to 41 wks) pregnancies were followed during spontaneous labor. During the last stage of vaginal delivery 100 ucg of LHRH was administered intravenously to the mother. Approximately 10 minutes later, after delivery, blood was obtained from the cord and at 15,30,45,60,90 and 120 minutes from an umbilical catheter in the neonate. Concentrations of BLH were determined in the serum by means of the in vitro RICT assay utilizing 2nd IRP-hMG as the standard. Of the 7 neonates 4 were male and 3 female. All had normal birth weights and Apgar scores. The BLH concentrations in the cord blood of boys and girls were 165± 112 and 158±17 mIU/ml (mean±1SD). These values were not significantly different from values in the cord blood of 7 neonatal boys and 7 girls whose mother did not receive LHRH. In boys and girls of LHRH injected mothers the maximum BLH was achieved between 30 and 45 minutes. The increase in boys varied from 168 to 1586%, whereas in the girls it was lower, between 125 and 336%. It is therefore concluded that: 1) LHRH administered to the mother during the last stages of labor does not significantly alter BLH concentrations in cord blood but may contribute to postnatal BLH elevations and 2) the rise in newborn boys exceeds that of girls.

● **352** DYNAMICS OF BIOACTIVE LH DURING THE FIRST SEVEN DAYS OF LIFE. M. Danon, I.Z.Beitins, O. Velez, T. Ostrea and J.D.Crawford. Harvard Med. Sch., Boston, and Facultad de Medicina, Universidad del Valle, Cali, Colombia.

The objectives of this study were to a) determine the concentrations of bioactive (B)LH in the blood of both boys and girls during the first 7 days of life and b) evaluate the pattern of B-LH secretion on day 7. Blood was obtained daily for the first 7 days of life in 7 full-term neonatal boys and 4 girls. The BLH was determined in the serum by means of the in vitro RICT assay utilizing 2nd IRP-hMG as the standard (expressed as mIU/ml).

Day (D)		1	2	3	4	5	6	7
MALE	mean	139.3	39.5*	17.1	13.7∞	15.1	23.1	23.7α
	±SEM	39.8	13.9	4.7	3.1	4.7	9.2	10.4
FEMALE	mean	74.6	33.8	19.3	9.4*	6.0	5.5	4.1β
	±SEM	24.1	10.5	5.6	1.6	1.8	0.5	0.6

*p<0.05 ∞p<0.01 vs D1; αp<0.05 βp<0.025 D4 vs D7 (paired t test)

To determine the pattern of BLH secretion on day 7, 4 girls and 5 boys had blood withdrawn Q 20 min for a period of 2 h. The % CV in 4/5 boys (17.9,14.0,52.4,15.2) and 3/4 girls (24.4,17.3,19.2) was at least 3 times greater than that of the assay (<5)suggesting the possibility of pulsatile secretion. These data demonstrate that a) BLH reaches a nadir on day 4 after birth in both boys and girls most probably corresponding to the disappearance of endogenous hCG activity; b) in boys BLH rises significantly by postnatal day 7, most probably the result of endogenous LH secretion; c) in girls BLH continues to decline and by postnatal day 7 is significantly lower than on day 4 and d) both boys and girls exhibit pulsatile secretion of BLH on postnatal day 7.

353 IMPROVED METHOD TO ACHIEVE GOOD DIABETIC CONTROL. John A. Duncan, Sponsored by John I. Malone. U. of So. Florida College of Medicine, Dept. of Pediatrics, Tampa, FL.

Ten insulin-dependent diabetic (IDD) youth were treated with continuous subcutaneous insulin infusions without pre-meal bolus injections for an average of 4.6 mos. (range 1-12 mos.). Continuous day infusions of 2.0 to 3.9 units regular insulin/hr. (33 to 65 mU/min) were utilized with the night infusion rate slowed to 0.9 to 2.5 units/hr. (10 to 42 mU/min). Infusion rate changes were made at 7AM and one hr. prior to sleep daily. Diets were self-selected, 1500 to 2300 kcal/day. At 3 mos. of therapy, patients' glucose levels were monitored and recorded every 60 sec. by a Biostator while insulin was administered by the continuous sc method outlined above. Meal-associated glycemic excursions, glycemic excursion times and free insulin levels were measured during a normal three-meal day. Free insulin levels were determined by RIA after removing interfering antibodies with PEG treatment. Values were compared to 6 non-diabetic controls. (†=m±S.D.)

Continuous Glucose Monitoring on CBII †

	IDD	ND
ΔGlucose baseline to peak:	68.1±53.9 mg/dl (N=20)	44.1±13.5 (N=6)
ΔTime baseline to peak:	1.29±0.60 hrs. (N=20)	0.77±0.44 (N=6)
ΔTime baseline to baseline:	2.61±1.08 hrs. (N=15)	3.05±0.72 (N=6)

HbAlc (% of total Hb) †

Pre-CBII	Post 30 Days of CBII	Non-Diabetic Range
11.3±4.0	7.08±1.4 (N=7)	3.7 to 6.9

These data reveal insulin levels achieved with continuous basal insulin infusion (CBII) are similar to the non-diabetic. Moreover, glycemic control, with non-diabetic glycemic excursions and glycemic excursion times, is possible on CBII without pre-meal boluses of insulin. This approach to the pump infusion of insulin is less complex than the variable bolus approach commonly used and is equally effective in producing good diabetic control.

354 PERSISTENT FEEDBACK ABNORMALITY IN THE PITUITARY-IODOTHYRONINE AXIS IN CONGENITAL HYPOTHYROIDISM (CH) John A. Germak, Carlie H. White and Thomas P. Foley, Jr., Dept. of Ped., Univ. of Pgh., Pittsburgh

In an attempt to elucidate the underlying mechanisms associated with the elevated threshold for TSH suppression in certain patients with CH. 12 infants with the apparent feedback defect (FBD) of 26 with CH were studied. FBD was defined as a serum TSH ≥8 uU/ml beyond 10 weeks of L-Thyroxine therapy with a total T4 (TT4) above the mean for age (≥ 9.0 µg/dl)and normal free T4 (FT4), ≥1.2 ng/dl and T3, ≥ 100 ng/dl. Of the 12 infants with FBD 8 had functional athyreosis (AT), 3 had ectopic or hypoplastic tissue (E/H) and 1 had dyshormonogenesis (DH). The mean bone age (BA) at diagnosis (dx) did not differ (p>0.1) between the 8 AT patients with (c̄) FBD, 32.4 ± 6 fetal wks (FW), and the 8 AT patients without (s̄) FBD, 35 ± 8FW.BA at Dx in the 3 infants with E/H and 1 with DH was not delayed. Of the 12 infants c̄ FBD, the TT4 was low in 9 (75%), T3 low in 4 (33%) and FT4 low in 10 of 11 (91%) at Dx. The mean TSH at Dx did not differ between the infants c̄ FBD and infants s̄ FBD (p>0.5). Serum prolactin (Pr) was elevated beyond 3 months of age in 3 of 4 AT c̄ FBD infants compared to age-matched controls. The E/H and DH patients c̄ FBD and 3 CH patients s̄ FBD demonstrated normal Pr levels.

In summary, FBD commonly occurs in CH. The duration of hypothyroidism as determined by BA at Dx and severity of hypothyroidism at Dx as determined by TT4, T3, or TSH do not differ in patients c̄ or s̄ FBD. A low FT4 at Dx was present in all but 1 infant c̄ FBD. In AT patients c̄ FBD there appears to be a persistent Pr elevation during infancy.

● **355** ACCELERATED GROWTH DURING CONTINUOUS SUBCUTANEOUS INFUSION OF GROWTH HORMONE (CSIGH) IN DEFICIENT PATIENTS. J.Gertner, S.Page, W.Tamborlane, Dept. Ped., Yale U. School Med., New Haven, CT.

Conventional growth hormone (GH) replacement often fails to induce growth rates that can restore stature to the normal range even in doses exceeding current recommendations. While dosage increments may alter the peak GH value, plasma GH levels are elevated for only ~15 hrs after intramuscular injection. Recently we showed that CSIGH could maintain sustained elevations in GH for 4 days. Because the natural secretory pattern of GH is pulsatile, the effectiveness of CSIGH in the stimulation of growth remained to be determined. 4 GHD boys (10.1±1.2 yrs) who had stable growth rates on conventional GH Rx (.3U/kg/wk in 3 doses) received CSIGH for 4 months in a dose which raised plasma GH to 9-11 ng/ml (.6-.9 U/kg/wk). During conventional Rx age adjusted growth velocity was normal (5.7±1.1cm/yr). CSIGH resulted in a striking acceleration to values in excess of normal (11.3± 1.2cm/yr, P<.01). Growth acceleration was accompanied by significant rises in somatomedin C (.16±.08 to .95±.4 U/ml, P<.05) and the insulin response to oral glucose (area under curve 5.8± .8 to 9.8±1.5(mU/ml)·min, P<.05). However, there was no impairment of glucose tolerance, cholesterol and triglycerides remained normal and CSIGH was well tolerated by patients.

Conclusions: These data demonstrate that the growth-promoting effects of GH are not dependent on pulsatile release of the hormone. Methods of GH delivery which provide mild sustained elevations in GH levels may be a favorable alternative in the Rx of GHD.

356 EVALUATION OF INTELLECTUAL, ACADEMIC AND VISUAL-MOTOR FUNCTIONING IN CHILDREN WITH CONSTITUTIONAL DELAY (CD). Michael Gordon, Ernest M. Post, Carol S. Crouthamel and Robert A. Richman. SUNY Upstate Medical Center, Departments of Psychiatry and Pediatrics, Syracuse, N.Y.

Most previous studies of the intellectual, academic and psychosocial functioning of children with short stature have focused on those with growth hormone deficiency, rather than the much larger group with CD. To assess the effects of CD on learning and visual-motor functioning, we administered a battery of psychological tests to 24 affected children, aged 6-12 years. The results were compared to those of 23 healthy children with normal stature matched for age, sex and socioeconomic status. The tests consisted of 8 subtests of the Wechsler Intelligence Scale for Children-Revised, the Peabody Individual Achievement Test and the Bender-Gestalt Test. School teachers completed the Child Behavior Checklist and the Conner's Teacher Rating Scale. There were no significant differences between the two groups for any of the 15 variables analyzed. About 1/3 of the parents in each group reported that their children had academic difficulties. Since we have previously demonstrated that the children with CD tend to have more somatic complaints, low self-esteem, and to be socially withdrawn, it may be that school teachers are more attuned to notice acting out rather than internalizing sorts of behavior problems.

In conclusion, children with CD are not more likely to have school-related difficulties than their taller peers. While they are apt to have increased behavioral difficulties, these do not seem to intrude significantly into the academic realm.

357 BIOACTIVE LH IN UNTREATED CONGENITAL ADRENAL HYPERPLASIA. Alice B. Granoff, Mary Witt, and Inese Z. Beitins*, St. Louis Children's Hosp., Washington Univ. Sch.of Med., St. Louis & Mass.Gen.Hospt.(Vincent Res.Lab),Boston.

In some patients with congenital adrenal hyperplasia (CAH) initiation of treatment with hydrocortisone (HC) when the bone age is 12 years or more results in changes of normal puberty regardless of the chronological age.

Two boys with non-salt losing CAH ages 3-6/12 and 4-8/12 with bone ages of 11 and 12 years respectively were assessed for serum bioactive LH (B-LH) and immunoreactive LH (I-LH) response to gonadotropin releasing hormone (GnRH) injection (100 µg) prior to HC therapy, 8 days and 4 months later. Basal levels of I-LH were prepubertal in both boys before therapy but basal B-LH levels were elevated with a B/I ratio of 14.8 in the older patient and 4.7 in the younger one. The I-LH response to GnRH was prepubertal in the untreated state whereas B-LH was not significantly responsive to GnRH. Both B-LH and I-LH patterns were pubertal and similar 8 days after therapy in both patients and 4 months later in the younger patient but the B-LH was much higher in the older patient. The disappearance rate of B-LH was different in that high levels persisted throughout the sampling period whereas I-LH declined to baseline levels. The higher levels of B-LH seen in the older child correlated with the physical signs of early puberty and a commensurate rise in serum testosterone.

In summary, basal as well as stimulated B-LH corresponded better than I-LH to the hypothalamic maturation seen in children with CAH who are exposed for prolonged periods to elevated levels of sex steroid prior to therapy with HC.

358 CURE OF SEXUAL PRECOCITY WITH REMOVAL OF LHRH-SECRETING HAMARTOMA. James P. Gutai, Leland A. Albright, Peter A. Lee, University of Pittsburgh, Children's Hospital of Pittsburgh, Pittsburgh, PA.

The onset of sexual precocity was noted at age 10 mo., marked by penile growth. Progressive pubertal development and growth ensued over the next year. At 22 months, height had increased 16cm to 98.8, weight 4.9kg to 17.8, R testes to 3.5 x 1.5cm, and L 3.0 x 2.0, penile length to 11.5cm, pubic hair to Tanner Stage III. Acne, a deepened voice, and faint axillary and facial hair were evident. Bone age advanced from 39 to 60 mos. Plasma testosterone was 379 and 428 ng/dl, androstenedione 35, and 17-OH progesterone 99 and 127. Basal LH levels were in the normal adult male range (49 & 64 ng/nl) and response to LHRH stimulation was markedly accentuated, greater than the range of normal adult male responses (peak response - 335ng/ml). Pubertal sleep-related episodic responses were documented. Serum FSH basal and response levels to LHRH were consistent with those of prepubertal males. Skull x-ray, EEG, CNS CT scan and IVP at 14 mo. were interpreted as normal. Repeat CT scan and amipaque cisternogram at 21 mo. showed a 4-5mm suprasellar cisternal mass posterior to the pituitary stalk. At neurosurgery, this mass of tissue, which appeared grossly normal and was connected with a thin stalk to the floor of the hypothalamus anterior to the basilar artery, was dissected and removed. A hamartoma was demonstrated and shown to secrete LHRH. Hormone levels returned to normal, growth plateaued, and sexual characteristics regressed.

359 DETERMINATION OF IGF-I, IGF-II AND ILAs FOLLOWING GH THERAPY IN HYPOPITUITARISM. Harvey J. Guyda & Barry I. Posner. Depts. of Pediatrics & Medicine, McGill University, Montreal Children's Hosp. Res. Inst., Montreal, Quebec.

GH was administered (0.2±.02 U/kg/wk) to 24 patients (18M, 6F) with GH deficiency, aged 7 to 25 years; 14 were idiopathic (IH) and 10 had CNS disorders (CNS). Fasting plasma was obtained at 0, 4,24 and 72 hr after a single injection of GH, and at 1 and 6 mos on chronic therapy. Increased growth velocity (ΔGR = 0.49±.05 cm/mo) with GH therapy was significantly correlated with GH dosage ($p < .005$). IGF-I/SM-C was determined by RIA of unextracted plasma utilizing ^{125}I-IGF-I (R. Humbel) and an antibody to SM-C (NPA). IGF-II and ILAs were determined by RRA following acid chromatography utilizing rat and human placental membranes respectively. All values were compared to the same normal adult male pool assigned a value of 1.0 U/ml. A variable but significant mean increase ($p < .05$) was seen in IGF-I/SM-C at 4 hr, and persisted at 1 and 6 mos ($p < .01$). A significant mean increase in ILAs seen at 24 and 72 hr ($p < .005$) was maintained at 1 and 6 mos ($p < .005$). A significant correlation ($p < .001$) between IGF-I/SM-C by RIA and ILAs by RRA was seen. There was no significant correlation between ΔGR and either ILAs by RRA or IGF-I/SM-C by RIA, nor a difference in ΔGR, ΔILAs or ΔIGF-I/SM-C during puberty. IGF-II determined in 7 subjects (3 IH, 4 CNS) showed a significant mean increase at 1 mo ($p < .05$). Marked individual responses in IGF levels and lack of correlation with ΔGR were evident. Our data indicate that both alkaline (IGF-I, SM-C) and neutral (IGF-II, ILAs) IGF peptides are increased following GH therapy in hypopituitarism.

● **360** RIA OF IGF-I/SM-C IN CHILDREN WITH NORMAL AND ABNORMAL GH SECRETION. Harvey J. Guyda & Barry I. Posner. Depts. of Pediatrics & Medicine, McGill University - Montreal Children's Hospital Research Institute, Montreal, Quebec.

Spontaneous 6 hr GH secretory profiles have been studied q 20 min in 57 male and 32 female subjects (Endocrine Society, 63rd Annual Program, 1981, p.101). Spontaneous GH secretory episodes (≥ 5 ng/ml) were evident in 40 short children (87%), 89% of 27 control children and adults, and were absent in 16 patients with hypothalamic-pituitary dysfunction (HPD). The number and amplitude of GH episodes increased significantly with increased pubertal development. We have now determined IGF-I/SM-C levels q 2 h in unextracted plasma by a RIA employing ^{125}I-IGF-I/SM-C (R. Humbel, Zurich) and an antibody to SM-C (NPA). The diurnal variation was <20% and a mean value of 4 determinations for each subject was obtained. A clear age-dependent increase in IGF-I/SM-C, correlated with Tanner staging, was evident. Adult subjects had significantly lower values than Tanner V adolescents. In HPD, low IGF-I/SM-C values were usually seen in Tanner I subjects. However a markedly elevated value (2.6 U/ml) was seen in a 14 y.o. male subject with an astrocytoma and rapidly progressive puberty, despite undetectable GH by RIA, which decreased to 1.25 and 0.90 U/ml following irradiation. Overlap with normal levels was noted for younger hypopituitary subjects. A clear correlation between age and pubertal status with IGF-I/SM-C RIA values has been demonstrated. Our results indicate that single determinations of IGF peptides in patients with HPD must be interpreted with caution, and that both spontaneous GH secretion and IGF-I/SM-C levels increase during the pubertal growth spurt.

361 GROWTH HORMONE (GH) EFFECT ON SERUM GASTRIN IN GH DEFICIENT CHILDREN. John H. Holcombe, Rebecca T. Kirkland, George W. Clayton, Leonard Johnson, Dept. of Pediat., U. of Okla. Sch. of Med., Oklahoma City, and Baylor Coll. of Med., Houston; Dept. of Physiol., U. of Tex., Houston.

Gastrointestinal function in man is altered in hypopituitarism. Serum gastrin (G), an important trophic hormone in normal gastrointestinal function, is low in hypophysectomized animals. The low serum G can be restored to normal by GH therapy. We studied serum G in 24 children (mean age 9.7 yr, range 5.6-15.0 yr) with GH deficiency before and after acute and chronic GH therapy (Rx) to determine the effect of GH on G levels. Fasting (F) and one hr post-prandial (PP) G was determined before and after 5 d. GH (2 I. U./d), and again at 6 and 12 months during GH therapy 2 I.U. T.I.W.

		Gastrin, pg/ml*	
	n	Fasting	Postprandial
Pre-Rx	19	118.0±22.8	380.1±103.6
5 days	18	208.3±61.9	474.6±130.7
6 mo	17	121.8±27.7	----
1 yr	18	98.3±25.2	275.5±71.3

* Mean ± SEM

As observed in normal children PP G was greater than F G in the GH def. children before and after GH Rx ($p < .05$). GH Rx did not alter F or PP G levels compared to pre-Rx levels nor did the G response to a meal differ. There was no correlation between age and G response. Thus, it appears that GH Rx in GH deficient children does not increase basal or stimulated G secretion. Sponsored by NIH-RR-0188.

362 AUTONOMOUS OVARIAN HYPERFUNCTION CAUSING SEXUAL PRECOCITY IN MCCUNE-ALBRIGHT'S SYNDROME. Francine R. Kaufman and Gertrude Costin, Univ. of So. Calif. Sch. of Med. and Childrens Hospital of Los Angeles, Dept. of Peds., Los Angeles, Calif.

A 5 year old girl presented with a 6 month history of breast development and one episode of vaginal bleeding. On physical examination she had hyperpigmentation of the right anterior and lateral thigh and right buttock, Tanner Stage III breast development and hyperpigmented areolae. Skeletal x-rays showed polyostotic fibrous dysplasia consistent with McCune-Albright's syndrome and a bone age of 5 years. Random serum FSH and LH levels were <1.7 and 3.8 mIU/ml and peak levels during sleep were <1.7 and 2.1 mIU/ml, respectively (prepubertal levels <5 mIU/ml). Following luteinizing releasing hormone (LRH), FSH level did not rise above the basal value of <1.7 and LH rose from 2.8 to 3.5 mIU/ml. Serum estradiol levels ranged from 189 to 1285 pg/ml, progesterone was 82 ng/ml and dehydroepiandosterone-SO_4 21 µg/dl. Multiple ovarian cysts up to 5 cm in diameter were present bilaterally on pelvic ultrasound. The normal T4 and T3 levels, normal TSH response to thyrotropin releasing hormone, as well as normal parathyroid hormone level, and normal cortisol response to ACTH stimulation and dexamethasone suppression ruled out hyperfunction of other endocrine glands. Following oral L-dopa, growth hormone rose to 23.7 ng/ml and prolactin decreased to 3.5 ng/ml.

In our patient, the occurrence of sexual precocity, in the absence of elevated gonadotropins (Gn) and a prepubertal Gn response to LRH suggests an autonomous hyperfunction of the ovaries not mediated through the hypothalamic-pituitary gonadal axis.

363 DIFFERENTIAL DEACTIVATION OF TESTOSTERONE (T)- AND 5α-DIHYDROTESTOSTERONE (DHT)-RECEPTOR (R) COMPLEXES: ANOTHER EXPLANATION FOR DIFFERENTIAL ANDROGENICITY OF T AND DHT IN 5α-REDUCTASE (5α-R'ase) DEFICIENCY. M. Kaufman and L. Pinsky. Lady Davis Institute for Medical Research, and the Centre for Human Genetics, McGill University, Montreal.

We have studied the rate and character with which T-R and DHT-R complexes dissociate within, and after extraction from [^{3}H]T or [^{3}H]DHT-labelled genital skin fibroblasts (GSF) of a subject with 5α-R'ase deficiency. Within GSF the T-R and DHT-R complexes dissociate with $t_{\frac{1}{2}}$ of 30 and 90 min at 37°, respectively, but each type of complex dissociates with monophasic, first-order kinetics and is in the «activated» state as determined from an Arrhenius plot (27-40°). After extraction from GSF and partial purification through a G-75 column, DHT-R complexes still dissociate monophasically with the same $t_{\frac{1}{2}}$ as above, but T-R complexes exhibit biphasic kinetics - an initial «rapid» (preactivated) phase (k_{-2}, 40×10^{-3} min^{-1}) followed by a «slow» (activated) one (k_{-1}, 10×10^{-3} min^{-1}). The dissociative behavior of the T-R complexes in vitro resembles that of DHT-R complexes from (i) GSF of subjects with activation-defective, receptor-positive androgen insensitivity, and (ii) normal GSF when dissociation occurs in the presence of 5 mM pyridoxal 5' phosphate. Conclusion: DHT-R complexes within intact GSF remain in the activated state when extracted, whereas T-R complexes revert to the preactivated state. This may reflect a physiologic difference between T-R and DHT-R complexes that underlies the division of labor between T and DHT in male genital organogenesis and the organotypic phenotype of 5α-R'ase deficiency.

● **364** HYPOSPADIAS (HS): ABNORMALITY OF 5α-DIHYDROTESTOSTERONE (DHT) BINDING IN SONICATES OF CULTURED GENITAL SKIN FIBROBLASTS. Bruce S. Keenan, Ronald McNeel, Edmond T. Gonzales. Baylor College of Medicine, Depts. of Pediatrics and Urology, Houston, Texas, 77030.

Receptor-like DHT-binding activity has been demonstrated in the intact skin fibroblast. To evaluate DHT-protein interactions under equilibrium conditions, dissociation constant (Kd,nM) and binding capacity (B_{max},fm/mg protein) were measured by Scatchard analysis in sonicates of cultured fibroblasts. Gel filtration of the sonicate was carried out prior to incubation to eliminate steroid metabolism and Na_2MoO_4 (.2M) added at sonication to stabilize binding activity. In this system, DHT binding in newborn (NB) fibroblasts was compared to methyltrienolone (MTr) and testosterone (T):

	DHT:		MTr:		T:	
	Kd	B_{max}	Kd	B_{max}	Kd	B_{max}
NB #8	.15-.41	10.3-14.7	.33	12.5	2.7	17.1
NB #6	.46-.65	15-15.2	.25-.54	9.7-10.3		

DHT binding was compared in controls (10 normal NB, 8 children undergoing circumcision) and simple HS (n=27). For controls Kd=.28 ± .04, s.e. and B_{max}=10.1 ± 1.3. Fibroblasts from HS gave significantly lower B_{max}=6.1 ± 0.7 $p<.001$ by Mann-Whitney test, but Kd, 0.25 ± .04 s.e. was not different from controls. B_{max} values were similar in distal (n=7), midshaft (n=10) and penoscrotal HS (n=10). Lack of correlation between B_{max} and severity of HS suggests that decreased B_{max} is incidental to another feature of a defective receptor, e.g., instability, or that other factors in utero contributed to the development of HS. Supported by NIH Grant USPHI ROI HD15018-01/03.

365 PERINATAL CHANGES IN THYROID FUNCTION AND TISSUE RESPIRATION IN THE LAMB. Alan H. Klein, Anita L. Reviczky, Paula J. Chou, James F. Padbury, Calvin J. Hobel, and Delbert A. Fisher, UCLA School of Medicine, Harbor-UCLA Medical Center, Department of Pediatrics, Torrance, CA.

The relationship between perinatal changes in thyroid function and tissue respiration was evaluated by measuring hepatic and renal cortical oxygen consumption (QO_2) with and without ouabain (1mM) in tissues from fetal lambs at 121-124 days gestational age (GA) (Group I, n=5), 136-140 days GA (Group II, n=5) and in newborn lambs between 1 and 7 days of age (Group III, n=8). Geometric mean triiodothyronine (T3) concentrations (±95% confidence levels) increased from 14.3 (<11.6-21.1) ng/dl in Group I to 40.7 (18.1-91.4) ng/dl in Group II and 504 (424-599) ng/dl in Group III. Serum T4 levels were similar in all 3 groups. Mean (±SEM) total hepatic QO_2 values were similar in Groups I and II (34.7± 4.3 and 24.9±4.1 µl O_2/100 mg·hr) and increased to 59.5±4.2 in Group III ($p<0.01$). Sodium transport dependent QO_2 (total QO_2-ouabain suppressed QO_2) was significantly greater in Group III (21.2±2.2) than in Groups I (11.4±2.7) or II (3.1±0.8), and was decreased in Group II compared to Group I. Non-transport dependent (ouabain suppressed) QO_2 was similar in Groups I and II (23.3±2.4 and 21.9±4.5) and increased in Group III (38.3±2.9, $p< 0.01$). Renal cortical total and ouabain suppressed QO_2 values were similar in the three groups. Conclusions: 1) The increase in T3 concentrations observed in the newborn lamb correlates with an increase in hepatic but not renal cortical tissue respiration; 2) the increase in hepatic respiration is due to an increase in both sodium transport dependent and non-dependent respiration.

● **366** EFFECTS OF THYROID HORMONES ON TISSUE RESPIRATION IN THE OVINE FETUS. Alan H. Klein, Anita L. Reviczky, James F. Padbury and Delbert A. Fisher, UCLA School of Medicine, Harbor-UCLA Medical Center, Department of Pediatrics, Torrance, CA.

The effect of T3 treatment on in vitro oxygen consumption (QO_2) of isolated brown adipose tissue cells (BAT), liver, kidney cortex, brain and heart was studied in fetal sheep. Thyroidectomy and insertion of a constant infusion pump was performed at 119-121 days gestation followed by 8 days of infusion with either T3 (4 animals, Group I, 24 mcg/hr) or vehicle (4 animals, Group II). After hysterotomy, animals were sacrificed with barbiturate and decapitation and the tissues were removed. Basal QO_2 (±ouabain, 1mM) was measured in all tissues; norepinephrine (NE, 10^{-6}M) (±ouabain) stimulated respiration was measured on BAT only. Cord T3 serum concentrations at hysterotomy ranged between 160 and 502 ng/dl in Group I and were undetectable in Group II. There were no significant group differences for basal QO_2 (± ouabain, 1mM) in any of the tissues studied. NE stimulated QO_2 significantly increased in Group I (123±18.5) (SEM) µl $O_2/10^6$ cells·hr) vs Group II (55±15.6) ($p<0.05$). Non-sodium transport dependent NE QO_2 (ouabain suppressed) was increased in Group I (70±4.7 vs 27.3±7.8) ($p<0.01$) but transport dependent NE QO_2 (NE QO_2 - QO_2 with ouabain) was not different in the two groups. Conclusions: Basal tissue respiration in the ovine fetus at 120-130 days is not thyroid hormone dependent. In contrast NE stimulated BAT respiration increased two-fold suggesting that thyroid hormones may play an important role in stimulated BAT thermogenesis in the ovine fetus.

● **367** PARTIAL PERIPHERAL RESISTANCE TO THYROID HORMONES IN CHILDHOOD: THE PROBLEM OF CLINICAL EVALUATION. Sobha Kollipara and Matthew H. Connors. University of California, Davis, School of Medicine, Department of Pediatrics Sacramento.

Three children aged 2, 11 1/2 and 15 years were shown to have variable degrees of thyroid hormone insensitivity. Prior to investigation all three received therapy with either thyroid blocking drugs or thyroid hormone due to wrong clinical diagnosis. Normalization of thyroid hormone levels resulted in hypothyroidism. The older two patients were first cousins. The youngest patient had signs of hypothyroidism including both developmental and skeletal delay which were possibly exaggerated with 8 months of propylthiouracil therapy. The older two patients had goiters and were clinically euthyroid. All subjects had increased levels of thyroxine 14.4 - 21.5 µg (nl 4.5 to 11.5), free thyroxine 2.7 - 4.0 ng/dl (nl 0.8 to 2.3), triiodothyronine 243 - 430 ng/dl (nl 100 to 200), and normal thyroxin binding proteins. Serum TSH was normal in 2 subjects and elevated in the 15 year old to 42 µIU/ml (nl 1.9 to 5). All subjects developed a 30 minute peak response to TRH which was normal in 2 (10 and 16 µIU/ml) and exaggerated in the 15 year old (291 µIU/ml).

These observations indicate that the diagnosis of partial peripheral resistance to thyroid hormone may be missed in the clinically euthyroid child with a goiter and elevated thyroxine levels. The TRH test is an important step in differentiating this disorder and is indicated before therapy with antithyroid drugs. The underlying abnormality in these patients is unknown.

368 ANALYSIS OF GASTRIC EMPTYING AND CARBOHYDRATE TOLERANCE IN CHILDREN FOLLOWING FUNDOPLICATION FOR GE REFLUX. Sobha Kollipara, Marilyn Swanson, Kenneth L. Cox, and Matthew H. Connors. University of California, Davis, School of Medicine, Department of Pediatrics, Sacramento.

Rapid gastric emptying of carbohydrate substances is thought to augment insulin secretion and result in the symptoms of reactive hypoglycemia. Seven children aged 1-12 years who had previous Nissen fundoplication alone or combined with pyloroplasty were studied. The rate of gastric emptying was measured by the disappearance of Technicium 99 sulphur colloid in apple juice vehicle. Serial imaging was done at 15 minute intervals. Simultaneous measurements of blood glucose and insulin levels were obtained at 30 minute intervals. No subjects were symptomatic during the procedure.

Gastric emptying in patients with fundoplication alone was 69 minutes (45-105 minute range) as compared to 129 minutes (35-288 minute range) in patients with fundoplication with pyloroplasty. There was no correlation between the rate of gastric emptying and the rise in blood glucose and insulin levels although three children had exaggerated insulin responses (50-72 µU/ml) with normal glucose levels at 30 minutes. This did not correlate with the type of surgery.

From these observations it is concluded that gastric emptying is variable with either fundoplication alone or when combined with pyloroplasty. The glucose tolerance and the insulin response did not correlate with the rate of gastric emptying.

369 SEASONAL GROWTH RATES IN HYPOPITUITARY DWARFISM WITH AND WITHOUT GROWTH HORMONE (hGH) THERAPY. Sobha Kollipara, Linda Wilcox and Matthew H Connors. University of California, Davis, School of Medicine, Department of Pediatrics, Sacramento.

Variation in linear growth rates with seasonal changes have been attributed to physical activity, sunlight exposure, or vitamin D influences. We compared the hGH-induced growth rates in 19 hypopituitary dwarfs aged 4 to 22 years during two 4 month periods. Subjects did not receive hGH 4 months before the study. Individual growth variation was analyzed. The growth rate during Spring - Summer (April - August) and Fall - Winter (October - February) did not differ significantly (8.19 vs 8.12 cm/yr). Growth for these same periods was compared with all subjects while off of hGH therapy. The growth rates were significantly greater ($p<0.05$) in the Spring - Summer period. While rates of growth during therapy exceeded those during periods without therapy ($p<0.005$), no correlation was found between rates of growth and skeletal age or with the degree of skeletal age retardation.

Our data support the concept that seasonal variations in growth rate persist in hypopituitary dwarfism, but do not influence growth rate during therapy with hGH.

370 THE SPECTRUM OF THE MC CUNE-ALBRIGHT SYNDROME, Peter A. Lee, Claude J. Migeon, James P. Gutai, Univ. of Pittsburgh, Children's Hosp. of Pgh., Dept. of Ped., Pgh., PA, Johns Hopkins Univ. & Hosp., Dept. Ped., Baltimore, MD

The presentation, progression and long-term follow-up of 14 patients with 2 or 3 of the triad of findings of McCune-Albright Syndrome have been evaluated. Twelve female patients had sexual precocity; 4 lacked bony lesions & 1 skin lesions. Four presented with vaginal bleeding, 7 with breast growth & 1 with pubic hair. Age of onset was 0.3 to 8 years. Three girls had temporary regression; 7 had irregular vaginal bleeding. Serum LH & FSH in 4 were prepubertal levels. One who menstruated regularly had a prepubertal response to LHRH & minimal suppression with estradiol & provera. Two patients have each had 2 normal children. Adult heights of 5 range from 159 to 176cm, within 3.3cm of predictions based on parent's heights. Two patients had thyrotoxicosis & 1 acromegaly. Thirteen had cafe-au-lait spots, ten had polyostotic fibrous dysplasia. All had progression of bone lesions during childhood, 6 had one or more pathologic fractures, none after age 18. In the nine patients with both bone and skin findings the laterality of the skin lesion was concordant with the bone lesion in 5 instances.

Findings suggest that the severity, and even presence, of the three classic criteria of the McCune-Albright Syndrome vary considerably. Gonadotropins are not consistent with hypothalamic-pituitary maturation. Bony lesions did not progress after growth was complete; skin lesions, with an exception, did not progress after birth; and the laterality of these lesions was poorly concordant.

● **371** THE EFFECTS OF CASTRATION ON PULSATILE GONDAOTROPIN SECRETION DURING SEXUAL DEVELOPMENT IN THE MALE SUBHUMAN PRIMATE. B.C. Lee, B. Spiliotis, J. Pineda, H.C. Sachs, T.J. Brown, and B.B. Bercu, NPMB, NICHD, NIH, Bethesda, MD 20205

During male sexual development, there are changes in the hypothalamic-pituitary-testicular axis which are modulated by alterations in 24 h secretory patterns of gonadotropins. In order to characterize the pattern in the absence of negative feedback, we studied pulsatile LH/FSH secretion (q 15 min samples drawn without anesthesia in animals fitted with a vest and mobile tether) in castrated monkeys. Of the 18 monkeys, 4 were castrated at birth, and one each at 1, 8, 10, 20, 26, 33, 42 and two at 25 months of age, and five were castrated as adults. Pulsatile secretion of LH/FSH occurred as: 1) micro-pulses, having amplitudes < 2X over baseline; 2) macro-pulses, where the increase in LH/FSH levels > 2X. The greatest frequency and largest amplitude of pulses occurred in adults. In early postnatal life, there were also large and frequent pulses but less than in adults. Pulsatile secretion was absent during prepubertal life and early puberty. In two animals, castrated at birth and studied at 33 months of age (midpuberty), markedly dichotomotous patterns were apparent. One animal had advanced into "puberty" and LH micro- and macro-pulses (up to 6X) were seen with an ↑ frequency and magnitude of FSH pulses. The other animal retained a prepubertal secretory pattern, even when restudied 4 months later. These data indicate that changes in amplitude and frequency of LH/FSH pulsatile secretory patterns occur in the absence of the testis suggesting pubertal maturation is independent of negative gonadal feedback.

● **372** URINARY EXCRETION OF EPIDERMAL GROWTH FACTOR (EGF) IN GROWTH HORMONE (GH) DEFICIENT CHILDREN BEFORE AND AFTER TREATMENT WITH GROWTH HORMONE. Lynne L. Levitsky, Deborah V. Edidin, and Robert Benveniste. Pritzker Sch. of Med., Univ. of Chicago, Michael Reese Med. Ctr., Dept. of Pediatrics and the Gynecic Endocrinology Laboratories, Dept. of Obstetrics & Gynecology, Chicago.

We have previously measured urinary EGF in children using a human placental membrane radioreceptor assay which does not crossreact with insulin growth factor I (IGF I), somatomedin A, or other growth factors or peptide hormones. EGF excretion in normal children was 33.0 ± 2.8 $\mu g/M^2/24$ hr. EGF excretion was significantly ($p < .02$) diminished in GH-deficient children before therapy and was similar to normal in a like group of children after prolonged GH therapy. In this study we have evaluated the relationship between EGF excretion and the length of GH therapy in order to determine whether EGF is a GH-dependent growth factor. Urinary EGF was measured in 5 GH-deficient children before and after .1 IU/kg of GH q 12 hr X 2. There was no significant rise in EGF excretion over 3 days. However, in 7 GH-deficient children treated for 1 month with .1 IU/kg of GH 3X/wk, excretion of EGF rose from 24.5 ± 3.4 $\mu g/M^2/24$ hr to 40.2 ± 4.8 $\mu g/M^2/24$ hr ($p < .05$). The rise persisted during treatment thereafter. Since EGF excretion is enhanced by prolonged (1 month) GH therapy, but not by short-term GH therapy, EGF is not a classic GH-dependent growth factor. Whether EGF represents a delayed intermediate in the mechanism of GH action or whether it is a product of the GH-induced growth effect remains to be elucidated.

● **373** EFFECTS OF AN LHRH AGONIST D-TRP^6-PRO^9-NET-LHRH (LHRH$_a$) UPON GROWTH AND SKELETAL MATURATION IN CENTRAL PRECOCITY, M. John Mansfield, Jacquelyn S. Loughlin, John D. Crawford, Hans H. Bode, William F. Crowley, Jr., Harvard Medical School, Mass. General Hospital, Dept. of Pediatrics, Boston.

We have previously demonstrated that short term LHRH$_a$-induced pituitary desensitization is a safe, effective and reversible means of suppressing the gonadotropins and sex steroids in subjects with central precocious puberty. However, the effects of this therapy upon growth and bone maturation is as yet unknown. 5 girls with well-established central precocity were treated with 4-8 ug/kg/d of the LHRH$_a$ for 12 consecutive months. Pubertal development regressed one full Tanner stage in 4/5, menses ceased, maturation index scores returned to prepubertal levels, and E2 values fell to < 20 pg/ml in all. In all patients growth velocity decreased to normal and bone ages which had been rapidly accelerating pretherapy all advanced ≤ 1 year during the 12 month treatment period. Parents remarked upon the decrease in hyperkinesis and emotional lability which had been unrelieved by previous therapy with medroxyprogesterone acetate in 2 patients.

	Growth Velocity[1]	B.A.[2]	E2[3]	M.I.[4]
Pre-Rx	9.7 ± .89 SE	11.1 ± .6 SE	31.2 ± 13.2 SE	64.1 ± 12 SE
Post-Rx	6.2 ± .45 SE+	11.7 ± .5 °	< 20°	14.6 ± 20*

All values = Mean ± SE; + = p < .01, ° = NS, * = p < .005.

Conclusions: The LHRH$_a$ is capable of normalizing growth velocity and skeletal maturation in central precocity and thus appears to be unique among the agents which have been used to treat this condition. 1 = cm/yr, 2 = bone age, 3 = pg/ml, 4 = maturation index score.

● **374** 1,25-DIHYDROXYVITAMIN D (1,25-D) AND IONIZED CALCIUM (Ca^{++}): RESPONSE TO BOVINE PARATHYROID HORMONE (bPTH) IN HORMONE DEFICIENT HYPOPARATHYROID (HP) CHILDREN. Morri E. Markowitz, John F. Rosen, Connie M. Smith, and Hector F. DeLuca. Dept. Peds-CRC, Einstein Coll. Med., Montefiore Hosp., N.Y.; Dept. Biochem., U. Wisconsin, Madison.

Blood Ca^{++} concentration is regulated tightly, in part, by PTH and 1,25-D. Stimulation of the renal 1-hydroxylase enzyme by PTH produces an increase in 1,25-D biogenesis from its precursor, 25-hydroxy D. This has been demonstrated in normal and HP adults but not in patients with pseudo HP. The present study was designed to evaluate the enzyme's responsiveness to bPTH in children with idiopathic HP. Four children (ages 4-10 years) received bPTH 5U/kg parenterally at 0 and 2 hours. Blood samples were drawn sequentially to measure blood Ca^{++}(mg/dl), PTH(µl-equiv/ml), and 1,25-D (pg/ml). The results (mean ± SE) were:

	0H	2H	4H	8H	12H	14H	24H
Ca^{++}	3.20 ±.05	3.19 ±.05	4.40 ±.08	4.52 ±.09	4.51 ±.08	3.21 ±.02	3.16 ±.03
PTH	0	36±3	62±10	12±2	0	0	0
1,25-D	16±.5	18±1	18±1	55±3	55±4	44±3	16±1

Conclusions: 1) Our 4 patients had appropriate calcemic responses to bPTH. 2) The sequence of changes in blood concentrations was: PTH, Ca^{++}, 1,25-D. 3) This order was followed both in the rise and fall of the serum levels of these blood constituents. 4) The rise in Ca^{++} preceding increases in 1,25-D may reflect PTH-stimulated osteoclastic activity; maintenance of peak Ca^{++} levels may be due to the additive effect of 1,25-D and PTH on osteocytic function.

● **375** INAPPROPRIATE TSH SYNDROME: RESPONSE TO DOPAMINE. Kenneth McCormick, Kitima Sriwatanakul, and Paul D. Woolf. (Spon. by Gilbert B. Forbes). University of Rochester Medical Center, Department of Pediatrics, Rochester, New York.

A 12 yr. old girl was evaluated with a history of recurrent goiter and high TSH after thyroidectomies. Clinically florid hyperthyroidism with goiter was diagnosed at age 5, and she had two thyroidectomies, four years apart, because of recurrent symptoms and dysphagia. Except for a maternal grandmother with hyperthyroidism, the family history was negative for endocrinopathies. On examination she was clinically euthyroid with moderate thyromegaly; T_4 8.1 µg%, TSH >40 µU/ml. Two months of thyroid hormone supplement slightly suppressed her elevated TSH (32 µU/ml), despite elevations in her T_4 (14.8 µg%), T_3 (353 ng%), and free T_4 index (4.6 units). Growth hormone, cortisol, LH, FSH, and prolactin levels were normal and responded appropriately to provocative tests. Cranial CT scan, suprasellar polytomogram and visual fields were normal.

The TSH response to TRH was grossly exaggerated (peak level 676 µU/ml) and was only slightly suppressed by pre-treatment with dexamethasone. However, a dopamine infusion (4 µg/kg/min) resulted in a 65% suppression of both basal TSH level and the response to TRH. A five month trial of a dopamine agonist (bromocriptine), up to 7.5 mg/day, was unsuccessful: basal TSH levels persisted and there was no alteration in the TSH hyperresponsiveness to TRH.

This study demonstrates the pituitary responsiveness of the non-neoplastic inappropriate TSH syndrome to dopamine but not to bromocriptine.

376 PROLACTIN IN SUBTYPES OF GROWTH HORMONE DEFICIENCY BEFORE AND DURING TREATMENT. J. Michael McMillin, Thomas Aceto, Jr., David R. Brown, Robert Bonner, Univ. of SD, Sioux Falls, SD; St. Louis Univ., St. Louis, MO; Univ. of MN and Minneapolis Childrens Hospital, MN.

We have studied the prolactin response to TRH in 15 control children, 20 with idiopathic growth hormone deficiency (IGHD) and 15 with organic growth hormone deficiency (OGHD). Baseline prolactin concentration (m of 3 samples ± SEM) was 8.5 ± 1 ng/ml in control children, 15.1 ± 3.7 ng/ml in the IGHD children and 64.7 ± 43.9 ng/ml in the children with OGHD. Eight with IGHD had a history of perinatal insult. Baseline prolactin was significantly higher in these children (20.7 ± 5.5 ng/ml) than children with normal perinatal history (8.7 ± 1.6 ng/ml, p <.03). Mean peak prolactin concentration after TRH was 45.8 ± 4.7 ng/ml in the control children, 46.9 ± 7.0 ng/ml in the children with IGHD and 95.0 ± 47.8 ng/ml in those with OGHD. Eighteen of the IGHD and ten of the OGHD children were restudied while being treated with GH (0.08 IU/kg t.i.w.). Intratreatment mean baseline and peak post TRH prolactin was not significantly different from pretreatment values. Considerable variability was found in the baseline values before and during GH Rx in the IGHD group. We conclude that: 1) Hypothalamic injury secondary to perinatal insult could be the etiology of growth hormone deficiency in a distinct subgroup of children with IGHD, 2) We find no evidence for an agonistic or antagonistic effect of growth hormone on prolactin secretion, 3) Baseline prolactin obtained on several occasions and TRH testing are valuable adjuncts in the evaluation of pathologic short stature.

377 ESTRADIOL (E2) AUGMENTATION OF LH RELEASE BY THE PREPUBERTAL PITUITARY IN VITRO. George W. Moll, Jr.* & Robert L. Rosenfield, University of Chicago Pritzker School of Medicine, Department of Pediatrics, Chicago, IL.

In order to explore the possible role of E2 feedback at the pituitary level in the onset of puberty, the following experiments were performed.

An in vitro perifusion system was developed to test the response of the isolated pituitary to E2 and pulsatile LHRH under physiological conditions. Five to six hemipituitaries from one month old (juvenile) female Sprague-Dawley rats were placed in paired perifusion cells. One cell was perfused with M199 medium (A), while the other cell was simultaneously perfused with M199 + 10^{-9} M E2 (B). LHRH pulses (10^{-8} M) were given synchronously every 1.5-4.2 hr. The LH production rates in response to each LHRH pulse were compared during 20 hours of perifusion at 38° C:

Pulse Time (hr)	0	2.2	3.8	7.4	11.6	13.2	14.8	16.2	17.8
Relative LH prod. (B/A + SD)	1.0	0.50 +.04	0.72 +.04	1.15 +.21	1.25 +.07	1.75 +.21	1.50 +.28	1.45 +.07	1.46 +.01

The data indicate 1) an early inhibition ($p < .05$) by E2 of LH response to LHRH and 2) a later gradual rise to persistently positively augmented LH surges in response to LHRH pulses ($p < .025$ between 12-18 hr).

These results directly demonstrate for the first time that E2 has a biphasic effect upon pituitary LH responsiveness to LHRH. The initial effect (within 2 hr) is transient early inhibition. This is followed by prolonged augmentation, which commences by about 12 hr. Furthermore, these effects are discernible prepubertally.

Thus, pituitary LH release is not persistently inhibited by E2 in the juvenile period. In fact, E2 would seem to play a role in promoting pubertal maturation at this stage of development by enhancing pituitary LH release.

● **378** PRIMARY HYPERALDOSTERONISM IN CHILDHOOD DUE TO UNILATERAL MACRONODULAR HYPERPLASIA. S.E.Oberfield, E.Stoner, L.S.Levine, D.Laurence Sr., M.I.New, Cornell Univ Med Col, New York, NY 10021

We present the first report of primary hyperaldosteronism in childhood due to unilateral macronodular hyperplasia. A 10 y o white male with severe hypertension (150/100mmHg), hypokalemia (1.9mEq/l), and suppressed plasma renin activity (PRA) (<.1ng/ml/hr) was extensively studied. Alterations of dietary sodium demonstrated fixed PRA and aldosterone levels. The paradoxical decrease in aldosterone on assumption of upright posture suggested a tumor. The marked hypertensive response to prolonged ACTH was accompanied by aldo escape. A minimal decrease in urinary aldo with dexamethasone was noted excluding dexamethasone suppressible hyperaldosteronism. Blood pressure normalized with spironolactone. CTT, iodocholesterol scanning, and adrenal venography were not diagnostic of a discrete adrenal lesion.

Adrenal vein hormone sampling with ACTH stimulation however, lateralized aldosterone secretion unequivocally to the left adrenal gland:

	Aldo (ng/dl)	DOC* (ng/dl)	B* (µg/dl)	F* (µg/dl)	Aldo/F Ratio
Left adrenal vein	5795.0	16,034.0	90.0	1896.0	3.06
Right adrenal vein	107.0	4885.0	140.0	2233.0	0.05
IVC below adrenal veins	89.2	192.9	2.352	22.2	4.0
Peripheral vein	62.3	187.0	3.4	25.0	

Although hyperplasia as a cause of hyperaldosteronism in childhood is more common than an adenoma, a tumor was predicted in this child since excessive aldosterone appeared to originate from one adrenal. However, left adrenalectomy revealed macronodular hyperplasia, adrenal pathology consistent with the patient's young age. Post operatively there has been a normalization of blood pressure, biochemical, and hormonal parameters which further support the unilateral secretion of aldosterone excess as the cause for the primary hyperaldosteronism. Thus in childhood, hyperaldosteronism due to unilateral hypersecretion may result from nodular hyperplasia, rather than a discrete adenoma.

* DOC, desoxycorticosterone; B, corticosterone; F, cortisol

379 NON SALT LOSING CONGENITAL ADRENAL HYPERPLASIA(CAH) DUE TO 3βOH STEROID DEHYDROGENASE(3βOHSD) DEFICIENCY. S.Pang, L.S.Levine, E.Stoner, J.M.Opitz, M.I.New, Cornell Univ Med Col, NY 10021; Shadair Childrens Hosp, Helena MT 59601

Both a 6 yr old boy and his non-HLA identical 8 yr old sister had biochemical evidence of 3βOHSD deficiency and lacked salt wasting symptoms. The sister did not manifest abnormal genital development at birth but developed premature adrenarche at 4 yrs with clitoromegaly and advanced bone age. The brother had 4°hypospadias at birth.In both sibs the baseline and ACTH stimulated Δ5 steroids, pregnenolone, dehydroepiandrosterone(DHA), 17-OHpregnenolone, were unequivocally elevated. The baseline Δ4 steroids, progesterone, 17-OHprogesterone, androstenedione and testosterone(T), were slightly high while DOC, B, F were in the normal range, and rose poorly or appropriately to ACTH. All steroids were promptly suppressed with dexamethasone(DEX). Baseline plasma and urinary aldosterone were normal and rose with ACTH and a low Na diet with prompt Na conservation. Baseline plasma renin activity was normal or slightly elevated and increased with ACTH and a low Na diet,and decreased following DEX suggesting the presence of an ACTH-dependent mineralocorticoid antagonist. HCG did not stimulate E2 in the sister. T rose poorly with HCG in the brother indicating a deficiency of 3βOHSD in the gonad. Following 3H-DHA-IV infusion, 3H T conjugate was detectable in a 24hr urine suggesting the presence of some peripheral 3βOHSD activity. We propose in these children a partial deficiency of 3βOHSD in the 17hydroxy, 17deoxy and androgen pathway in zona fasciculata and intact 3βOHSD in zona glomerulosa supporting the concept that zona glomerulosa and zona fasciculata function as separate glands.

380 RELATIONSHIP OF ORAL GLUCOCORTICOID THERAPY TO URINARY FREE CORTISOL (UFC) EXCRETION Frank C. Papacostas, James P. Gutai and Thomas P. Foley, Jr., Univ. of Pgh., Dept. of Ped., Pittsburgh, PA

A positive correlation between UFC excretion and cortisol production rate has been reported previously in normal children. In the present study UFC was measured on 34 patients aged 5-16 yrs. who were on oral hydrocortisone (F) therapy. 20 patients had congenital adrenal hyperplasia (CAH), (13 salt losers, 7 nonsalt losers). There were 14 patients with panhypopituitarism (PHT) of which 12 were postop craniopharyngioma and 2 were idiopathic. All patients received F therapy for 1 mo. prior to each study time. A second UFC determination was obtained on 21 of the 34 patients at least 1 month after a change in the F dose. There was a significant positive correlation between UFC excretion ($\mu g/M^2/24$ h.) and oral F dose ($mg/M^2/24$ h.) in each group of patients studied.

CAH: 1st specimen n=20 r=.73 p<.001
CAH: 2nd specimen n= 9 r=.77 p<.05
PHT: 1st specimen n=14 r=.68 p<.01
PHT: 2nd specimen n=12 r=.74 p<.01
CAH: mean dose of F=17.7 $mg/M^2/d$; mean UFC 71.0 $\mu g/M^2/d$
PHT: mean dose of F= 9.8 $mg/M^2/d$; mean UFC 31.9 $\mu g/M^2/d$

The positive correlation between UFC excretion and replacement F therapy may be helpful to determine the appropriate dose of F in children with PHT on exogenous F therapy in order to minimize the inhibitory growth effects and other complications secondary to glucocorticoid administration.

381 DEVELOPMENTAL CHANGES IN TESTICULAR STEROIDOGENESIS FROM EARLY POSTNATAL THROUGH ADULT LIFE IN THE SUBHUMAN PRIMATE. J.L. Pineda, B.C. Lee, B. Spiliotis, H.C. Sachs, T.J. Brown, and B.B. Bercu. NPMB, NICHD, NIH, Bethesda, MD 20205.

Systematic longitudinal and cross-sectional studies to characterize steroidogenesis in monkeys have not been previously done. Monkeys (N=46) were studied from 2 weeks of age through adult life with hCG and GnRH stimulation tests. HCG (100 IU/kg was given i.v. and blood was drawn for testosterone (T), dihydrotestosterone (DHT) and Δ^4 androstenedione (Δ^4) prior to and 60 min after hCG. On another day, GnRH (10 μg) was given i.v. and blood was drawn at 0, 15, 30, 60, 90 and 120 min for T, LH and FSH. The data can be subdivided into the following developmental categories on the basis of the hCG stimulated 60 min values:

	age (mo.)	n	T (ng/dl)	DHT (ng/dl)	Δ^4 (ng/dl)
postnatal	(1/2-6)	10	564 ± 53	55 ± 17	95 ± 32
prepubertal	(7-24)	20	62 ± 6	12 ± 2	29 ± 6
early pubertal	(25-31)	6	85 ± 16	< 10	19 ± 5
midpubertal	(32-39)	12	456 ± 136	37 ± 19	14 ± 3
late pubertal	(40-50)	12	2166 ± 245	63 ± 13	37 ± 7
adult	(> 60)	12	2158 ± 238	98 ± 16	65 ± 10

T response to GnRH stimulation also correlated with age. Histological changes in light microscopy paralleled T secretion. In conclusion, the subhuman primate is a useful model to study human sexual development. Because of the known pulsatility of T secretion, a short hCG stimulation test may substitute for single static measurements in staging male sexual development.

382 CLOMIPHENE CITRATE IN THE TREATMENT OF ADOLESCENT GYNECOMASTIA: CLINICAL AND ENDOCRINE STUDIES. Paul V. Plourde, Howard E. Kulin, Richard J. Santen, and Steven J. Santner. The M.S. Hershey Med. Ctr. of The PA State Univ., Div. of Endocrin., Depts. of Med. and Ped., Hershey, PA

Antagonism of estrogen action and stimulation of androgen production with the anti-estrogen clomiphene citrate have been proposed as the physiologic basis for use of the drug in the treatment of adolescent gynecomastia. To compare the clinical and hormonal effects of such therapy we administered 50 mg/day of Clomid® for 4-13 wk to 11 late pubertal boys (ages 12-19) with 1.5-7.0 cm of breast enlargement. Mean breast size decreased 20-36% in 5 boys with 0-17% change in the remainder; 4 individuals required reduction mammoplasty.

Radioimmunoassay of urinary gonadotropins and serum testosterone and estradiol revealed significant ($p < 0.01$) mean increases in all hormones following treatment. LH rose from 560 to 2380 mIU/hr 4-7 wk after intitiation of treatment; by 8-12 wk of therapy levels had stabilized at 1400 mIU/hr. FSH increased from 360 to 940 mIU/hr and then decreased to 630 mIU/hr. Although testosterone rose from 490 to 1360 ng/dl and estradiol from 26 to 90 pg/ml, the ratio of T:E decreased significantly ($p < .05$) during the regimen. There were no differences in hormone patterns between boys who experienced a decrease in breast size and those who did not.

In conclusion, clomiphene causes only small improvement in (late) adolescent gynecomastia. Since the drug does not promote a more favorable androgen-estrogen milieux its anti-estrogenic effects are achieved primarily at the level of breast tissue.

383 DETERMINING THE DOSE OF L-THYROXINE REPLACEMENT IN INFANTS WITH CONGENITAL HYPOTHYROIDISM. Ernest M. Post and Robert A. Richman. SUNY Upstate Medical Center, Department of Pediatrics, Syracuse, New York.

In three infants (2-6 months old) with congenital hypothyroidism, we found that treatment with L-thyroxine (50 mcg/day, 5.7-11 mcg/kg/day) resulted in suppression of their TSH response to thyrotropin releasing hormone (change in TSH < 0.5 uIU/ml), indicating overtreatment. To determine the optimum dosage of L-thyroxine replacement, we studied 19 affected infants and gradually reduced the doses we prescribe. In the table below, we compared, for each age, the mean L-thyroxine dose (mcg/kg/day) that resulted in TSH levels being elevated with that producing a normal level.

Age(months):	1.5-3	4-6	7-9	10-12	13-18	19-24	25-30
TSH <10 uIU/ml	7.68	6.28	5.21	5.00	4.92	4.45	3.97
TSH >10 uIU/ml	5.27	4.63	4.88	-	3.91	4.29	5.20

All 13 patients now more than 12 months old, had a normal TSH before their first birthday on doses of 2.7-7.5 mcg/kg/day (mean 5.2). The comparable doses at later ages in the two TSH groups suggests that those children with the recurrence of an elevated TSH level may not be receiving the medication as prescribed. Growth and development of all the children has been normal. For the children > 12 months old, the means on the Bayley Scales of Infant Development have been: mental 108.6 ± 12.6 S.D. (range 84-124), psychomotor 113.3 ± 12.5 (range 91-125).

We have demonstrated that normalization of TSH levels in infants can be achieved using doses of L-thyroxine 25%-50% lower than those previously recommended.

384 PITUITARY HORMONE EFFECTS ON ESTROGEN-2-HYDROXYLASE IN THE MALE RAT. MERRILY POTH AND DIANE PROIA. PEDIATRIC ENDOCRINOLOGY SECTION, DEPARTMENT OF PEDIATRICS, UNIFORMED SERVICES UNIVERSITY, BETHESDA, MARYLAND 20814

Some microsomal cytochrome P450-dependent liver enzymes show sexual dimorphism, that is, they are significantly higher in one sex than the other. In addition to direct effects of the gonadal steroids on the liver there appears to be other pituitary "factors" which contribute to the enzyme differences between male and female. We investigated this phenomenon in the rat, looking at the enzyme estrogen 2-hydroxylase which converts estrogens into catecholestrogens. This enzyme is 8-10 times higher in the adult male than the female and is a major degradation pathway which may "protect" the male from estrogen exposure. We have previously slown a 20% decrease in liver enzyme activity in the castrate male rat, and a doubling of activity in the female rat treated with high doses of testosterone. Thus testosterone can not totally account for the sexual difference in enzyme activity. Twelve experimental and 12 "sham" operated rats were killed for enzyme assay 7-10 days after surgery. Estrogen-2hydroxylase was assayed in liver microsomes by a radio-enzymatic assay. Hypophysectomy of male rats resulted in a slight (~20%) decrease in enzyme activity. Pituitary stalk transection of the male rat caused a decrease of enzyme activity of over 80% resulting in complete "feminization" of the level of enzyme activity. The major hormonal change in the pituitary stalk sectioned animals is a large increase in prolactin. We hypothesize that prolactin may suppress liver enzyme activity. The decrease in inactivation of estrogen could help to explain the hypogonadism of hyperprolactinemic men.

385 USE OF ESTRONE SULFATE (E_1S) MEASUREMENTS TO EVALUATE ESTROGEN LEVELS IN LOW ESTROGEN STATES. Edward O. Reiter and David J. Watson, University of Massachusetts Medical School, Baystate Med. Ctr., Dept. Peds., Springfield, MA.

Serum estrogen levels (especially estradiol (E_2)) are often below limits of RIA sensitivity in prepubertal(PRE) children. E_1S, the most abundant estrogen in adult serum, with stable high levels about 10-20-fold greater than unconjugated estrogens, arises largely from precursor sulfurylation in peripheral tissues. To examine other means of evaluating estrogen levels in PRE and hypogonadal subjects, we improved our RIA for E_1S and related its concentrations to those of E_1 and E_2 in children of varied pubertal status. Estrogens were quantitated in 35 PRE and pubertal (PUB) children and in 5 girls with Turner's syndrome. Mean (±SE) E_1S levels in PRE girls (106±13 pg/ml) and boys (82±16) were significantly lower than in PUB (406±76) or adult female (follicular phase, 880±117) subjects. All E_1S levels were above assay sensitivity (6 pg/ml). In contrast, E_2 in PRE girls (3.4±.4) or boys (2.8±.5) was often below or at the limits of detectability (2 pg/ml); E_1 was 10.6+1.6 in PRE girls and 12.7+3.5 in PRE boys. E_1S levels correlated strongly (r>.90) with those of E_1 and E_2. In patients with Turner's syndrome, mean E_1 and E_2 levels were 17.5 ±6.3 and 3.3±.8, while E_1S was 204±56. These data suggest: (1) E_1S levels are easily measurable in sera from PRE subjects and permit assessment of integrated estrogen status when E_1 or E_2 levels are barely detectable; (2) Quantitation of E_1S in patients with Turner's syndrome may help to further define neuroendocrine feedback controlling gonadotropin suppression during mid-childhood or during conjugated estrogen therapy.

386 DOSE-RESPONSE CHARACTERISTICS OF PLASMA LH BIOACTIVITY DURING PUBERTY. Barry H. Rich* & Robert L. Rosenfield, University of Chicago Pritzker School of Medicine, Department of Pediatrics, Chicago, IL.

We have performed a detailed dose-response analysis of plasma LH bioactivity (B-LH) throughout puberty to better understand the basis for the changing ratio of bioactive LH to immunoreactive LH (B/I) which we have reported to occur during maturation.

Rat interstitial cell testosterone assay data after metametric transformation of LH or plasma dose vs testosterone response (log dose vs $\sqrt{T}$) permitted parallel line analysis. The dose-response curve was linearized between 2.5-25 ng LER-907/1st IRP per aliquot (r=0.80-0.92). The slope was parallel to the more biopotent (2.3x) 2nd IRP. Results in males:

GROUP (n)	SLOPE, mean ± SD (avg B-LH, ng/ml) Standard	Pre-GnRH	Post-GnRH
PREPUB (6)	6.7±0.86	2.1±1.2* (17)	6.5±1.5 (299)
PUB (10-15)	7.6±0.57	5.7±2.3 (37)	8.3±2.2 (1189)
		7.5±1.6 (146)	
ADULT (9)	6.5±0.81	7.0±0.63 (172)**	6.4±1.4 (1022)

* $p < .05$ vs std slope **34 ng LER-907 or 10 mIU 2nd IRP/ml by RIA

These data show that circulating LH bioactivity has dose-response characteristics like LH throughout puberty. There is a possible exception in basal samples from prepubertal children. For B-LH over 35 ng/ml, we find no evidence for an independent species of interstitial cell interactor which differs from standard LH.

Consequently, the most likely explanation for changes in B/I commencing in the course of puberty is that LH is heterogeneous and that during puberty there are changing proportions of biologically inactive material within plasma radioimmunoassayable LH.

● **387** PHENOTYPIC HETEROGENEITY IN FAMILIAL ISOLATED GROWTH HORMONE DEFICIENCY (IGHD) TYPE A. Marco A. Rivarola, John A. Phillips III, Claude J. Migeon and Brian J. Hjelle, Hosp. General de Ninos, Buenos Aires and Dept. of Peds. Johns Hopkins Univ. Sch. Med. Baltimore.

We have studied an Argentine family in which the parents are normal (I-1,2) and 3 of 4 sibs are affected with IGHD (II-1,2-male and II-4-female). Both parents are of Spanish ancestry and denied consanguinity. Because of the similarity of the findings in this family to those described in Swiss families with IGHD type A (early onset of severe dwarfism, typical physical findings, absence of growth hormone (GH) production following stimulation tests) we examined their DNA for deletion of the GH genes. Restriction endonuclease analysis of DNAs isolated from leukocytes was done using ^{32}P-labelled GH cDNA sequences as a probe. The 3 affected Argentine sibs were homozygous while the parents and sib (II-3) were heterozygous for a deletion of about 7.5-kb which included the normal GH gene, in agreement with an autosomal recessive mode of inheritance as well as the clinical phenotype. While the GH gene deletion in this family seems identical to that seen in the Swiss families, the phenotype of the Argentine children differed in 3 respects. First, there was variation in birth length (II-1 : 44, II-2 : 51 and II-4 : 50 cm) although all 3 were born at term after normal gestation. Secondly, prior to treatment, at 7 years of age, II-1 and II-2 differed in height (75 and 83 cm). Thirdly, during the first 18 months of GH treatment, yearly growth was good in II-2 : 10 cm, but poor in II-1 and II-4 (4 and 4.5 cm) despite high Anti-GH titers in all 3 sibs. The differences in rate of growth of these 3 sibs must be due to factors other than the GH gene deletion. Prior to therapy, these factors may include other genes which modify growth and during therapy genes which effect immune response.

388 SUPPRESSION OF SEX HORMONE SECRETION IN PRECOCIOUS PUBERTY (PP). Thomas F. Roe and Gertrude Costin. Univ. of So. Calif. Sch. of Med., and Childrens Hosp. of Los Angeles, Dept. of Pediatrics, Los Angeles.

In adult males administration of megestrol acetate (MA) and low-dose diethylstilbesterol (DES) completely suppresses gonadotropin (Gn) and testosterone (T) levels in plasma. We have studied the effects of these medications in 2 boys with PP, ages 3½ and 4 years. Each boy received MA, 35 mg/M^2/day orally; patient (pt) 1 also received DES, 50 µg/day. Morning plasma LH, FSH (mIU/ml) and T (ng/dl) and peak responses to sleep and Gn releasing hormone (GnRH) before and at 2 and 6 months (mo) Rx were:

	Pt 1							Pt 2						
	Morning			Sleep		GnRH		Morning			Sleep		GnRH	
Rx	LH	FSH	T	LH	T	LH	T	LH	FSH	T	LH	T	LH	T
None	2.7	<1.7	225	5.1	483	25	462	6.9	5.5	667	18	590	211	977
2 mo	<1.7	<1.7	<15	<1.7	<15	2.3	<15	2.9	<1.7	<15	3.3	<15	2.9	<15
6 mo	2.0	<1.7	24	2.8	23	7.6	25							

Basal and stimulated plasma Gn and T fell to prepubertal levels after 2 mo therapy in both boys and remained low in Pt 1 at 6 mo of therapy. In Pt 2 plasma LH rose to 11 mIU/ml and T rose to 744 ng/dl when treatment was inadvertantly stopped for 2 weeks. The Pts' growth rates were 1.41 and 1.17 before and 0.71 and 0.7 cm/mo respectively during therapy. The rate of skeletal maturation decreased during therapy in Pt 1.

These data indicate that MA administration with or without DES, 1) suppresses plasma Gn and T levels in PP, 2) decreases the rate of linear growth and bone maturation and, 3) may prove effective in treatment of PP.

● **389** RECOMBINANT DNA-DERIVED HUMAN GROWTH HORMONE IS BIOLOGICALLY ACTIVE IN HUMANS. Ron G. Rosenfeld, Darrell M. Wilson, Ann Bennett and Raymond L. Hintz, Stanford University School of Medicine, Dept. of Pediatrics, Stanford, CA.

The membrane binding characteristics and biological activity of N-terminal methionyl human growth hormone (met-hGH), expressed in E. coli by recombinant DNA techniques, were compared to pituitary hGH (pit-hGH). By both IM-9 lymphocyte and rat liver membrane radioreceptorassays, met-hGH and pit-hGH were equipotent, and the two proteins were equivalent in their ability to induce hGH receptor loss in IM-9 cells. The in vivo activity of both hGH preparations was assessed in a double-blind, randomized, crossover study of 22 normal adult males. Each subject was given 4 daily I.M. injections of 0.125 mg/k/d of one hGH preparation, followed by a 10 day rest, then 4 daily injections of the other hGH. Plasma hGH levels rose rapidly to peak levels of 220 ng/ml within 4 hours of I.M. injection of either hGH. Plasma SM-C levels rose from a baseline of 1.29 ± 0.12 U/ml (mean ± SEM) to 3.64 ± 0.19 U/ml following 4 injections of pit-hGH, and from 1.34 ± 0.10 to 3.67 ± 0.15 U/ml following met-hGH. Insulin-resistant carbohydrate intolerance was observed with both hGH preparations, with the integrated plasma glucose following an oral glucose load rising 34% above pretreatment values following pit-hGH, and 37% following met-hGH. Concurrently, the integrated plasma insulin level rose 194% with pit-hGH and 204% with met-hGH.

We conclude from these data that 1) the receptor binding activity of bacterially produced met-hGH is indistinguishable from that of native pituitary hGH, 2) pure monocomponent met-hGH is capable of producing insulin resistance and 3) met-hGH is biologically active in humans.

390 GLUCOSE (G) TOLERANCE & INSULIN LEVELS (I) IN TURNER'S SYNDROME (TS). Deborah Rotenstein, Dorothy Becker, Trevor Orchard, Ronald LaPorte, Allan Drash Children's Hospital of Pittsburgh, Graduate School of Public Health, Pittsburgh, PA

Although glucose intolerance (GI) in TS is well documented, its relationship to age, wt., & early I secretion is unclear. We examined G&I responses to oral GTT in 14 untreated TS girls. G&I secretion were expressed as 3 hr. G&I areas (GA & GI, resp.). Results were compared with 113 non-diabetic sibs of diabetics (C) matched for age & sex. HLA A1 (8/14) & B8 (7/14) were frequent in TS. Impaired G tolerance (ADA criteria) was seen in 21% of TS. GA, G, & I responses were consistently higher in TS than C. The significant differences for GA were not eliminated by body mass index (BMI) or HLA B8 matching with C. However, increased IA in TS was not significant when BMI matched. Early (15 min.) I hypersecretion was present in TS, but its statistical significance was lost when matching for BMI in the younger but not the older TS.

TABLE: $\bar{x}$ ± SE P *p<.05, **p<.01, ***p<.001

AGE		BMI	GA (mg min)	IA (uU min.)	15 min (uU/ml)
7-12.9 yrs.	TS	21.3±2.1	172±34	196±58.4	63± 9.6
	C	*16.7± .34	***68± 4.2	*95± 7.7	*40± 3
13-17 yrs.	TS	21.3± .96	141±12	172±13	87±13
	C	20.7± .41	**78± 8	137± 8	**47± 3.2

TS is associated with GI with consistently higher G levels than C, not accounted for by increased BMI. Except at 15 min., elevated G levels are accompanied by I levels similar to C. The pathogenesis of GI in TS includes relative I deficiency with possible I resistance.

391 NORMAL GROWTH DESPITE SOMATOMEDIN-C DEFICIENCY. Mary C.J.Rudolf, Joseph M.Gertner, Raymond L.Hintz, Myron Genel. Yale Univ. Sch. Med., Dept. of Peds., New Haven and Stanford Univ. Med. Ctr., Dept. of Peds., Stanford

According to current concepts growth is mediated by growth hormone (GH) stimulated peptide factors of which IGF I/somatomedin-C (SmC) is best characterized and most GH dependent. However we have observed normal linear growth in 3 subjects with deficient GH release and low SmC by RIA. Subject A is status post craniopharyngioma, B has septo-optic dysplasia with associated diabetes insipidus, and C has obligatory autosomal dominant GH deficiency detected due to affected sons, sister and nephews. All have absent GH response to L-DOPA and insulin hypoglycemia (ITT) and low SmC levels by RIA.

	Age yrs	Growth	Peak GH (ng/ml) ITT	L-DOPA	SmC (RIA) U/ml
A	12	7.5 cm/yr	1	2	0.18
B	12	8.0 cm/yr	<1	<1	<0.10
C	40	176 cm	4	2	0.14

A & B are obese with hyperinsulinemia and hyperprolactinemia. In B somatomedin by porcine bioassay was low normal for age (0.45, 0.54 & 0.82 U/ml), but clearly out of the range observed with other hypopituitary patients.

Normal growth in these subjects could be ascribed to elaboration of growth promoting substances other than SmC. The contrast in the bioassay somatomedin compared to RIA SmC in patient B supports this hypothesis. Alternatively, the apparently deficient SmC detected by RIA may reflect deficiency of the obligatory carrier protein, with normal "free" somatomedin-C.

● **392** NALOXONE INCREASES DAYTIME LH SECRETION IN HYPOTHALAMIC AMENORRHEA (HA) BUT NOT IN EARLY PUBERTY. S.E. Sauder, R.P. Kelch, N.J. Hopwood and J.C. Marshall. Univ. of Mich., Depts of Ped. and Int. Med., Ann Arbor, MI

Recent studies indicate that antagonism of endogenous opiates acutely increases gonadotropin secretion in women with HA. To determine whether the mechanisms which inhibit daytime gonadotropin secretion in early puberty are similar to that in HA, two groups of patients with increased nocturnal secretion of LH were studied: 4 early pubertal children (3 male, 1 female; CA range 11.9-15.1 yr; BA 8.5-13.5 yr) and 2 adult women with HA (CA 21&31 yr). Plasma LH and FSH (mIU/ml) were measured every 20 min. during three 6-8 hr. study periods on consecutive days: samples were drawn from 1200h (DAY); 2400h (NIGHT): and from 1200h (DAY + NALOXONE). The opiate antagonist, Naloxone, was administered iv (1.6 mg/m^2/hr) for 4 hrs. (puberty) or 6 hrs. (HA).

	Mean LH ± SE (range) DAY	NIGHT	DAY + NALOXONE
EARLY PUBERTY	2.3±1.0 (0.7-5.3)	5.7±1.6 (2.7-9.5)	2.7±1.3 (0.8-6.7)
HYPOTHALAMIC AMENORRHEA (HA)	3.2 (2.5-3.9)	7.2 (5.3-9.1)	7.2 (5.6-8.7)

Naloxone had no discernible effect on daytime gonadotropin secretion in early pubertal children. In contrast, opioid antagonism in the women with HA significantly increased mean LH; LH pulse frequency averaged one pulse q4.8h before and q2.4h during Naloxone. We conclude that endogenous opiates do not mediate the day-night gonadotropin differences in early puberty. Moreover, the mechanisms of gonadotropin suppression in early puberty differ from that acting in HA. Grants 5M01RR42 and HD11311

393 EFFECTS OF THYROXINE ADMINISTRATION TO PRETERM INFANTS. Todd Scharnberg, Rebecca Kirkland, Martha Taylor, John Burdine, George Clayton, Departments of Pediatrics and Nuclear Medicine, Baylor College of Medicine, Houston, Texas (spon. by Reba M. Hill)

This study was undertaken to examine the physiology and effects if any, of administered thyroxine (T_4) in the normal preterm infant. Group 1: 11 well, AGA, preterm infants weighing from 1180-1820gm (mean 1487 ± 198 gm) on day 3 or 4 of life were given 25 micrograms of L-thyroxine daily for 20 days. These were paired with 11 matched control infants. Weight, length, and head circumference (HC), as well as T_4, T_3 RIA and reverse T_3 (RT_3) were measured on days 1, 10, and 20. Group 2: In 5 similarly treated infant pairs, weight 1200-1580 gm (mean 1392 ± 153), T_4 and free T_4 were measured. Weight, length, and HC between matched pairs of both groups were not significantly different by the paired t-test on day 1, 10, or 20. In group 1, mean T_4 and T_3 were not significantly different in treated vs control patients on days 1, 10, and 20. Mean RT_3 were similar on day 1: 1889 ± 566 vs 1970 ± 616 in treated vs control patients respectively, but significantly higher in treated patients on day 10: 1201 ± 277 vs 830 ± 236 ($p < 0.005$) and on day 20: 1048 ± 280 vs 736 ± 203 ($p < 0.02$). In group 2, mean serum T_4 and free T_4 were not significantly different in treated vs control patients on days 1, 10, and 20. These studies show that administration of thyroxine to the preterm infant does not affect serum levels of T_4, T_3, or free T_4, and suggests that monodeiodination of T_4 to RT_3 plays a role in thyroid homeostasis in these infants.

● **394** VITAMIN D METABOLISM IN PREGNANT AND LACTATING RHESUS MONKEYS. H. Schedewie, J. Bailey, M. Ho, W.Slikker, D. Hill, R. Tsang, J. Elders. UAMS, Little Rock, AR., NCTR, Jefferson, AR., UCCM, Cincinnati, O.

Although pregnancy and lactation present a maximun challenge to maternal mineral metabolism, little is known about endocrine factors maintaining mineral homeostasis during gestation. We have performed longitudinal studies in 22 pregnant Rhesus monkeys and 11 non-pregnant controls. All animals were kept protected against daylight and fed a standard Purina chow diet. Blood specimens for the measurement of 1,25- and 24,25-calcitriol (1,25 and 24,25) concentrations were obtained at monthly intervals during pregnancy and for 3-5 months after delivery. Serum D-metabolites were extracted, separated by standard HPLC procedures, and measured by chick intestinal radioreceptor assay. Mean serum 1,25 levels of 167 pg/ml (SE±26) during the first 50 days of pregnancy were not different from controls. However, hormone levels increased significantly after 50 days ($P<.001$) reaching a peak between 80-120 days (481±42). 1,25 levels after termination of pregnancy dropped rapidly to values slightly above controls and did not appear to be different in lactating and non-lactating mothers. Mean 24,25 concentrations of 3.3±0.6 ng/ml during the first 50 days of pregnancy were not different from controls. Although sterol levels increased in the majority of animals after 50 days, mean concentrations of 4.2±0.58 ng/ml between 80-120 days were not determined different ($P>.05$). In conclusion: The marked changes in D-metabolism occurring in pregnant monkeys suggest that D-sterols play an important role in the control of gestational mineral homeostasis.

395 PSYCHOSOCIAL DWARFISM (PSD): A REAPPRAISAL OF ENDOCRINE STATUS. Selma Siegel and Dorothy Becker, University of Pittsburgh, Department of Pediatrics, Pittsburgh, PA

PSD is characterized by growth failure & bizarre behavior, particularly related to food intake. Reversible growth hormone (GH) deficiency is thought to be the etiology of the short stature. We assessed the frequency of GH & cortisol (F) deficiency on 25 occasions in 23 children, $\bar{x}$ age 6.5 yrs. (1.8-15.5 yrs.) with classical clinical features of PSD. Tests were oral glucose tolerance (GTT), arginine and/or insulin stimulation (AITT/ITT), & nocturnal sampling (N) on Days 1&2 (init.) & during the 3rd week of hospitalization (subs.). Bone age ($\bar{x}$ 4.1±SE .5 yrs.) was less retarded than ht. age ($\bar{x}$ 3.6±.6 yrs.) ($p<.001$). Significant ht. & wt. increments in the hospital ($\bar{x}$ 1.57 cm & 1.62 kg) did not correlate with init. GH peaks. Normal GH responses (>7 ng/ml) were seen in 13/25 init. AITTs. N & GTT showed GH levels >7 ng/ml in 5/11 & 8/21, resp. Two pts. had normal GH levels on N or GTT, but did not achieve adequate responses on AITT. Responses were persistently low in 5/20 subs. AITT; 2 of these 5, who underwent GTT or N, showed normal GH levels; 4 of these 5 had normal follow-up growth, & 1, whose environment did not change, did not grow on GH therapy. There was no correlation between init. peak GH response & ht. age (HA), wt. age (WA), or HA/WA. F response to ITT was >17µg/dl in 19/20 tests. T4,TSH, & 3TRH tests were normal. On the basis of subs. testing, our population separates into 3 groups: 1) normal init. & subs. GH response (60%); 2) abnormal init. GH response which normalized (25%); 3) abnormal init. & subs. GH response (15%). Thus, normal pituitary function is frequent in PSD & does not exclude its diagnosis.

396 IS THERE AN INCREASED PREVALENCE OF MITRAL VALVE PROLAPSE IN CHILDHOOD HYPERTHYROIDISM? Santokh Sindhu, Richard A. Meyer, David C. Schwartz & Mark A. Sperling. University of Cincinnati, Department of Pediatrics, Children's Hospital Medical Center, Cincinnati, Ohio.

It has been proposed that the prevalence of mitral valve prolapse (MVP) is significantly increased in adults with hyperthyroidism (N Engl J Med 305:497, 1981). To test this association in a pediatric population, we studied 20 patients (15 F, 5 M aged 8-20 yrs) treated for hyperthyroidism. At onset T4 was 21 ± 2 µg/dl and T3 480 ± 39 ng/dl; at the time of study T3 was 202 ± 15 ng/dl. Each patient had M-mode echocardiograms (ECHO) obtained and interpreted by two independent observers one of whom was unaware of the patients' condition. Auscultation was performed by a Cardiologist unaware of the ECHO findings. Only one child with Marfan's syndrome had clinical features of mitral valve disease, while another had a non-specific apical systolic murmur. ECHO findings in patients were compared to those of 53 age-and sex-matched controls. Using our published criteria, none of the controls had MVP although two (5%) had some ECHO features suggestive of MVP. In contrast, among the 20 patients, two had definite MVP (10%). An additional two (10%) had ECHO features suggestive of MVP. Thus, the overall prevalence of positive or suggestive ECHO findings was 20% ($p < .05$). There was no correlation between clinical or biochemical indices of thyrotoxicosis and presence of MVP. These results suggest the need for further study of larger numbers of hyperthyroid children to validate our findings. Further, this association may represent a spectrum with prevalence increasing over time necessitating longitudinal evaluation.

397 ROLE OF C'AMP IN ANGIOTENSIN MEDIATED ACTH SECRETION
D.O.Sobel.Dept of Internal Medicine and Pediatrics,National Naval Medical Center,Uniformed Services University, Bethesda, Maryland 20814

We recently demonstrated that angiotensin II(AII)directly stimulates in vitro ACTH secretion in rat pituitary cells.To investigate the role of cyclic AMP as a mediator of AII stimulated ACTH secretion,we studied 1)the generation of extracellular and intracellular C'AMP induced by AII(10nM)& 2)the effect of ^{8}Br C'AMP,and two phosphodiesterase inhibitors,isobutyl-3-methylxanthine(IBMX) and caffeine on AII mediated ACTH release.Minced anterior rat pituitaries were dispersed in trypsin/DNAase solution and placed in monolayer cell culture.After 3 days,test media was incubated 3.5 hours and then stored for ACTH measurement by RIA.AII(10nM)stimulated a 150-180% increase of ACTH(1.3ng/3x10^{5}cells/3.5hours).AII (10nM)did not stimulate an increase of intracellular or extracellular C'AMP.IBMX(0.25-2.5mM),^{8}Br C'AMP(0.1-2mM)and caffeine(5-50mM) each stimulated ACTH dose dependently.AII+IBMX(50μM a non stimulatory dose)stimulated a 170% increase of net ACTH over AII alone. ^{8}Br C'AMP(2and20nM)+AII released a 190% and 230% increase of ACTH over AII stimulation.The net ACTH release(Test-control)is diagramed.

2nM ^{8}Br C'AMP	20nM ^{8}Br C'AMP	10nM AII	2nM ^{8}Br C'AMP+AII	20nM ^{8}Br- C'AMP+AII	IBMX	AII+ IBMX
NC	NC	100%	190%	230%	NC	170%

NC=no change from control.ACTH release with AII+Caffeine(10nM) were not significantly different from AII alone.In summary,although AII did not increase intracellular or extracellular C'AMP, ^{8}Br C'AMP and IBMX potentiate the AII mediated release of ACTH. Data suggests that AII stimulated ACTH maybe mediated by C'AMP.

398 ACTH INCREASES GROWTH RESPONSE TO TREATMENT IN HYPOPITUITARISM. Edna H. Sobel. Albert Einstein College of Medicine. Department of Pediatrics, Bronx, New York. Four hypopituitary patients were treated with hGH and thyroxine for 3 to 5 years. ACTH (ACTHAR gel 0.05mg/kg) was added for 6 months of each year. Growth rates were calculated as cm/year. In 9 of 14 comparisons, the rate was greater in the immediately adjacent ACTH period, in 3 it was less and in 2 the rate with ACTH treatment was the same as without ACTH. These findings are significant by the Sign test ($p < 0.019$). The explanation for these results remains unclear because we previously found that hGH depressed endogenous ACTH secretion (Sobel, E.H. and B. Zumoff. Interactive effects of ACTH and growth hormone on adrenocortical hormone secretion. Ped. Res. 15:514,1981).

The data, however, show that ACTH augments growth response to hGH in hypopituitarism.

● **399** PULSATILE GONADOTROPIN SECRETION DURING SEXUAL DEVELOPMENT IN THE MALE SUBHUMAN PRIMATE. B. Spiliotis, B.C. Lee, J. Pineda, H. Sachs, T.J. Brown, and B.B. Bercu. NPMB, NICHD, NIH, Bethesda, MD 20205.

We have used the primate as an animal model to study the pubertal process and male sexual development. We report here cross-sectional and longitudinal studies characterizing changes in 24 h secretory patterns of LH and FSH in monkeys (Macaca mulatta and fascicularis) from 9 days of age through adult life. Monkeys (N=46) were fitted with a vest and mobile tether permitting chronic cannulation. Blood was drawn at 15 min intervals over 24 hours without anesthesia. LH, FSH and testosterone were measured by radioimmunoassay. Pulsatile secretion of LH and FSH occurred as: 1) micro-pulses, having amplitudes < 2 times over baseline; 2) macro-pulses where the increase > 2 fold over baseline. Throughout, FSH secretion occurred mostly as a steady state undulating pattern with occasional micro- and macro-pulses at all ages. On the other hand, the largest LH pulses (up to 15 times, from a baseline of < 0.9 to a maximum of > 15 μg/ml of approximately 2 hours duration) occurred in the prepubertal animal and LH micro-pulses at all ages. Large testosterone macro-pulses occurred in the early postnatal period, late puberty and adult life. Gonadotropin secretory patterns associated with normal sexual development was highly individual; uniformly the amplitude and frequency varied. In this large series of animals, these data indicate that changes in frequency and amplitude of gonadotropin pulsatile secretion correlate with testicular maturation.

● **400** IS THE LEVEL OF VASOPRESSIN (VP) IN AMNIOTIC FLUID (AP) A MARKER OF FETAL HYPOXIA? Raymond I. Stark, Salha S. Daniel, M. Kazim Husain, Alan K. Zubrow and L. Stanley James. Columbia U., Coll. of P & S, Div. Perin. Med., Depts. Ped., Anes., Med., NY.

Hypoxia is a potent stimulus to release of VP. We have shown up to 10% of plasma VP is cleared by the fetal kidney and excreted in urine. We propose that AF-VP may be a marker of fetal hypoxia in the fetal lamb. AF and plasma samples were obtained from 15 chronically catheterized fetal lambs (116 to 141 d gestation) (1) during steady state conditions (control), (2) following exposure of the ewe to 10% FIO_2 or partial umbilical cord occlusion x 30 min. (hypoxia), and (3) after exogenous VP infusion into AF. VP was reliably extracted from AF in acetone with an 80 ± 4% recovery. VP measured by RIA of AF has an interassay variability of 8% at 4 pg/ml and 10% at 25 pg/ml. Parallel biologic activity of AF VP was confirmed by bioassay. (1) In control state plasma VP (1.8 ± 1.4 pg/ml) did not correlate with AF-VP (1.7 ± 1.4, range 0.5 to 7.5 pg/ml) or change with gestational maturation. (2) With hypoxia (PO_2 25.5 ± 1.4 to 11.8 ± 1.6 mmHg) fetal plasma VP rose to 242 ± 266 pg/ml at 30 min. returning to control by 1 hr. Maternal levels did not change. AF-VP rose to 22 ± 20.4 pg/ml by 2 hrs. and remained significantly elevated ($p<0.01$) for at least 24 hours. Plasma VP following hypoxia was positively correlated with AF-VP at 24 hrs. ($r = .87$, $p<.001$). (3) After AF infusion of VP levels remained elevated for 24 hrs. with $T_{½}$ clearance of >8 hrs. No increase in uterine activity or meconium passage were noted following hypoxia or infusion except in animals close to term. We conclude that measurement of VP in AF may be a useful marker of fetal hypoxia.

401 IONIZED CA (ICA) IN WHOLE BLOOD & SERUM OF NEWBORN INFANTS. Shyan Sun, Anita Baldomero, Kamtorn Vangvanichyakorn, Minerva Castillo.(Spon. F. Behrle) New Jersey Med. School. Div. Neonatology, Newark, New Jersey

The actual iCa is influenced by momentary pH changes, which may be irrelevant for the calcium problem under study, but the standardized iCa at pH 7.4 can be misleading if the patient suffers from a persistent pH change. An instrument that measures both actual pH and iCa and calculates a standardized iCa at pH 7.4 will therefore be ideal. We report our experience with such an instrument, the ICA1 Radiometer's Ionized Calcium Analyzer. The concentration of iCa was measured both in the whole blood and serum of 20 neonates. Specimens were collected at the same time and the determinations of blood and serum were done within 5 minutes.

	iCa mmol/L	pH	iCa at pH 7.4 mmol/L
Blood	1.29+1.8	7.33+0.05	1.23+0.14
Serum	1.19+0.18	7.53+0.12	1.28+0.20
P	<0.001	<0.001	<0.01

The serum became significantly alkalotic (pH 7.53 vs 7.33) after being separated from the original whole blood. (Centrifuge effect) The pH changes in turn affect significant changes of iCa concentration in the blood and serum. (Δ iCa 0.1 mmol/L) After pH correction, the difference was lessmarked (Δ iCa 0.5 mmol/L). Awareness of these variations is important in clinical management of patients. Hypoionized calcemia can be due to true deficiency or simply alkalosis. Treatment differs accordingly. Accurate diagnosis cannot be made without simultaneous measurement of pH and iCa. Additional knowledge of iCa corrected at pH 7.4,helpful.

402 GONADOTROPIN (GN) RESPONSE TO LHRH IN PRUNE BELLY SYNDROME (PBS) AT DIFFERENT AGES. CHANDRA M. TIWARY, & E. ZEIDMAN (SPONSORED BY MELVIN E. JENKINS) DEPT. OF PED. & UROLOGY, WALTER REED ARMY MED. CTR. AND HOWARD UNIV. MED. SCH. WASH. D.C. AND UNIFORMED SVC. U. OF THE HEALTH SCIENCES, MD

I analyzed GN responses to IM injection of LHRH on three occasions in two children. Both showed features of PBS, chronic renal failure and had intra-abdominal testes. AA was 5 10/12 old, his height was 35", weight 29 lbs and BP 94/58. The serum electrolytes were normal. Serum testosterone rose to 1.8 ng/ml after HCG injections. The basal serum LH, FSH and the LH response to LHRH was similar to that in a 4 year old control subject with undescended testes but the FSH response was much less (9.7 vs 25.3 (peak), 7.5 vs 21.55 (mean)). The second patient TS was evaluated twice; in January 1979 (15 11/12 age) and in January 1981 (17 11/12 age). Left orchiectomy was done in Aug., 1979. His maternal cousin suffered from PBS. In 1979 his height was 56 1/2", weight 69 lbs and BP 120/90 and no sign of sexual maturation. In 1981 his height was 60", weight 94 1/4 lbs, pubic hair stage IV, axillary hair +, but no facial hair. His bone age was 14 years. Basal, peak and mean LH/FSH values (mIU/ml) after LHRH in 1979 were 22.1/19.3, 104/32.1, 86.5/28.7 respectively and the corresponding values in 1981 (after orchiectomy) were 32/138, 313/299, 164.6/191 respectively. CONCLUSION: In PBS the impairment in FSH regulation is more pronounced and is seen at an early age. The LH response in 1979 was similar to that of castrate subjects, but the FSH was normal. In 1981 the more marked rise in FSH than in LH suggests greater limitation of inhibin than testosterone production by the remaining testes.

403 PATTERNS OF TSH RESPONSE TO TRH IN HYPOTHALAMIC-PITUITARY-THYROID DISORDERS. Val Abbassi. Georgetown Univ. Sch. of Med.,Dept. of Peds. Washington, D.C.

TRH was employed to evaluate hypothalamic-pituitary-thyroid function in 31 children with suspected thyroid disease. 7 ug/kg TRH (min.25,max.200μg) was administered IV. Baseline, 30' & 60' blood samples were obtained for TSH assay by RIA. Results are shown in table.(*denotes significant difference from controls).

Condition (# of pts)	TSH response μu/ml Baseline	30'	60'
Prim.hypothyroid. (10)	59.7±28*	358.6 ±252*	197.8±113*
GH deficiency (6)	5.2±1.3	13.7 ±2.0	11.2±1.7
Hyperthyroidism (4)	2.1±0.4	1.95±0.3*	2.2±0.6*
TBG deficiency (5)	4.6±0.8	16.6 ±1.2	14.3±2.0
Auton. adenoma (2)	2.9	16.6	11.7
Control Group (10)	3.6±0.32	13.1 ±1.7	9.7±1.0

Exaggerated TSH response was observed in primary hypothyroidism, regardless of duration or baseline TSH level, and in one neonate with TRH deficiency. In four of these children T4 was normal & in two baseline TSH was minimally elevated. Suppressed TSH response was observed in 4 with borderline clinical toxicosis & normal T4, one with hypopituitarism and one with a functioning adenoma. Normal TSH response was obtained in 6 with GH deficiency and 2 with functioning adenoma. In these diverse disorders of hypothalamus, pituitary & thyroid, TRH test was consistently diagnostic & useful not only in localizing the pathology but also in the assessment of the physiologic status,particularly when clinical findings were obscure and thyroid levels non-diagnostic.

● **404** EFFECT OF MAGNESIUM INFUSION ON PARATHYROID HORMONE (PTH) AND CALCITONIN (CT) HOMEOSTASIS IN INFANTILE HYPOMAGNESEMIA; COMPARISON WITH NORMOMAGNESEMIC INFANTS. P.S. Venkataraman, R.C. Tsang, D. Buckley, M. Kirk, Department of Pediatrics, University of Cincinnati

The importance of Mg in PTH and CT homeostasis in infancy is unclear. Magnesium deficiency theoretically may be associated with decreased secretion of PTH. We evaluated 6 infants with hypomagnesemia (HM), serum Mg 1.18±0.06 mg/dl (mean± SE) and 4 with normomagnesemia (NM), following infusion of 6 mg/kg of elemental Mg over one hr. In HM infants, mean serum Mg rose to 2.25±0.1 mg/dl with Mg infusion; mean serum PTH was 42±11μl-Eq/ml (RIA 1-84 PTH, N ≤ 57) initially and rose to 77±15, 82± 19, 66±18, 60±27 and 41±14 μl-Eq/ml at 1,2, 4,6,12 and 24 hrs vs 45±24, 44±19, 40±14, 41±19, 27±4 and 42±14 μl Eq/ml in NM infants. By analysis of covariance there was a significant difference between the groups, $p < 0.01$. Serum CT was 50±17, 54±19, 31±15 and 31±19 (RIA, N ≤ 107 pg/ml) at 0,1,2, and 6 hrs with Mg infusion in HM infants and 221±36, 243±56, 226±38 and 231±40 pg/ml in NM infants (HM lower than NM, $p<.0001$, no changes with infusion). Thus 1) in hypomagnesemic infants, serum calcitonin is low and does not significantly respond to Mg infusion, 2) serum PTH rises with Mg infusion in hypomagnesemic infants, 3) PTH response with Mg infusion was significantly greater in hypomagnesemic vs normomagnesemic infants. Thus serum Mg appears to play a significant role in neonatal parathyroid hormone homeostasis, supporting the thesis that infantile hypomagnesemia results in hypoparathyroidism.

405 LACK OF PARATHYROID HORMONE (PTH) SUPPRESSION BY "PHARMACOLOGICAL" DOSES OF 1,25-$(OH)_2$ VITAMIN D IN NEONATES. P.S. Venkataraman, R.C. Tsang, J.J. Steichen, Univ. of Cincinnati Medical Center, Cincinnati, Ohio.

While receptors for 1,25-$(OH)_2$ vit D are known to exist in parathyroid glands and PTH is a known stimulus for 1,25-$(OH)_2$ vit D production, it is unclear whether this metabolite has feed-back control on PTH secretion, and especially without concomitant elevation of serum Ca. We evaluated 8 infants who were given calcitriol (1,25-$(OH)_2$ vit D) within the first 12 hrs, at 24 to 36 hrs and at 48 to 60 hrs of age as prophylaxis for neonatal hypocalcemia. Gestational age was 30.6±1.1 wks (mean±SE) and birth wt 1188±178 gms. Doses studied were 0.1, 0.3, 0.5 and 0.75 mcg/kg/dose given intramuscularly; the "physiologic" dose of the vitamin is approximately 0.05 mcg/kg/day. Serum Ca and PTH levels were evaluated through the first 5 days of life. Serum Ca was 7.67±0.46 mg/dl prior to calcitriol injection and 6.8±0.22, 8.5±0.45, 7.2±2.0 mg/dl at 24 to 36 hrs of age, 48 to 60 hrs of age and at 24 hrs after the last injection of calcitriol. The corresponding serum PTH (radioimmunoassay, 1-84 PTH, N ≤ 57) concentrations were 21±4, 19±3, 20±3.5, and 22±1 μl-Eq/ml. There was no significant change in serum Ca and PTH over the first 5 days. By analysis of variance, there was no significant dose related difference in the Ca or PTH response elicited. Thus in preterm neonates, administration of relatively high doses of 1,25-$(OH)_2$ vitamin D does not suppress parathyroid hormone secretion.

● **406** MATERNAL LIPEMIA ALTERS GLYCEROL METABOLISM IN THE FETAL RAT. Raul A. Wapnir and Lily Stiel (spon.: F. Lifshitz). Dept. of Peds., N. Shore Univ. Hosp., Manhasset, NY 11030 and Dept. of Peds., Cornell Univ. Med. Col., New York, NY 10021.

In a model of maternal lipemia (L) in the rat, mimicking the conditions occurring in poorly controlled maternal diabetes (DB), we investigated whether glycerol (Gc) metabolism or the levels of its intermediary metabolites were altered in fetal liver and brain. L was induced in pregnant rats by feedings of a high-fat (45%) diet during the second half of gestation. Controls (C) were fed a commercial ration (4.5% fat). Serum triglycerides were elevated in L dams and fetuses. 3-HO-butyrate was higher in L pups (303 ± 45 vs 179 ± 22 μM, $P< 0.05$). Fetuses were studied one day before term. Liver dihydroxyacetone phosphate (DHAP) was higher in L than in C fetuses (means ± SEM: 0.86 ± 0.03, n=26, vs 0.64 ± 0.03, n=26, nmoles/g tissue, $P< 0.001$). The ratio of $GcPO_4$ to DHAP in liver was lower in L fetuses (3.87 ± 0.17 vs 4.55 ± 0.28, $P< 0.05$). However, there were no changes in hepatic Gc kinase, $GcPO_4$ dehydrogenase and $GcPO_4$ oxidase. Gc metabolism enzymes were also unaltered in brain. These data indicate that in gestational L, fetuses are exposed to a more reduced redox potential environment than in normal conditions. This may contribute to alterations of glucose utilization and be an additional deleterious factor in the intrauterine development of fetuses of DB individuals (Supported in part by NIH grant S08 RR-09128-03).

● **407** THYROID STATUS AND THE DEVELOPMENT OF MYOCARDIAL β-ADRENERGIC RECEPTORS (β-AR) IN THE RAT. Jeffrey A. Whitsett, Jennifer Pollinger, Susan Matz, Children's Hospital Medical Center, Cincinnati

The role of thyroid status on ventricular growth and β-AR's was determined in rat pups rendered 1) Hypothyroid with propylthiouracil (PTU), 2) Euthyroid with PTU and thyroxine (T_4), 3) Hyperthyroid with T_4 or 4) Control, sham saline injections. Myocardial weight, protein and DNA were similar in Euthyroid and normal rats at postnatal days 5, 15 and 28. Growth in Hypo pups was normal until postnatal day 14 after which heart weight and protein content were significantly decreased ($p< .01$). Ventricular DNA content was not decreased in Hypo rats, thus postnatal hypertrophic but not hyperplastic ventricular growth, is dependent on thyroid hormone. The number of β-AR's was decreased in Hypo myocardium at all ages studied, e.g. on day 5 of the (-)-[^{3}H]DHA binding (Bmax) was 37±9 in Hypo compared to 63±8 fmole per mg protein m± S.D. in Euth myocardium, $p<.01$. The function of the β-AR's was also decreased in Hypo as compared to Euth as demonstrated by a decrease in catecholamine sensitive adenylate cyclase, $p<.01$. Treatment of Hypo or control pups with T_4 (Hyperthyroid) resulted in an increase in heart size, and β-adrenergic receptors. β-AR's are decreased in ventricles from Hypothyroid rats at all ages studied and the decreased production of c-AMP in response to (-)-epinephrine may relate to the decreased numbers of β-adrenergic receptors present on the sarcolemmal membrane. We speculate that thyroid hormone is an important regulator of both myocardial hypertrophic growth and β-adrenergic receptors during development.

408 SERUM FREE THYROXINE LEVELS IN TERM, PRETERM, AND SICK INFANTS. Darrell M. Wilson, Andrew O. Hopper, I. Ross McDougall, Monika F. Bayer, Raymond L. Hintz, David K. Stevenson, Ron G. Rosenfeld. Stanford University School of Medicine, Depts. of Pediatrics and Radiology, Stanford, CA.

Free thyroxine levels (FT4) were determined by radioimmunoassay in 96 infants from our Intensive Care Nursery (ICN) and in 32 healthy term infants. Sera for FT4 levels were obtained simultaneously with filter paper specimens for total T4. The mean FT4 level in infants from the ICN was 3.48 ± 0.18 (SE) ng/dl and in the healthy term infants was 4.24 ± 0.23 ng/dl. FT4 levels from both groups of infants were significantly higher than levels found in normal adults (1.38 ± 0.03 ng/dl, $p < 0.001$). A correlation was noted between FT4 and T4 levels (r=0.52). Like T4, FT4 correlated with increasing gestational age (r=0.60) and birth weight (r=0.59) and was lower in infants with RDS ($p < 0.001$). Although 66% of the ICN infants had total T4 levels below the statistically selected screening level (5th percentile), these infants all had FT4 levels > 0.8 ng/dl. All of these infants had normal TSH levels and were judged clinically euthyroid. Two additional infants with untreated congenital hypothyroidism had FT4 levels of 0.3 and 0.4 ng/dl. The high incidence of hypothyroxinemia observed in sick newborns confirms the observation that T4 screening for hypothyroidism results in a high false positive rate in this group of infants and that additional tests are necessary to determine thyroid status in ICN infants. The measurement of FT4 appears to be an accurate indicator of thyroid function in newborns and may represent a more direct method of screening infants for hypothyroidism.

409 HYPOKETONEMIA: THE PRINCIPAL CAUSE OF FASTING HYPOGLYCEMIA IN GROWTH HORMONE DEFICIENCY. Joseph I. Wolfsdorf, Abdollah Sadeghi-Nejad, and Boris Senior. Tufts University School of Medicine, New England Medical Center, Boston.

Fasting children quickly become ketotic and ketones, as an alternative fuel for the brain, spare glucose. Because utilization of ketones relates directly to their concentration, children with the highest concentrations of ketones use the most and by being most dependent on ketones for fuel would be most prone to develop hypoglycemia were ketones in short supply.

We examined whether fasting hypoglycemia of growth hormone deficiency could be ascribed to a shortage of ketones. We studied 45 normal and 17 growth hormone deficient children. In both groups fasting concentrations of ketones varied over a 20-fold range and correlated inversely with both the glucose levels and with the ages of the subjects.

KETONES vs. GLUCOSE	r	P	KETONES vs. AGE	r	P
CONTROLS y=6.47-1.16x	-0.63	<0.001	y=4.8-0.25x	-0.84	<0.001
GH DEFIC y=4.02-0.78x	-0.80	<0.001	y=3.9-0.22x	-0.83	<0.001

Adjusted for glucose levels and age, by analysis of covariance, the concentrations of ketones in the growth hormone deficient patients were significantly lower than in the control children, $P<0.01$. Only the five youngest growth hormone deficient patients became hypoglycemic. These were precisely the patients with the greatest degree of relative hypoketonemia.

Accordingly we propose that hypoketonemia is the principal factor in the genesis of fasting hypoglycemia in growth hormone deficiency.

● **410** PANCREATIC POLYPEPTIDE (PP) DEFICIENCY IN PRADER-WILLI SYNDROME (PWS): William B.Zipf, Thomas M. O'Dorisio, Samuel Cataland, (Spon.Juan F. Sotos)College of Medicine, Departments of Pediatrics and Medicine, The Ohio State University, Columbus, Ohio.

Children with hyperphagia and obesity of the PWS have blunted PP responses to low protein(LP) meal stimulation (Zipf et al.JCEM: 52,1264). Since PP responses are directly related to the amount of protein ingested, we wished to determine if the blunted response was due either to an altered response threshold or to PP deficiency. We gave both LP (0.2g/kg) and high protein(HP)(2.0g/kg) meals to 11 PWS children, 10 normal obese(NOb) children and compared the PP responses measured at 0,15,30,45,60,90,120 and 180 minutes to LP meal stimulated PP responses observed in previously studied normal weight children(NWC) on growth hormone therapy for GH deficiency (Zipf et al,JCEM:53,574). All hormone values are expressed as mean ($\bar{X}$)±SEM, ng/ml. 50 pg/ml is the lower limit of the assay sensitivity. ΔMAX, is the rise above basal values.

GROUP	N	AGE ($\bar{X}$, RANGE)	% IDEAL BODY WT.	BASAL PP	LP Δ MAX	HP Δ MAX
PWS	11	12, 6-17	197%	50±5 *	40±29 *	209±81 *
NOb	10	11, 7-14	162%	92±25	348±168	678±210 †
NWC	7	11, 7-15	116%	140±60	435±53	——

(*Sig. different than the other groups, $p<0.05$; †, N = 7)

To test further for releasable PP, 10 PWS children received an i.v. pentagastrin PP stimulation test. Only 2 had a positive PP response although all showed a positive insulin response. These studies show that PWS children have a functional deficiency of PP and not an altered stimulus response threshold. This observation, 1)may have etiologic significance to the hyperphagia and obesity as suggested by recent animal studies and 2)suggests PP response may be a useful diagnostic test for PWS.

● **411** CARTILAGE METABOLISM IN CATCH-UP GROWTH SUPERIMPOSED ON GROWTH STUNTING RESULTING FROM DIFFUSE BRAIN INJURY. Oscar F. Zuniga, Regina A. Jansons, Cindy B. Good, Charles A. Sondhaus, and H. David Mosier, Jr., University of California, Departments of Pediatrics and Radiological Sciences, Irvine, California.

Cartilage of rats with growth retardation due to neonatal head-irradiation (X) has paradoxically increased protein and collagen synthesis. Females exhibit greater growth recovery than males. We have tested whether cartilage metabolism reflects this sex difference. Incorporation of ^{35}S-sulfate (S), ^{3}H-thymidine (T), ^{14}C-leucine (L) and ^{3}H-proline (P) by cartilage of irradiated rats were determined with and without superimposed fasting (F) and during a subsequent recovery period. The groups were non X-non F; non X-F; X-non F; and X-F. 600 rads were given to the head only at 2 days of age; all non X rats were sham-X littermates. Fasting was for 2 days from 40 days of age. At 70 days of age cartilages from each rat were divided among media containing the labeled substrates. In males, X had greater L incorporation than non X ($p<0.05$); however, in females X had both significantly increased L ($p<0.025$) and P ($p<0.05$) incorporation than non X. In addition, in females and not in males, X-F showed increased L ($p<0.05$) and P ($p<0.025$) incorporation than non X-F. Neither sex had a difference between non X and non X-F or between X and X-F. We conclude that greater protein and collagen synthesis in females correlates with greater growth recovery. In both sexes this was independent of the catch-up growth from fasting; thus, a different growth mechanism is involved in the slow growth recovery after brain injury than is involved in catch-up growth after F.

412 THE CATCH-UP GROWTH MECHANISM IN THE STUNTED BRAIN-INJURED RAT. Oscar F. Zuniga, Charles A. Sondhaus, Regina A. Jansons, Cindy B. Good, and H. David Mosier, Jr., University of California, Departments of Pediatrics, and Radiological Sciences, Irvine, California.

X-irradiation (X) of the head of the neonatal rat results in a dose related growth retardation which is resistant to growth hormone and/or thyroxine. In order to determine whether the stunting results from damage of catch-up growth controls we have observed growth during recovery after fasting (F) in X rats and sham-X littermate controls. 36 males and 35 female rats were distributed among non X - non F, non X - F, X - non F, and X - F. 600 rads X-irradiation was given to the head only at 2 days of age. Fasting lasted for 2 days from 40 days of age. Head irradiation per se resulted in a highly significantly lower body weight ($p<0.0005$) and tail length ($p<0.025$). At the end of the fast there was a highly significant added reduction of body weight in both sexes in X ($p<0.0025$) as well as in non X ($p<0.0005$). At 70 days of age, however, X-F and non X-F of both sexes did not differ from their respective controls with respect to body weight, tail or tibial length. We conclude that although X creates a permanent growth deficit, the catch-up control continues to operate after F. Growth stunting after diffuse head irradiation thus results in a new setting for body size which in turn becomes the new limit for catch-up growth.

EPIDEMIOLOGY

413 THE EPIDEMIOLOGY OF HOSPITAL ACQUIRED NEONATAL CYTOMEGALOVIRUS (CMV) INFECTIONS. Stuart Adler, T. Chandrika, Linda Lawrence, and Jane Baggett. (Spon.by H. Maurer) Medical College of Virginia, Department of Pediatrics, Richmond.

135 newborns were cultured for CMV on admission and weekly after 4 weeks of age until discharge. 6 (all weighing <1100 gms.) acquired CMV while hospitalized. Mothers of all infected infants were CMV seronegative (CMV ELISA). 50% of all infants were born to seronegative mothers. The risk of a seronegative infant weighing <1200 gms. of acquiring CMV was 50%. There was no correlation between length of hospitalization and birth weight for all infants hospitalized over 30 days. There was a significant correlation ($p<0.0001$) between the number of blood donors for an infant and the acquisition of CMV. Infected infants received blood from >8 donors prior to CMV shedding. Infected infants received blood from an average of 6.6 CMV antibody + donors while uninfected infants <1200 gms. received blood from an average of 3.3 CMV antibody + donors. Seronegative mothers are unlikely to have infected their infants. No infant received non-maternal breast milk. Restriction enzyme analysis of all isolates is being completed to exclude infant to infant transmission. After acquiring CMV, 2 infants died (only 1 autopsied and had proven disseminated CMV), 2 developed clinically significant hepatitis, and 1 developed pneumonia and hepatitis. These results strongly suggest that acquired CMV infections are a significant risk to the infants <1200 gms. born to seronegative mothers and the source of this infection is seropositive blood donors.

414 RED CELL CYTIDINE PHOSPHATES: A STABLE INDEX OF LEAD EXPOSURE UNAFFECTED BY CHELATION. Carol R. Angle, Mark S. Swanson, Matilda S. McIntire, Sidney S. Stohs. University of Nebraska Medical Center, Department of Pediatrics and Biomedicinal Chemistry, Omaha, NE 68105

Blood lead (PbB) itself is a relatively unstable index of lead exposure. An increase in red cell cytidine phosphates (rbc CP) occurs with excess lead exposure during erythrocyte maturation and thus provides evidence of cumulative lead exposure over the antecedant three months. Pyrimidine-5'-nucleotidase (Py5N) is an enzyme of the red cell and reticulocyte cytosol that dephosphorylates UMP and CMP and permits their diffusion from the cell. Rbc Py5N activity is directly and rapidly inhibited by increases in the PbB. Although rbc Py5N fluctuates with PbB, rbc CP remains elevated. Stability of rbc CP was shown in four children, 2-5 years old, with PbB of 58.3 ± 3.8 ug/dl. Chelation with I.M. CaEDTA 50mg/kg/d x 4 rapidly reduced PbB to 28.5 ± 1.5 ug/dl. Py5N was restored from <40 units/g hemoglobin to normal values of above 100 u/g. Rbc CP remained elevated at 10-50 nmoles/10^{10} rbc. Persistence of rbc CP despite correction of Py5N suggests that Py5N has limited function in the mature rbc. Fluorescent erythrocyte protoporphyrins (FEP) are also cumulative during rbc maturation in the presence of increased PbB and reflect the inhibition of heme synthesis. Although rbc CP and FEP result from two distinct modes of toxicity of Pb for the developing rbc, both can be used as indices of cumulative exposure to lead. (Supported in part by USPHS Grant 1RO1ES01857).

● **415** PROTECTIVE EFFICACY OF LIVE ATTENUATED VARICELLA ZOSTER VIRUS (VZV) VACCINE AGAINST NATURALLY ACQUIRED VZV INFECTION. Koichi Baba, Hyakuji Yabuuchi, Michiaki Takahashi, Sarah Bogger, and Pearay L. Ogra. Dept. of Pediatrics, State University of N.Y. at Buffalo, Osaka University, Osaka, and Research Institute for Microbial Diseases, Osaka, Japan.

Groups of normal infants and children in a closed institution in Japan were immunized subcutaneously (S/C) or via inhalation (I/N) with OKA strain of live attenuated VZV vaccine in a dose ranging from 50 to 2500 PFU of the vaccine virus. The immunized subjects, non-immunized seronegative and previously infected seropositive subjects (controls) were followed through four epidemics of VZV infection in this institution over a period of five years. No subjects with prior natural VZV infection developed varicella during subsequent VZV outbreaks. However, 100% of seronegative subjects developed varicella during exposure. Of particular importance is the observation that 10% (17/178) VZV vaccinated subjects developed varicella during re-exposure. The development of varicella in such immunized subjects was limited to those who had been vaccinated with either <80 PFU of the S/C vaccine or <800 PFU of the I/N vaccine. These observations suggest that vaccination with VZV vaccine in a dose over >800 PFU offers 100% protection against heavy exposure to wild virus even under closed institutional settings.

418 ROTAVIRUS GASTROENTERITIS AND WEATHER. Carl D.Brandt, Hyun W. Kim, Wm. J. Rodriguez, Julita O. Arrobio, Barbara C. Jeffries and Robt. H. Parrott. Research Fdn of Children's Hospital and the George Washington University School of Medicine and Health Sciences, Washington, D.C.

During 5½ years of study in Washington, D.C., hospitalization of children for rotavirus gastroenteritis tended to be more common following a month of cold or dry weather than following a corresponding calendar month of warm or wet weather. Overall, there were 84% more (178 vs 97) inpatients with rotavirus following a set of relatively colder individual months taken as a group than following an equal number of warmer corresponding calendar months taken as a group. Comparable differences were not seen with non-rotavirus gastroenteritis patients. There also were 45% more rotavirus hospitalizations following a set of months with the least depth of precipitation as compared to a set of corresponding calendar months with the greatest depth of precipitation. Rotavirus infection in young infants, the children least likely to be directly exposed to outdoor conditions, showed some of the most marked weather-associated effects. These findings suggest that weather-related low indoor relative humidity and indoor crowding may be key factors in the epidemiology of rotavirus disease.

● **416** DETERMINANTS OF BIRTH-WEIGHT IN SINGLETON BIRTHS IN A PREDOMINANTLY WHITE MIDDLE CLASS COMMUNITY. Ilsa N. Blidner, Gary D. Anderson, and John C. Sinclair, Departments of Pediatrics and Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Canada.

The effects on birth-weight (BW) of gestational age (GA), fetal sex, maternal anthropometric measurements, sociodemographic characteristics, and smoking were studied in a stratified random sample of 1501 singleton pregnancies delivered in Hamilton hospitals over an 18-month period. Information was collected prospectively by maternal hospital chart review, maternal postpartum interview and anthropometric assessment, and newborn examination. Mean BW among singletons was 3316 g. At 40 weeks GA, the 50th percentile BW was 3540 g for males and 3350 g for females. After controlling for GA and fetal sex, the following maternal variables were positively correlated with BW: prepregnant weight, weight gain in pregnancy, stature, bicristal diameter, biacromial diameter, calf circumference, upper arm circumference, triceps skinfold, upper arm muscle area, and subscapular skinfold. Stepwise multiple linear regression, controlling for GA and sex, showed that the most important predictors of BW were: for primigravidas, weight gain in pregnancy, pre-pregnant weight and number of cigarettes smoked daily during pregnancy; for multigravidas, birth-weight of the last sibling, number of cigarettes smoked daily, weight gain during pregnancy, and prepregnant weight. Smoking during pregnancy reduced birthweight by 13.3 g per cigarette smoked daily. Women who smoked before pregnancy but not during pregnancy delivered infants of BW's similar to infants of non-smokers.

● **419** TEMPORAL AND GEOGRAPHIC CLUSTERING OF BILIARY ATRESIA Linda S. Book, John Gardner, Michael Matlak, Chris Gillies. (Spon. by Lowell Glasgow) University of Utah Medical School, University of Utah Medical Center, Department of Pediatrics, Salt Lake City.

Cases of extrahepatic biliary atresia have generally been observed to occur sporadically. We compared the incidence of extrahepatic biliary atresia in Utah and Idaho to U.S. incidence and evaluated cases for time-space clustering. Cases from 1974-1981 in Utah and Idaho were ascertained by contact with all pediatricians and pediatric surgeons in the two states as well as pediatric surgeons and gastroenterologists in Denver, Seattle, and Portland; the closest referral centers outside the two states. Death certificates were also reviewed in the two states for the past 10 years to assure complete ascertainment. Diagnosis was confirmed by surgical exploration or autopsy in most cases. Expected cases were calculated from the U.S. mortality rate for biliary atresia in 1975 (5/100,000 births). Relative rates were calculated as observed to expected ratios for each time period and geographic area. The incidence of biliary atresia in Idaho was double that in Utah. Cases were found to cluster in eastern Idaho with a 3-4 fold increase over that expected from national rates ($p<.01$). In both states the majority of cases for the 8 year period occurred in the past three years. Our data suggests that time-space clustering of biliary atresia occurs. This suggests that environmental factors may play a role in the etiology of biliary atresia, but changing diagnostic practices must also be considered.

417 ANTIBACTERIAL EFFICACY AND SAFETY OF NEONATAL BATHING WITH HIBICLENS^{R} (HIB). Jeffrey L. Blumer, Marcia P. Husak, Joan Wiltshire, Avroy A. Fanaroff, and William T. Speck. Case Western Reserve University School of Medicine, Rainbow Babies and Children's Hospital, Departments of Pediatrics and Pharmacology, Cleveland, Ohio 44106.

The present study was undertaken to evaluate the effect of total body bathing with 4% Hibiclens^{R} (chlorhexidine gluconate) on the rate and extent of neonatal bacterial colonization. Full-term newborn infants were randomly assigned to receive either bathing with HIB or a control solution (castile soap). Blood samples were obtained on days 1, 2, and 3 of life and analyzed by GC for chlorhexidine. Cultures of the anterior nares and umbilical area were obtained on days 1, 2, 3 and 14 and analyzed bacteriologically. A total of 38 infants (19 in each group) have been studied to date. During the first three days of life HIB had little effect on the bacterial colonization of the anterior nares but resulted in marked protection against colonization of the umbilical region. Eighteen of 19 infants had no bacterial growth by the third day of life. By day 14 colonization of HIB infants was indistinguishable from those washed with castile soap except for a slight increase in colonization by gram-negative bacteria. No percutaneous absorption of chlorhexidine was observed during the first three days of life. In addition, washing with HIB resulted in no increase in adverse clinical reactions when compared with castile soap. Thus perinatal infant bathing with 4% chlorhexidine gluconate is effective in preventing colonization with bacterial pathogens. Its use results in no systemic absorption of the antiseptic and no increase in cutaneous or systemic perinatal disease.

420 PREDICTION OF RISK OF BRONCHOPULMONARY DYSPLASIA (BPD) Aaron Cohen and H. William Taeusch, Jr. Harvard Medical School, Dept. Pediatrics, Boston.

Studies of approaches to decreasing the risk of BPD have been hampered by failure to define prospectively a high risk population. Therefore, we tried to design a screening test that could be easily applied early in the hospital course that would predict which infants would develop BPD. From a population of infants ≤ 1250g, who were alive at 48h, we selected those who had received ventilator support (IMV) within 48h after birth. From this group we selected those receiving IMV for $\geq$24h/48h and $F_IO_2 \geq .6$ for $\geq$ 2h/48h. If these criteria were met, the screen was positive. BPD was defined as $F_IO_2 \geq .24$ at 1 month of postnatal age AND a chest radiograph consistent with BPD. For 166 infants ≤ 1250g born between 1978-1981 at Brigham & Women's Hospital for whom we could analyze records, we found that the screening procedure had: sensitivity (34/43) = .79, positive accuracy (34/42) = .81, false positive rate (8/42) = .19, and specificity (18/26) = .69. We conclude that this screening procedure is a useful one for early prediction of BPD risk and selection of a study population. In order to study a treatment designed to produce ~20% reduction in BPD at $p<.05$, approximately 190 infants would have to be enrolled.

	BPD	NO BPD	
+ screen	34	8	42
- screen	9	18	27
	43	26	69

421 IMPACT OF NEONATAL INTENSIVE CARE UNITS(NICUs) AND THE WIC PROGRAM ON EXPECTED CEREBRAL PALSY(CP) RATES. Richard J. David and Janet M. Reis. (Spon. by Carl E. Hunt). Northwestern Univ., Dept. of Pediatrics, Chicago.

Two major trends affected the BW distribution of neonatal survivors in opposite directions in recent years: a decline in low birth weight(LBW) was attributed to primary prevention (such as the WIC nutrition and prenatal care program) while increased survival rate among LBW infants was attributed to NICUs. We calculated the impact on expected CP rates of these two trends, using three data sources: (1) two studies, each of which provided BW data on all CP cases in a geographic population; (2) computerized vital records from North Carolina for 1968-77; and (3) BW and mortality data from the Massachusetts WIC Evaluation Project. We first quantitated the relationship between BW and CP risk(R_{CP}) using data sources 1 and 2: R_{CP} rose exponentially with decreasing BW using data from either of the CP studies ($R_{CP}=83e^{-1.01BW}$, $r=-.93$, and $R_{CP}=239e^{-1.43BW}$, $r=-.97$). We then applied the derived regression equations to the observed changes in BW-specific survival data (data source 2), using 500g BW categories. Proportionally fewer total births and fewer survivors occurred in most weight categories below 3500g in 1977 compared to 1968, resulting in a predicted fall in CP rates of about 6%. Applying the same analysis to WIC program data (source 3), we found a calculated decline in CP rate of about 4%. These results indicate that recent advantageous shifts in population BW distribution such as noted with improved nutrition and prenatal care have more than compensated for the increased LBW survival attributed to NICUs in their impact on predicted CP rates.

422 FATAL HEPATITIS B IN INFANTS OF $HB_sAg\oplus$ MOTHERS: IMPORTANCE OF MATERNAL SCREENING AND NEONATAL IMMUNOPROPHYLAXIS. Dietra Delaplane, Ram Yogev, Frank G. Crussi, and Stanford T. Shulman. Northwestern University Medical School and Children's Memorial Hospital, Chicago.

Infants born to asymptomatic $HB_sAg\oplus$ mothers are at high risk of hepatitis B (HBV) infection. The spectrum of disease in infants includes mild acute hepatitis B, chronic active hepatitis with or without cirrhosis, chronic persistent hepatitis, chronic asymptomatic HB_sAg carriage, and very rarely fatal fulminant hepatitis B. Maternal seropositivity for HB_sAg and HB_eAg is associated with increased risk of HBV transmission from mother to infant. We report four unrelated infants 2½ to 16 weeks of age who died of fulminant acute hepatitis B. In each instance the asymptomatic mother was found retrospectively to be seropositive for HB_sAg. One mother was found to have chronic active hepatitis B. Two mothers were U.S. immigrants from areas of high HB_sAg endemicity. Since recent trials have demonstrated the efficacy of hepatitis B immunoglobulin (HBIG) in reducing the rate of infantile HBV acquisition, these fatalities likely were preventable. The potential value of hepatitis B vaccine in prevention of vertical transmission of HBV is being explored. These four infant deaths dramatize the importance of screening pregnant women for HB_sAg, particularly those from populations at increased risk of HB_sAg carriage: Orientals, medical personnel, drug addicts, prostitutes, and those with history of hepatitis. Such prenatal HB_sAg screening, with HBIG and/or hepatitis B vaccine immunoprophylaxis for infants at risk, will reduce the incidence of infantile HBV infection, with its potentially fatal outcome.

423 SOCIODEMOGRAPHIC CHANGE AND RECENT IMPROVEMENT IN LOW BIRTHWEIGHT RATE(LBWR) IN THE U.S. Hakuyo Ebara, Chuwen-Yuh Kuo, Kwang-sun Lee and Lawrence M. Gartner. The University of Chicago, Pritzker School of Medicine, Dept. Pediatr., Chicago, IL.

This study analyzes the relationship between net change in LBWRs of 50 states and Washington, D.C. and the concomittant alterations in sociodemographic and prenatal care status in the years between 1969 and 1977. There have been significant reductions in both white and black LBWRs.

LBWR	1969	1977	% Change
White	7.16±0.86	6.05±0.77*	-15.3±6.4#
Black	14.17±1.61	12.52±1.46*	-11.9±9.2#
Total	8.07±1.31	7.01±1.45	-13.6±6.2

*Difference, 1969 vs. 1977, $p<.01$. #White vs. black, $p<.05$.

Correlation analyses between net changes in LBWRs and sociodemographic and prenatal care status are shown below:

% Change LBWR	% Change Age (≤19&≥35)	Parity (1&>5)	Education (<12 yrs.)	Illegitimacy	No Prenatal Care
White	-.22*	-.13	.19	-.19	-.11
Black	.18	-.04	.21	.27	-.24
Total	.08	.18	.10	-.02	.22

*Correlation coefficients (r), all, $p>.05$.

The results of this study suggest that the recent improvement in LBWR in the U.S. can not be attributed to alterations in maternal sociodemographic or prenatal care status in the same time period.

424 MATCHED CASE CONTROL POPULATION <2500G TO DETECT EFFICACY OF NEONATAL TRANSPORT. Angelo Ferrara, Melvin Schwartz, Mort Israel, Helen Page, Susan Highhouse, Ed Smith, Leon Landowitz. NYU/Bellevue Med. Ctr. Dept.Environ. Med., Dept. Peds. & CUNY, NYC.

To note the efficacy of neonatal transport, 1292 NB charts <2500G were reviewed from 50 NYC hosp. for calendar yr. '79. The hosp. records of all 222 transported (T) NB <2500G. & a randomized sample of non-transported (NT) (N=1070) matched population were audited by trained RN's. Besides the physiological perinatal data, the independent variables included hosp. of birth (6 levels), severity by APGAR(<6&>6),Wt in Gm(<1500&1500-2500) & transport status (2 levels-yes.no).Additional matching variables included sex & race. Between the (T)&(NT) study pop. there was no signif. diff. in maternal age, in incidence of illegitimacy, in maternal education, in position at birth (most were occiput) & in financial coverage. Major outcome measure was mortality. Analysis of data was done by χ^2 testing including Mantel-Haenszel (M-H) test. Data in Table I reflects Phase I of the study. RESULTS:(1) In a matched pop., the (T) showed an improved survival if the pt. was in a severe category, <1500G (2)All (NT)>1500G did better than (T). (3)These results are preliminary, but suggest that only a reduced # of selected neonates would benefit from transports & judicious decision re, transport is essential.

TABLE I: ANALYSIS MATCHED POP. BY M-H TEST BY SEVERITY BY WT.

CATEGORY		ALIVE	DEAD	CATEGORY		ALIVE	DEAD
Mild-Mod.>1500	T	111	7	Mild-Mod.<1500	T	51	21
P<.001 favor (NT)	NT	983	0	P<.001 favor (NT)	NT	30	3
Severe>1500	T	8	3	Severe<1500	T	9	12
P<.07 favor (NT)	NT	23	3	P<.09 favor (T)	NT	8	20

425 THE EPIDEMIOLOGY OF CHRONIC OTITIS MEDIA IN CHILDREN. G. Scott Giebink, Chap T. Le and Michael M. Paparella. University of Minnesota, Departments of Pediatrics, Biometry and Otolaryngology, Minneapolis, Minnesota.

To describe the contents of the middle ear in chronic otitis media (OM), a population of 898 children less than 12 years of age having chronic OM of at least three months duration was studied at the time of myringotomy for tympanostomy tube placement. Mucoid effusion, which was found in 48% of the 1,796 operated ears, occurred more often in younger than in older patients, and was bilateral more often than was serous or purulent effusion. Serous effusion was found in 10% of operated ears and occurred more often in older than in younger patients. Purulent effusion was found in 7% of operated ears and was equally distributed by patient age. No effusion was found in 36% of operated ears. Mucoid effusion was the most stable chronic OM state among 117 patients that had repeat surgery an average of 13 months after initial surgery. Preoperative otoscopy showed subtle differences between effusion-free and effusion-containing ears, but did not distinguish among effusion types. Known middle ear bacterial pathogens were cultured from 23% of effusion samples, other bacteria were cultured from 7% of samples, and 17% of the sterile effusions showed bacteria on gram-stain. Effusions which cultured bacterial pathogens contained more phagocytic cells than sterile effusions. Thus, chronic OM is characterized by mucoid, serous and purulent effusion or by absence of effusion. Respiratory bacteria may contribute to the pathogenesis of chronic OM. These observations provide a descriptive base for further investigation of chronic OM.

426 INCONSISTENCY OF NEUROLOGICAL OUTCOME WITH INTENSIVE CARE OF VLBW INFANTS. M.Hack and A.Fanaroff. Department of Pediatrics, Case Western Reserve Univ., Cleve., Ohio.

It has been postulated that the improved survival and long term outcome of VLBW (<1.5Kg) infants in the early and mid 1970's are the result of neonatal intensive care. Alarmingly, since 1978 we have noted an increased incidence of cerebral palsy (spastic diplegia, quadruplegia) in infants followed to at least 20 months (60% transport 40% inborn). In order to elucidate this problem we compared the outcome of 205 infants (BW 1.2Kg, GA 29.9 wks) born in 1976 and 1977 who survived until discharge with 232 infants (BW 1.2Kg, GA 29.8 wks) born in 1978 and 1979. Survival in 1976-77 was 71%(205/289) and in 1978-79 66%(232/354) N.S.

Cohort	Infants Followed n (%)	Cerebral Palsy n (%)	Total Neurological Abnormality and/or D. Q.<80 n (%)
1976-77	179(87%)	6(3.4%)	17 (9.5%)
1978-79	228(98%)	17(7.5%)*	36 (15.8%)**

*$p<.001$, **$p<.01$

There were no differences between the two periods in BW, GA or Hobel antepartum, intrapartum and neonatal risk scores. Also the incidence of transport, asphyxia (Apgar <6 at 5 min), RDS, apnea and necrotizing enterocolitis did not differ. However, significantly more infants were intubated for RDS [17/205, 8% vs 38/227, 17% ($p<.001$)], and had documented sepsis [15/205,7% vs 37/227, 16% ($p<.001$)].

The findings suggest that more active intensive care is not necessarily accompanied by a better long term outcome and may lend itself to iatrogenic problems. Prevention of prematurity must remain the top priority.

● **427** A PROSPECTIVE STUDY OF RESPIRATORY VIRUSES AND BACTERIA IN THE ETIOLOGY OF OTITIS MEDIA WITH EFFUSION (OME): Frederick W. Henderson, Univ. of North Carolina School of Medicine, Dept. of Pediatrics, Chapel Hill, N.C.

Data from a 14 year longitudinal study of respiratory infection in young children were analyzed to examine the relative importance of viral infection and nasopharyngeal carriage of Streptococcus pneumoniae and Haemophilus influenzae (Str. pn. and H.inf.) as etiologic determinants in OME. The study was performed in a research day care center. Children had nasopharyngeal cultures for viruses and bacteria at the onset of each illness and every two weeks routinely. The incidence of OME was increased significantly ($p<.0001$) in the two weeks following infections with respiratory syncytial virus(RSV;33.3%), adenoviruses(AV;28.2%), influenza viruses(Inf A and B;27.9%), parainfluenza and mumps viruses (15.5%), and enteroviruses(16.0%), in comparison to the OME incidence when viral infections were not identified(6.6% per 2 weeks). Colonization of the nasopharynx with Str. pn. and H. inf. had smaller but significant effects on OME incidence(relative risk for OME: Str. pn. 1.35; H. inf. 1.76). Primary acquisition of Str. pn. serotypes was not identified as an OME precipitant. Prevention of OME cases attributable to these bacteria would have reduced OME incidence approximately 25%. Early and repeated infections with the closely OME-linked viruses were correlated with more frequent OME; no parameter of bacterial colonization was identified as a correlate of OME frequency. The data identify microbiologic parameters which deserve consideration in future design of preventive intervention programs.

428 ASSESSMENT OF SOCIO-ECONOMIC STATUS IN A DEVELOPING URBAN COMMUNITY. Janet Hollingshead, Christopher D. Molteno, Maurice A. Kibel (Spon. by Sydney S. Gellis) University of Cape Town, Children's Hospital, Dept. of Paediatrics and Child Health, Cape Town, Rep. of South Africa.

Research in community paediatrics frequently requires an objective assessment of socio-economic status. Traditional methods e.g. the Registrar General's classification in the United Kingdom, are not always applicable in developing countries. The Child Development Study required such an assessment.
In the study a cohort of 1000 consecutive live births was identified and a random sample of 187 selected for follow-up over a 5 year period. A socio-economic index was developed for the sample comprising 5 items viz 1) marital status, 2) family cohesiveness and child orientation, 3) available income expressed as a percentage of a household subsistence level, 4) the degree of crowding measured by an occupancy ratio and 5) the presence of social pathology e.g. alcohol abuse. Item analysis was applied. On the basis of the reliability indices, the items were weighted to give a total score out of 14.
The theoretical hypothesis that socio-economic status would influence growth and development was used to evaluate the validity of the index. The index of socio-economic status correlated significantly with growth ($r = 0.83$) and development ($r = 0.47$) at 5 years.

429 BETA HEMOLYTIC STREPTOCOCCI IN NORMAL NEONATES. M. Hosmer, K. Sprunt. Dept of Pediatrics, Columbia Presbyterian Medical Center, New York, N.Y. 10032.

Since March, 1977, infants discharged from our nurseries have had umbilical cultures (umb) to detect as early as possible the appearance of Group A (A) β-hemolytic streptococci (BHS). The colonization rate of BHS has varied from 1 to 48% per month, usually 20-30%. However, <1% of the strep are A. In 1979 an average 15% of the infants carried Group B (B) (8-30%). The 30% B peak in June fell to 4% by Dec as Group G (G) increased (18% in Nov and Dec). The shift to G peaked (36%) in Feb 1980, fell to 4% in March, and has been occasional since. From March through Nov overall BHS colonization dropped (1-14%). The common group was B, but in July 1% were Group C, in Oct 2%, and in Dec 7%. C increased to 27% in March 1981 and has been the common group since.

In Nov 63/103 infants in 1 nursery carried C (umb) at discharge: 3 carried B; no staff throat cultures (T) yielded C. C colonization rate of infant umb varied from 0% to 100%/day. Infants who became colonized had positive (+) cultures on day 1 (or at first culture) with one exception (positive at 2nd culture). Eleven sets of cultures (umb, T, and axilla) were taken from infants with known positive umb cultures. C colonization did not spread to other sites. The data suggest maternal origin of C rather than nursery dissemination. There has been no Group C disease. Knowledge of this extensive colonization is essential in evaluating the meaning of clinically pertinent positive cultures.

● **430** EPIDEMIOLOGY OF NEONATAL ENTEROVIRUS INFECTIONS. Jerri A. Jenista, Marilyn A. Menegus, and Keith R. Powell (Spon. by Robert A. Hoekelman). Univ. of Rochester, Strong Mem. Hosp., Dept. of Pediatrics, Rochester, NY

Although enteroviruses can cause overwhelming neonatal disease the incidence and prevalence of these infections in infants less than a month of age are unknown. The proportion of symptomatic cases, demographic and medical risk factors associated with infection, and the probability of illness requiring hospitalization in this age group are poorly defined. We prospectively studied Monroe County, NY residents born at Strong Memorial Hospital from June 24 through Sept. 30, 1981. Within 48 hours of delivery, medical history, demographic data, and throat and rectal cultures were obtained from the mother. A history of infant and household member symptoms and throat and rectal cultures from the infant were collected within 24 hours of birth, at 1, 2, 3, and 4 weeks of age, and at all hospital admissions. Cultures from 628/654 eligible mothers grew 6 enteroviruses, 3 rhinoviruses, and 18 herpes simplex viruses. Cultures taken shortly after birth from 666/668 eligible neonates grew 0 enteroviruses and 4 cytomegaloviruses. The minimal incidence of non-polio enterovirus infection during the first 4 weeks of life was 12%; prevalence ranged from 4 to 10% at each week. Enterovirus infection was associated with lower family income, bottle feeding, fever, maternal concern sufficient to contact a physician, and week of the year. The hospitalization rate was 4% overall and 24% in infants from whom enterovirus was isolated at weeks 2 or 4 Thus, enterovirus infection is common in neonates and frequently causes hospitalization.

431 VARICELLA VACCINE: USE TO PREVENT VARICELLA IN SUSCEPTIBLE ADULTS. Philip LaRussa, Margaret Hammerschlag, Sharon Steinberg, Melvin Marks, Ann Arvin, David Amler, Anne Gershon, & N I H Coll. Gp; Dept. Peds: NYU, Downstate, U. Okla, Stanford Med. U.

Varicella may be severe or fatal in adults, and hospital staff with varicella may spread disease to their patients. Numbers of susceptibles may vary in different locales. At NYU the incidence of varicella in pediatric residents was 1 every other year from 1973-78 (1%). In 1980 4 pediatric residents (8%) contracted varicella at Downstate. Serologic testing for antibody (Ab) to varicella-zoster (VZ) virus by indirect immunofluorescence (FAMA) is now widely available. Most adults with no history are immune; in 1981, only 5% of Downstate residents with no history had a VZ-FAMA of $\leq$ 1:2.

Varicella vaccine, developed by Takahashi in 1974, has been used mainly in children. We have immunized 19 susceptible adults, mostly medical personnel. All developed VZ-Ab and CMI, with no significant side effects. The VZ-FAMA geometric mean titer at 6 mo (11 pts) and 1 yr (10 pts) was 1:10. No cases of clinical varicella have occurred, despite 4 close exposures to patients. Varicella vaccine may prove useful to prevent clinical varicella in susceptible hospital staff.

432 REGIONAL VARIATION IN BIRTHWEIGHT DISTRIBUTION IN THE UNITED STATES. Kwang-sun Lee, Yucel S. Atakent, and Lawrence M. Gartner. University of Chicago, Pritzker School of Medicine, Chicago, IL and New York University, New York, N.Y.

Birthweight distribution of live births is closely linked to indices of maternal sociodemographic and biologic status. This study evaluates the relative importance of maternal factors on regional variation in very low birthweight rates (VLBWR) and low birthweight rates (LBWR) in the 50 states and Washington, D.C. in 1975.

Both VLBWR and LBWR of individual states and D.C. were significantly related to the prevalence rates of maternal sociodemographic status (age, parity, education, illegitimacy and race) and prenatal care status (r, 0.44 to 0.93, all $p < 0.01$). Racial composition of maternal populations alone accounted for approximately 83% of variance in VLBWR and 65% of variance in LBWR. Prevalence rates of sociodemographic factors in individual states and D.C. were unfavorable for black mothers compared to those for white. When white and black populations of states and D.C. were examined separately, the previously observed correlations between VLBWR/LBWR and prevalence rates of these maternal factors other than race were either absent or greatly reduced.

Results of these analyses suggest that the regional difference in racial composition of the maternal population is the single most important factor related to regional variations in birthweight distribution in the United States.

433 RUBELLA SEROEPIDEMIOLOGY AMONG AMISH FAMILIES IN LANCASTER COUNTY, PENNSYLVANIA. Martha S. Linet, Wilma B. Bias, Dorothy M. Horstmann (Spon. by Leon Gordis). ɔhns Hopkins U. Sch. Pub. Health, Dept. of Epidemiol.; Johns ɔpkins U. Sch. of Med., Dept. of Med., Baltimore; Yale U. Sch. ⁻ Med., Dept. of Pediatrics, New Haven, Conn.

A serosurvey of 52 Amish families with 391 children in Lancaɜr County, Pa., was carried out to determine rubella susceptiility levels (HAI titer <1:8) in this poorly immunized populaion, the distribution of rubella in families, and the efficacy f immunization in those who have been vaccinated. Overall 71% f the 269 children tested but only 2% of the parents were susɛptible. Age specific analysis showed 76% of children ages 6-10, 3% of those 11-15, 65% of those 16-20 and 17% of those 21-25 ɜre susceptible. (Children 0-5 weren't tested.) These rates iffer from those found in most other subgroups of the U.S. popuation in which 25-60% of those ages 6-10, 10-25% of those 11-15 ɲd 12-21% of those 16-20 are susceptible. Twenty-four of the 52 amilies tested had all children in the family susceptible to ubella; 2/52 families had all children immune. Immunity was not ssociated with family size. Only 8.5% of the study children had ɜen vaccinated against rubella. Of the 32 children vaccinated, 1% had negative serology titers. It is postulated that the high evels of susceptibility among the Amish children are due to bsence of epidemics (since rubella vaccine became available in 969 in the general population), as well as a low level of ndemic disease in this isolated population. We are currently xamining the possible role of HLA in rubella susceptibility.

434 ANALYSIS OF PEDIATRIC BLOOD LEAD LEVELS IN COLUMBUS AND THEIR RELATION TO AMBIENT AIR LEAD LEVELS. A. Harold Lubin, Barbara L. Jaffe, Irwin Billick. The ɲio State University, Department of Preventive Medicine, Columɹs, Ohio 43205.

Mean blood lead levels of 10,065 Columbus, Ohio, preschool ɲildren were evaluated from 1975 through 1979 to determine the ɔtential relationship to ambient air lead levels, race, and age. ɔwnward trends in the blood lead levels sampled as well as in ɲbient air lead levels were apparent in the study period. In ɜneral, blood lead levels sampled in 1979 were significantly ɔwer than four years previously. Absolute values for black childɜn fell more during this period than they did for white childɜn. Age related values for both races followed a virtually idenical pattern. When the three independent variables, race, age, ɲd ambient air lead levels were employed in a regression analyis, ambient air lead proved to be the best predictor of blood ɜad. Apparently, the regulation of lead in the air is associated ith lower lead levels in preschool children.

MEAN BLOOD LEAD LEVELS (ug/100ml)

RACE	YEAR	0-12 MOS	25-36 MOS	49-60 MOS
Black	1975	19.05	24.55	25.70
	1979	14.80*	18.20*	16.60*
White	1975	16.60	22.39	22.91
	1979	14.45	17.78*	17.38*

*p < .01

435 ON THE DEFINITION OF FEEDING GROUPS IN BREAST VS FORMULA FEEDING STUDIES. A. Harold Lubin, Janet S. Kasler, Ruth O. Shrock. The Ohio State University, epartment of Pediatrics. Columbus, Ohio 43205.

Infant feeding methods and their relationship to health have ɜen the focus of numerous studies. Differences in the definition f breast and formula feeding groups, however, has made the aplicability of subsequent findings difficult. Breast feeding to ome refers to being exclusively fed from the breast while to thers it includes cow's milk, formula and/or solid food supplɜentation. Where a given health outcome may be influenced by ɜeding method or in fact precipitate that outcome careful defnition of the feeding groups is essential. For example, in the ase of infection, the introduction of new foods may predispose o gastrointestinal illness and in the case of obesity, the arly introduction of solid foods may influence early weight ain regardless of breast or formula feeding. Preliminary findngs from our investigation on the effects of maternal nutritionl and environmental factors on infant growth and development ndicate that consideration of precise infant feeding groups is ecessary to determine iron status differences - infants exclusively breast or formula fed were found to have higher serum ron levels than infants who were not. We emphasize that the ɩost important criterion is that of "exclusivity". Children ɜither exclusively breast or formula fed constitute a difficult o control and compare group, who confound a large number of ɩtherwise well designed studies.

● **436** PROTECTIVE INFLUENCE OF BREAST FEEDING (BF) ON THE RISK OF DEVELOPING INVASIVE H. INFLUENZAE TYPE b (HIB) DISEASE. Milton K. Lum, Joel I. Ward, Thomas R. Bender. (Spon. by B. Anthony) UCLA School of Medicine, Harbor-UCLA Med. Ctr., Dept. Pediatrics; CDC, Anchorage, AK.

Alaskan Eskimos have the highest known incidence of invasive HIB disease, with 3% of Eskimo infants developing bacteremia or meningitis before 1 yr. of age. To evaluate measures which might prevent disease in infancy, we studied the influence of BF by assessing nutritional histories in a matched case-control study. We also measured levels of HIB anticapsular antibody in breast milk (BM) and sera of Eskimo mothers. Infants with invasive disease (N=19) and 2 controls for each case, matched for age (susceptibility) and village or neighborhood (exposure), were studied. A history for BF was considered positive if the subject was predominantly BF until an age equal to that of the case at the time of hospitalization. BF was significantly less prevalent among cases 1/19 than controls (18/38) (p<.01, Pike-Morrow).

HIB anticapsular antibody (Ab) was measured in breast milk specimens and sera from 10 Eskimo mothers 2-6 months postpartum by RIA and ELISA. Ab in BM was predominantly IgA (ELISA: IgA 67%, IgM 33%, IgG 0%) and total levels ranged from 10-390 ng/ml (RIA mean 95 ng/ml). These levels were similar to controls from elsewhere in the U.S. Antibody in maternal sera was predominantly IgM (ELISA: IgM 72%, IgG 21%, IgA 7%) and total levels ranged from 2.0-6.4 µg/ml (RIA mean 3.4 µg/ml). There was no correlation between levels in BM and sera.

Breast feeding appears to reduce the risk of developing invasive HIB disease, but the mechanism needs further clarification.

437 CURRENT BATHING TECHNIQUES IN NEWBORN NURSERIES IN THE UNITED STATES. Gilbert I. Martin, Joel Streng, Marjorie Miller. The Hagan Medical Clinic and the ueen of the Valley Hosp., West Covina, Calif.(Spon. by P. Wu).

A questionnaire was sent to 2400 hospitals in the United States with more than 250 deliveries per year to determine current bathing techniques. 1294 (54%) were returned. The following data were recorded: Admission bath-1248 (96%); daily bath-1162 (93%) umbilical cord care: alcohol-518 (40%), triple dye-401 (30%), alcohol and triple dye combined-181 (14%), Iodophor 43 (3%), Bacitracin-66 (5%). Materials used for infant bathing:

SUBSTANCE	ADMISSION BATH	DAILY BATH
pHisohex*	320 (26%)	113 (10%)
Ivory Soap	200 (16%)	222 (19%)
Safeguard soap or Phisoderm	233 (19%)	221 (19%)
Dial soap* or Betadine*	60 (4%)	34 (2.6%)
Hibiclens* or Baby Magic*	100 (8%)	90 (7.6%)
J&J Baby bath or Castile	96 (7%)	86 (7%)
Gammophen* or Mennen's Baby Lotion	105 (9%)	81 (7%)
Water	135 (11%)	315 (27%)

*materials with anti-bacterial properties.

Phisohex was used full strength in 201 (63%), and diluted in 119 (37%). Routine post-discharge cultures were done in 130 (10%). Post-discharge follow-up, 260 (20%).

Although the American Academy of Pediatrics Standards and Recommendations for Hospital Care of Newborn Infants recommends a "Dry Bathing Technique", few hospitals follow these guidelines.

438 PREDICTING FETAL GROWTH FROM NUTRITIONAL STATUS OF THE MOTHER AT MIDPREGNANCY. J. Metcoff, P. Costiloe, W. Crosby, L. Bentle, S. Dutta, F. Weaver, G. Burns, H. Sandstead, C. Bodwell. Depts of Pediatrics, Biochemistry, Epidemiology & Biostatistics, Obstetrics & Gynecology, Univ. of Oklahoma Health Sci. Ctr, Oklahoma City, OK 73190, Human Nutr. Research Lab, USDA/ARS, Grand Forks, North Dakota 58201, & Protein Nutr. Research Laboratories, USDA/ARS, Beltsville, Maryland 20705.

A single measurement of blood nutrient levels & other characteristics at midpregnancy in 539 women, 215 having uncomplicated pregnancies, was used to develop an equation to predict birth weight. The equation could account for 64% of the variance in birth weight, allowing for gestational age & sex of the baby. The correlation between observed and predicted birth weight for the 215 babies was r=0.74. In a field trial, a screening equation involving only demographic/clinical variables derived from 1290 mother/baby pairs was used at midpregnancy for preliminary stratification of mothers likely to have babies in the lower or upper thirds of a birth weight frequency distribution. Measurements of blood levels of those nutrients & leukocyte bioactivities at midpregnancy comprising the prediction equation were added to further narrow the identification of mothers likely to have fetally malnourished or large babies. Two thirds of the mothers in each of these selected groups were randomly assigned a food supplement. The remaining third were controls. To date, data have been analyzed for 245 initially screened mothers. For the selected test mothers, correlation between observed & predicted birth weights was r=.68. Thus prediction is both feasible & practical but the number of babies born to mothers whose fetus was thought to be nutritionally disadvantaged is still too small to evaluate the effect of a selective nutritional intervention on fetal growth.

● **439** PATHOGENICITY OF STREPTOCOCCUS VIRIDANS (S. VIRIDANS) IN THE NEONATE. Ara Moomjian, Myron Sokal and Suya Vijayan. SUNY Downstate Med. Ctr.-Brookdale Hospital, Brooklyn, New York. (Sponsored by T.W. AvRuskin)

S. viridans has been thought to be nonpathogenic in the neonate although it has been widely accepted as pathogenic in SBE and other conditions. During a 30 month period in the NICU, we have identified 18 infants with septicemia having S. viridans as the causative organism. During this period it was the most common etiologic agent in neonatal sepsis. Mean birthweight of the infants was 2990 g (range 900-4500g): mean gestational age was 39 weeks (range 28-42 weeks). 5 of the infants were premature and 6 were low birthweight. There was prolonged rupture of the membranes (PROM) in 8/18 patients and 1 mother had fever prior to delivery. 5/18 infants developed respiratory distress: 3 of these were term. No infant with PROM developed respiratory distress. The majority of the infants presented within 24 hours of birth with signs of sepsis. All infants had blood and other cultures drawn prior to beginning antibiotic therapy. Blood cultures were taken from a peripheral vessel. The blood was incubated in trypticase-soy broth at 37°C for 3 days. The organism was subcultured in SXT medium and after inoculation in Todd-Hewitt broth it was centrifuged and the supernatant was tested with specific alpha-hemolytic streptococcal antibody. The single mortality in the group was the smallest and most premature who also had findings consistent with severe hyaline membrane disease. In the remainder there was a good correlation with the beginning of antibiotic therapy and clinical improvement. The findings suggest that S. viridans is pathogenic in the neonate.

440 EPIDEMIOLOGY OF ACQUIRED MONOSACCHARIDE INTOLERANCE (AMI). Veda Nichols, Kim Evans, E. O'Brian Smith, Janice E. Stuff, G.S. Gopalakrishna, J. Ken Fraley, Herbert L. DuPont, and Buford L. Nichols. USDA/ARS, Children's Nutrition Research Center, Baylor College of Medicine, Houston.

Acquired monosaccharide intolerance (AMI) is a form of chronic diarrhea which is relieved by fasting and is characterized by the recurrence of diarrhea after feeding any form of dietary carbohydrate including monosaccharides. An epidemiological descriptive study of AMI is being conducted at the Ben Taub General Hospital in Houston, TX. All patients 3 months of age or less with diarrhea who visit the Pediatric Outpatient Service or who are admitted to the hospital are seen and entered into the study. Information concerning history of the diarrhea, feeding history, home and family conditions, nutritional assessment, collection of stool samples for viral and bacterial pathogens, and clinical course are obtained. The data at the present time do not implicate specific pathogens, feeding practices, maternal health factors, and socioeconomic conditions in the etiology of AMI. Malnutrition is prevalent among all patients. These children fit the normal distribution for weight at birth. The nutritional deficit suffered by these infants by the time of admission (mean age, 37 days) is evidenced by a reduction in the mean weight/height, height/age, and weight/age Z scores (standard deviations from the NCHS mean). AMI infants have lower mean Z scores than non-AMI infants. (Supported by USDA/ARS).

	Wt/Ht Z Score	Ht/Age Z Score	Wt/Age Z Score
AMI	-1.60 ± 0.96	-1.06 ± 1.07	-1.84 ± 0.83
Non-AMI	-0.93 ± 0.99	-0.79 ± 1.19	-1.24 ± 0.99

● **441** AN EPIDEMIC OF INFANTILE GASTROENTERITIS IN NORTHWESTERN QUEBEC: A CASE STUDY IN NATIVE HEALTH CARE Gary S. Pekeles and Ivan B. Pless, Montreal Children's Hospital, Community Pediatric Research, Montreal.

In 1980, infants in two Inuit (Eskimo) villages in northern Québec were struck by an unusually severe gastroenteritis which then spread to other settlements in the region. A retrospective study was carried out through visits to the villages and review of medical records to delineate predisposing factors, clinical course and mode of spread. In most affected villages, a majority of children under two had clinical symptoms; 82 were hospitalized with symptoms of gastroenteritis (mean hospitalization 39.5 days) of whom 77% had stool cultures positive for E. Coli 0111:K58. Thirty-seven percent required parenteral nutrition and 18% required rehospitalization because of prolonged or recurrent symptoms respectively. Seven infants died. Control cultures of adults and children in two villages were all negative. Several conditions facilitating fecal oral transmission of the disease within villages were noted: relatively inaccessible clean water, inadequate sewage disposal, open sewage ditches and preparation of infant formulas with contaminated water. Regional hospitals and foster homes were the major source of spread between villages Fifteen % of the hospitalized cases were nosocomially acquired and there were several instances of infants hospitalized for other problems who returned to their villages with diarrhea. This epidemic illustrates several of the problems faced by the native-run health board responsible for local care; inability to implement many preventive measures, poor organization of medical services, and inadequate back-up support.

442 THE INFLUENCE OF THE RESPIRATORY DISTRESS SYNDROME (RDS) AND ASPHYXIA ON NATIONAL NEONATAL MORTALITY BETWEEN 1968-1978. Robert Perelman and Philip Farrell, University of WI., Department of Pediatrics, Madison, WI.

A progressive reduction in total neonatal deaths began in 1971 such that only 56% as many newborn deaths occurred in 1978 as in 1968 (31,618 vs. 66,456). The total live births in the United States began to increase in the last few years of the decade with approximately 7% of deliveries resulting in a neonate weighing less than 2.5 kg. RDS was the leading cause of death during 9 of the 11 years analyzed, accounting for an average 19.5% of neonatal fatalities. The percent of all neonatal deaths attributable to RDS increased from 14.7% in 1968 to a maximum of 21.3% in 1974, before declining to17.5% in 1978. Although there was a modest male predominence in all major underlying causes of death identified, (male:female ratio = 1.35) a more striking discrepency exists in the sex distribution of deaths due to RDS (male:female ratio = 1.60). These data indicate that despite the declining incidence of fatal RDS the disorder accounted for an increasing percent of total deaths through the later part of the 11 year period. Prevention and/or improved management of asphyxia made the most significant (29%) contribution to reduced neonatal mortality rates. Asphyxia began the 11 year period accounting for 18.1% of all neonatal deaths, whereas in 1978 it only accounted for 9.3%. Less change occurred in fetal complications of pregnancy implying a continuing need for improved maternal/fetal care. These data have implications for future planning for perinatal care services, outreach education and financial allocations.

443 MECONIUM ASPIRATION SYNDROME: A PREVENTABLE DISEASE. Jeffrey J. Pomerance and John Kanegaye. UCLA School of Medicine, Cedars-Sinai Medical Center, Department of Pediatrics, Los Angeles, California.

In a review of the 7 year period between 7/1/74 and 6/30/81, the diagnosis of Meconium Aspiration Syndrome (MAS) was made in 63 of 31,423 infants (0.2%) born at Cedars-Sinai Medical Center (CSMC). Ventilatory support (VS) was required in 16, 4 of whom developed pneumothorax (PT). Another 14 infants developed PT, but did not require VS. One infant diagnosed as MAS died of apparent persistence of the fetal circulation. On autopsy, the lungs did not show meconium staining or aspiration of squamous cells.

In the same time period, 48 outborn infants with MAS were treated at CSMC. Twenty infants required VS. All 3 infants who developed PT were in this group. Seven infants died. Six of 15 outborn MAS infants died in the first 14 months of the study, while only 1 of 33 infants died during the next 70 months ($X^2_{YATES} = 8.5$; $p < 0.005$).

The factors responsible for the extremely low MAS mortality of infants cared for at CSMC are unknown. Since relatively few infants required VS or chest tube insertion, the role of Neonatal Intensive Care cannot receive major credit for outcome. It does seem that the pathophysiology of severe MAS is preventable or at least reversible by some combination of antepartum, intrapartum and immediate neonatal care. It is our impression that antenatal monitoring for fetal well-being, automatic intrapartum fetal heart rate monitoring, and constant availability of obstetric anesthesiologists and pediatric residents for neonatal resuscitation (automatic endotracheal suctioning for meconium stained amniotic fluid), play significant roles.

444 NON-SELECTIVE MEDIA IN PREDICTION OF EARLY ONSET GBS (EOGBS) DISEASE, Suma P. Pyati, Rosita S. Pildes, Norman Jacobs and Devyani Raval. Cook County Hosp. Dept. of Pediatr., Chicago, Ill.

Selective media have been generally used in studies of GBS colonization in neonates; attack rates among colonized (col) newborns vary from 1 to 8%. Since non-selective media are used routinely and are more readily available, we studied the value of this medium in detecting GBS diseased neonates. During a 52-month period, 1187 inborn neonates <2000gms were enrolled in a study of PEN Rx in EOGBS dis. Blood, throat and cord (T,C) cultures were taken on 994 infants (84%) within 1 hr of birth and before antibiotics. T and C swabs were inoculated directly onto non-selective medium (sheep blood agar plate). Sixty-six of 994 were col (+T&/C); 16/66 col had EOGBS dis. (bacteremia plus symptoms); 3/928 non-col infants had EOGBS dis. The attack rate among col infants found by non-selective media was 25% (16/66). Validity and predictive value of surface cultures using routine media in detecting disease is shown:

		T&/C Cultures +	T&/C Cultures -
Blood Culture	+	16	3
	-	50	925

Sensitivity=84%
Specificity=95%
+ predictive value=24%
- predictive value=97%

Non-selective media selectively identified col infants at birth who are at maximum risk for developing disease. Non-selective media, may therefore, be more useful than selective media in studies of prophylaxis or therapy of GBS in the newborn.

445 VERTICAL TRANSMISSION OF GROUP B STREPTOCOCCI (GBS) DURATION OF MEMBRANE RUPTURE IS NOT A FACTOR.
Joan A. Regan, Jeffrey Siracuse, Jane O'Neill and L. Stanley James, Columbia U., Coll. P&S, Div. Perin. Med., Dept. Ped., NY.

In a prospective study of 11,945 mothers at the time of admission for labor and delivery 12.4% were found to be GBS ⊕. 38% of the infants born to culture ⊕ mothers were colonized. 28 infants (2.3/1000 live births) developed early onset group B streptococcal disease (EOGBSD).

Time of membrane rupture (MR) as reported by the mother and or labor room staff was recorded for each patient. Patients in whom time of MR was uncertain were excluded; for the remaining 1099 colonized patients, incidence of infant colonization, non-colonization and disease were plotted against duration of membrane rupture at 2 hour intervals through 12 hours, then at 6 hour intervals to 24 hours and at 24-36 hours and >36 hours.

At no point in time of duration of MR was colonization among infants born to colonized mothers significantly increased. Only 18% of mothers whose infants had culture proven sepsis had membrane rupture for >24 hours.

This leads us to conclude that duration of MR among GBS ⊕ mothers does not increase the incidence of GBS colonization in their infants and leads us to speculate that factors other than duration of exposure to the pathogen predispose to infant colonization.

448 RUBELLA IMMUNITY IN OLDER PATIENTS IN A PEDIATRIC GROUP PRACTICE. R.G. Robinson, F.E. Dudenhoeffer, H.J. Holroyd, L.R. Baker, D.I. Bernstein, J.D. Cherry; Descanso Ped. Med. Group, LaCanada, Ca; and UCLA Sch. Med., Dept. Pediatrics, Los Angeles, Ca.

Because rubella continues to be a common illness in adolescents and young adults and because it has been suggested that booster rubella immunizations should be performed, we studied antibody prevalence in 459 predominantly adolescent patients. Of the total group 86.5% had antibody (PHA titer ≥1:13.5). Rubella antibody in documented previously immunized patients (89.6% of 386) was significantly more common than antibody in unimmunized patients and patients with a questionable history of immunization (70.3% of 74) ($p = <0.005$). Of 33 seronegative patients that we immunized all but 1 seroconverted (HAI titer ≥1:8). Of 23 with a documented history of prior immunization, only 1 had a specific IgM antibody response (determined by sucrose gradient separation and HAI antibody determination). In contrast 3 of 3 patients with a history of clinical rubella and 1 of 4 patients with a questionable history of past immunization had a specific IgM antibody response. Since 89.6% of previously vaccinated patients had demonstrable antibody and since 96% of those without measurable antibody had a secondary immune response following revaccination it seems likely that the level of protection in previous vaccinees is considerably greater than 90%. Because of this high degree of protection in vaccinated persons and the rarity of documented rubella vaccine failure, attention today should be directed at finding and immunizing unvaccinated teenagers and young adults and not in major unnecessary booster vaccine programs.

● **446** SEVEN YEAR EXPERIENCE WITH NECROTIZING ENTEROCOLITIS (NEC): ASSOCIATION WITH FEEDING. C. Joan Richardson, David K. Rassin and Michael H. Malloy. University of Texas Medical Branch (UTMB), Department of Pediatrics, Galveston.

The incidence of NEC among 27,540 inborn infants at UTMB has fluctuated markedly from 1974 to 1981. Attack rates per 1000 births were 1.9, 6, 1.3, 1.4, 4.1, 2.1, 0.9, and 5.6 in '74, '75, '76, '77, '78, '79, '80 and '81 respectively. Three formulas were used on a rotation basis in the nursery. Attack rates calculated by formula years were as follows:

Time Period:	9/74-8/75	9/75-8/76	9/76-8/77	9/77-8/78	9/78-8/79	9/79-8/80	9/80-8/81
Formula:	A	B	C	A	B	C	A
NEC Attack Rate per 1000:	6.9	2.4	0.5	4.8	2.3	0.7	4.0

By χ^2 analysis, NEC incidence in Formula A years was significantly higher and in C years significantly lower than expected based on total population. When attack rates for each formula year were combined for the same formula, differences among formulas were even greater. Occurrence of NEC was higher than expected during Formula A years ($p < 0.001$) and lower than expected during Formula C years ($p < 0.005$). These retrospective data indicate year to year variability in incidence of NEC and a strong association with type of formula in use in the nursery at that time. Further investigation with changes in order of formula use will be required to confirm the association between use of a particular formula and incidence of NEC.

449 LACK OF ROLE OF CHLAMYDIA TRACHOMATIS (CT) IN UPPER RESPIRATORY INFECTIONS (URI) OF CHILDREN. Venusto H. San Joaquin, Philip J. Rettig, and Melvin I. Marks. University of Oklahoma Health Sciences Center, Department of Pediatrics, Oklahoma City, Oklahoma.

Previous studies show progressive, age-related acquisition of antibodies to CT in children. The antecedent infection(s) causing seroconversion is unknown. Because of the observed association of CT with infantile pneumonia and conjunctivitis, we searched for the stimulus for this seropositivity among children with URI.

From November 1980 to November 1981, 164 children older than 6 months who presented to the Oklahoma Children's Memorial Hospital outpatient clinics for URI were cultured for CT. Patients who had received antibiotics within the past 7 days were excluded. Clinical presentations included coryza, nasopharyngeal congestion, cough, and sore throat with or without fever. Nasopharyngeal specimens were collected with calcium alginate swabs, placed in transport media, and kept at 4°C for 1-8 hours prior to freezing at -70°C, or prior to inoculation into cycloheximide-treated McCoy cells. Frozen specimens were inoculated, in most cases, within one week of collection. Eighty-eight females and 76 males were studied; 156 were ≤ 10 years. Twenty-one had otitis media, 10 had conjunctivitis. Sixty-two patients had pharyngeal cultures for group A streptococcus; 27 were positive. CT was not isolated from any subject. CT does not appear to be an important cause of URI in children. By Poisson distribution, a sample size of 156 has a 97% chance of yielding at least 1 positive culture if the incidence of CT-URI were 1/30 and 67% chance if the incidence were 1/100.

447 RETINOPATHY OF PREMATURITY (ROP) IN AN OUTBORN POPULATION BIRTHWEIGHT 501-1500 GM (LBW) 1975-1980. S.P. Riley, J.V. Aranda, E.W. Outerbridge, J. Little. McGill Univ-Montreal Children's Hospital, Montreal, Quebec, CANADA

The incidence of ROP in an outborn population of LBW survivors was determined for 1977-1980. Occurrence of ROP was compared to that previously reported in 1975-1976. In the 6 years, 1975-1980, 186/225 (82.3%) of LBW survivors were evaluated. ROP (active and/or cicatricial) was present in 57/186 (31%). The incidence of cicatricial disease (all grades) was 24% for all LBW infants but was 46% for infants <1001 gm. Eight children are visually handicapped (blind or visual acuity <20/200).

CLINICAL DATA	1975-1976		1977-1980	TOTAL
Infants admitted < 1501 gm	154		194	348
Survived to discharge	94		131	225
Ophthalmology evaluation(n)	80		106	186
Incidence of ROP(%)	27(34%)	NS	30(28%)	57(31%)
Cicatricial disease(%)	25(31%)	p< .05	19(18%)	44(24%)
Cicatricial grade II or more(%)	8(10%)	NS	6(5.7%)	14(7.5%)
Visual handicap(%)	5(6.3%)	NS	3(2.8%)	8(7.5%)
Cicatricial disease -				
501-1000 gm	11/22(50%)	NS	7/17(41%)	18/39(46%)
1001-1500 gm	14/58(24%)	NS	12/89(14%)	26/147(18%)

The incidence of cicatricial disease was significantly decreased in the LBW population as a whole in 1977-1980. However, the risk for the smallest infants (501-1000 gm) has not changed since 1975.

450 PREVALENCE OF YERSINIA ENTEROCOLITICA (YE) ANTIBODIES IN CHILDREN. Venusto H. San Joaquin, Jimmie Y. Newton, David F. Welch, and Melvin I. Marks. University of Oklahoma Health Sciences Center, Department of Pediatrics, Oklahoma City, Oklahoma.

YE infection is well recognized worldwide but only infrequently described in the USA. Serotype O:8 is, reportedly, the predominant US strain in contrast with O:3 & O:9 in Canada and Europe, respectively. Efforts to isolate YE in 3,000 stool specimens submitted to our laboratory during the past year have been unrewarding. We tested the sera of 643 children, ages 1-15 yrs., for antibodies against YE O:3, O:8, & O:9 - the serotypes commonly responsible for human yersiniosis. Formalin-inactivated organisms, suspended in saline to McFarland #1 density, were used as antigens in a tube agglutination test. A reciprocal titer of 40 or higher was considered positive. Sixty-two (9.6%) of 643 were seropositive - 42 (6.5%) to O:3, 18 (2.8%) to O:8 and 4 (0.6%) to O:9. Two had titers against 2 serotypes. Titers ranged from 40 to 320. Antibodies to O:3 were observed from infancy through adolescence with comparable frequency whereas antibodies to O:8 and O:9 were not seen before age 4 and 8 years, respectively.

These sero-epidemiologic data suggest that, in Oklahoma: 1) YE infection may be more prevalent than reports indicate, 2) humoral antibody to serotype O:3 is more common than to O:8, 3) subclinical or clinical experience with YE other than gastrointestinal infection, or with YE-related antigens, may be responsible for the observed seropositivity.

451 BACTERICIDAL ANTIBODY TO ANTIGENICALLY DISTINCT NONTYPABLE STRAINS OF *Haemophilus influenzae* ISOLATED FROM OTITIS MEDIA. Paul A. Shurin and Colin D. Marchant. Case Western Reserve Univ. Sch. Med., Cleveland Metropolitan Gen. Hosp., Dept. of Pediatrics, Cleveland, Ohio.

Nontypable strains of *Haemophilus influenzae* were obtained from middle-ear exudates of children with otitis media. Two strains (BCH-37567 and H-Pr) were shown to have different antigenic determinants of complement-mediated killing by immune rabbit sera. Rabbit antisera to these isolates contained bactericidal antibody in varying titer to additional strains of a small collection. Each of six otitis media isolates cross-reacted with one or both of the two test strains. Circulating antibody in humans may protect against middle-ear infections caused by these bacteria. Sera of healthy humans were assayed for bactericidal antibody directed against strains BCH-37567 and H-Pr. Specific absorption of human sera with bacterial cells showed human antibody to be directed against strain-specific surface determinants. The importance of IgM in the bactericidal reaction of human serum was indicated by failure of bactericidal antibody to cross the placental barrier in most cases and by the susceptibility of this antibody to reduction by 2-mercaptoethanol. The distribution of antibody by age was similar for the two strains. Antibody was not detectable in most cord sera or in those of young infants but had developed in most subjects by two years of age. Thus, prevalence of bactericidal antibody to each of the test strains was inversely correlated by age with the period of greatest susceptibility to otitis media.

● **452** THE INFLUENCE ON ICU NEONATE INFECTION RATE OF INDIVIDUAL ORGANISMS AS COLONIZERS. K. Sprunt, W. Redman, G. Leidy. Dept. Pediatrics, Columbia University, College of Physicians & Surgeons, New York, N.Y. 10032.

An unexpected decrease in infection rate in ICU neonates was investigated. We reported that infection in our ICU occurs in 15-20% of infants with high titer abnormal bacterial colonization of the pharynx. 50-60% of those given antibiotics (during and/or after Rx) and 8% of those not so treated were abnormally colonized. Infection occurred rarely in infants with "normal" flora (∝-streptococci predominant).

Investigation of the decrease in infection rate in 1980 showed that (1) infection occurred in infants with technically "normal" flora (∝-strep predominant) who carried S. aureus in appreciable but not dominant concentrations in the pharynx. There were 20 infants in this culture category: 4 developed sepsis with S. aureus, a 20% infection rate in this subgroup with "normal" flora. (2) 129 abnormally colonzed infants had an infection rate of 5%. Breakdown of data showed that 109 of the 129 were abnormally colonized by S. epidermidis with an infection rate of 1.8%. The infection rate of the remainder (20) who abnormally colonized by all other organisms was in the expected range 20%. It is not necessarily abnormal colonization per se which influences the infection rate. Persistence of some strains as nursery colonizers may alter the findings considerably. The definition of "normal"flora requires modification to include the exception presented by S. aureus colonization.

● **453** VARICELLA-ZOSTER IN HOSPITAL PERSONNEL: SKIN TEST REACTIVITY TO MONITOR SUSCEPTIBILITY. Russell W. Steele, Mary A. Coleman, Robert Bradsher. Depart. of Pediatrics and Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas

An outbreak of chickenpox, including three patients and one nurse on a pediatric ward, necessitated rapid identification of susceptible employees in conjunction with standard epidemiologic intervention in order to prevent spread to other high-risk patients. Fifteen of 46 hospital personnel (33%) gave a negative or unknown history of prior disease. Response to a varicella-zoster (VZ) skin test was compared to antibody determination as measured by fluorescent antibody to membrane antigen (FAMA). Correlation of these two screening methods was absolute. Four of 46 hospital personnel (9%) were susceptible to infection (negative skin test and antibody < 1:4) requiring their removal from the ward. All with positive histories for prior disease with the virus and 11 of 15 (73%) with negative or unknown histories were immune as indicated by both tests. A readily available VZ skin test would be an extremely useful epidemiologic tool for screening hospital personnel.

454 SUDDEN INFANT DEATH (SIDS): ASSOCIATION WITH DPT IMMUNIZATION. Wm. C. Torch (sponsor, Burton A. Dudding), U of Nevada, School of Medicine, Dept. Pediatrics, Reno

Because of recent reports of DPT-associated SIDS and familiarity with 5 cases of sudden death in 4 infants and a 3 yr. old, 3-5 to 20 hr after vaccination, the immunization, clinical and autops records of 70 of over 200 SIDS cases reported in Nevada and surrounding States in the past 5 years were analyzed. 48 infants had received one or more DPT immunizations prior to death (DPT-SIDS); 22 had received none (n-DPT-SIDS). Mean age of DPT-SIDS at death was 4.5 mo; of n-DPT-SIDS, 2.3 mo. Age-frequency analysis at deatl showed a single peak at 2 mo. of age in the n-DPT-SIDS group, and a biphasic peak at 2 and 4 mo. in the DPT-SIDS group. The distribution of SIDS cases following DPT #1, 2, 3 & 4 was 32:11:4:1. SIDS was not sexually related in either group. Although n-DPT-SIDS clustered during the Fall-Winter months, DPT-SIDS was non-seasonal. Obvious clustering of DPT-SIDS occurred within the first three post-vaccinal weeks: 6.5% died within 12 hr of immunization, 13% within 24 hr, 26% within 3 d., and 37%, 61%, and 70% within 1, 2, and 3 wl respectively. Such clustering occurred irrespective of the DPT dose received. In both groups death occurred most often in sleep, in healthy, allergy-free infants following brief periods of irritability, crying, lethargy, upper respiratory tract symptoms and sleep disturbance. Autopsy findings typical of SIDS (pulmonary and thymic hemmorhage and petechia, pneumonitis, vascular congestion, brain edema) were seen in both groups. In conclusion, DPT immuniza tion is a major associated and possible causally related factor in SIDS. Modification of current immunization practices may be indicated if further epidemiological studies continue to link DPT to SIDS

● **455** FAILURE OF SEROCONVERSION FOLLOWING MEASLES, MUMPS, RUBELLA (MMR) VACCINE. IS THE PROBLEM VACCINE OR SEROLOGY? Kristen Weigle, M. Dianne Murphy, Elaine Cobb, Philip A. Brunell. Dept. of Pediatrics, Univ of Tex Health Science Center, San Antonio, Texas.

It has been suggested that the efficacy of MMR vaccine in "routine" use is less than reported in initial vaccine trials under "experimental" conditions. To test this hypothesis a group of 301 children who had received their routine immunization in their physician's office or health clinic, between 15 and 26 months of age, were bled 2-21 months after immunization. All serologic tests were standardized such that sera obtained from 50 children 15 months of age who had not had MMR or MMR vaccine were identified as susceptible. Sera from 20 health care workers over 30 years of age were "immune" controls. It was found that 12.3% of vaccinees and 2 of 20 adults had mumps neutralizing antibody (NA) of <1:2. Only 0.3% of vaccinees and none of the adults had rubella HAI antibody of <1:8. 5.3% of vaccinees and 2 of 20 adults had measles HAI antibody titers of <1:5. Using a more sensitive plaque reduction NA assay, only 1.6% of vaccinees and no adults had measles antibody of <1:10. At a single site where vaccine handling was observed to be inadequate, the failure rate for measles was about three times that found at other sites. It would appear that in acceptable "routine" use there is no problem with rubella or measles vaccine. There may indeed be a problem with mumps vaccine.

456 DRUG INGESTION IN PREGNANCY: INITIAL FINDINGS OF A STUDY DURING ALL THREE TRIMESTERS. T Wells, J Naisbit, & P Gardner, (Spon. by L. Glasgow). Utah Dept. of Health and Dept. of Pediatrics, University of Utah, Salt Lake City

Following identification of Thalidomide as a teratogenic agent numerous studies to determine not only the drugs women take during pregnancy but which drugs might cause congenital anomalies have been done. Most have been retrospective using chart reviews or questionnaires during the postpartum period. The current study represents an attempt to do a prospective study and to obtain the pattern of current drug usage by pregnant women in Utah. Questionnaires were randomly distributed by the Utah M&I project and private obstetricians to 3500 women in all trimesters of pregnancy. To date nearly 900 questionnaires have been returned. Though the largest group (65%) responding were in the 3rd trimester many were in the 1st and 2nd trimester. The questionnaire requested prescribed, over the counter and social drugs. Although we concluded that the data appears to be consistent with that of earlier studies by Hill, Forfar, and Peckham there are differences. Acetaminophen has replaced aspirin (50% vs 13%) as the most common OTC drug other than vitamins and iron. Antacid and analgesic usage was higher in early rather than late pregnancy. Diuretic consumption dropped (32% to 1%). Lastly, alcohol and nicotine consumption appear to have a much lower incidence in these women. Whether these differences represent a more accurate picture of drug ingestion by women during pregnancy or whether they can be attributed to medical practice and population differences is as yet unclear. Further analysis of data plus a review of birth and death certificates to determine the incidence of various congenital anomalies is planned.

GASTROENTEROLOGY AND NUTRITION

457 CYSTIC FIBROSIS: (CF) COMPENSATORY ROLE OF LINGUAL LIPASE IN GASTRIC AND DUODENAL FAT DIGESTION. Cynthia K. Abrams, Margit Hamosh, Van S. ıbbard, Sudhir K. Dutta and Paul Hamosh. Georgetown University edical Center, Washington, D.C.; Univ. Maryland Hosp.; and ıtional Institutes of Health, Maryland. (Spon. by J.W. Scanlon.)

Fat digestion starts in the stomach with the action of lingual lipase .L), an enzyme that hydrolyzes long chain triglycerides (TG) at ł optimum 4.0 - 6.0. We have investigated whether LL is active in ? by quantifying LL activity in gastric (GA) and duodenal aspirates)A) of 6 patients with exocrine pancreatic insufficiency (no detecble trypsin). GA and DA were collected after an overnight fast and . activity measured by hydrolysis of tri ^{3}H olein.

	pH	Lipase Activity (TG hydrolysis nmol FFA/ml/min)		
		pH 4.2	pH 5.4	pH 8.1
A	4.60±0.3	271 ± 45	286 ± 56	47 ± 14
A	4.80±0.3	231 ± 70	137 ± 59	10 ± 6

he data show that: 1) enzyme activity in GA and DA has the characeristics of LL; 2) The pH of GA and DA differs markedly from normal alues (3.5 ± 0.3 and 7.0 ± 0.2 respectively); 3. LL is higher in GA f CF patients than in normal controls (230±40 nmol/ml/min at pH 5.4) . Considerable amounts of LL are found in the duodenum. The ata indicate that: 1. The lingual serous glands are not affected by F; 2. because of high pH in GA and low pH in DA, LL activity reains high both in the stomach and intestine; 3. LL compensates for ow pancreatic lipase in CF. (Support NIH Grant AM 26641.)

458 LIVER DEPENDENT CLOTTING FACTORS AND TOTAL PARENTERAL NUTRITION (TPN) HEPATITIS IN NEONATES RECEIVING TPN. David H. Adamkin, Shirley A. Wilkerson, Paula ıdmacher, Rosemary Morris, (Sponsored by Billy F. Andrews), ıiversity of Louisville, School of Medicine, University Hospital, ;partment of Pediatrics. Louisville, Kentucky.

Sixteen premature neonates ranging in gestational age from ı-35 weeks and weighing between .64-2.4kg whose diagnoses ·ecluded enteral feedings where maintained on TPN for a minimum of) days. Growth, calories, fluid volumes, liver dependent clotting ıctors and liver enzymes were evaluated serially.

Mean caloric intake increased from 44Kcal/kg/d to .Kcal/kg/d over the four week study period. Fluid intake for .l patients decreased while overall body weight increased ıroughout the study period.

Liver dependent clotting factors, (II, VII, IX, X) were ›rmal throughout the study period including those neonates with .evated liver enzymes and/or TPN hepatitis.

Abnormal values for liver enzymes (SGOT, SGPT) were not ;eful in predicting which neonates would eventually develop TPN ;patitis (direct bilirubin >2.2mg%). Although those enzymes ;re frequently elevated in patients with elevated direct bilirubin ılues.

Three neonates (18.7%) developed TPN hepatitis. The mean ıration of TPN for the 13 neonates who did not develop ;patitis was 16.2 days; while 41.7 days was the mean for those ıat did. Mean time to onset of hepatitis was 22.3 days.

In summary, premature neonates maintained on TPN exhibit ›rmal synthesis of liver dependent clotting factors.

459 INTESTINAL $^{45}Ca^{2+}$ TRANSPORT IN IUGR RAT PUPS. M. Loghman-Adham, M. Ocampo, E.S. Moore. Pritzker Sch. Med., Univ. Chicago, Michael Reese Med. Ctr., ;pt. Peds., Chicago, IL

Bone mineralization in low birth weight (LBW) human infants ; significantly less than that demonstrated to occur in utero. ıese infants often develop metabolic bone disease (MBD) despite ıpplemental vitamin D. To test the hypothesis that MBD in LBW ıfants may be due to difference in intestinal Ca^{2+} absorption, ; studied gut Ca^{2+} transport in intrauterine growth retarded ıt (IUGR) pups. A uterine artery was ligated or sham ligated ;ontrols) on the 17th day of gestation in pregnant Sprague-ıwley rats. After normal delivery, the rat pups were equally .stributed among the dams. At age 3 days, pups were sacrificed ıd 2 cm slices of duodenum (Duo), jejunum (je), ileum (Il) and ›lon (Co) were incubated with $^{45}Ca^{2+}$. Values are mean and ± ;M.

)GR	Weight	Duo^{+}	Je^{+}	Il^{+}	Co^{+}
;.0 mg	5.10*	12.6	13.6	14.2	28.7
:11	±.17	±1.7	±1.7	±1.4	±8.9
1-8 mg	7.02*	12.5	14.8	12.2	54.7
:19	±.4	±1.3	±1.1	±1.0	±11.2
›ntrols	8.68	12.3	12.4	12.7	37.5
:11	±.10	±0.7	±1.1	±1.1	±3.5

ım Ca/mg prot/30 min x 10^{-3}; * = $p<.001$ compared to controls. ı both IUGR and control pups, $^{45}Ca^{2+}$ uptake was greatest in the ›lon and there was no difference among the groups. These data ıdicate that decreased Ca absorption is not present at age 3 ›ys in IUGR rat pups.

460 INTRACTABLE DIARRHEA SYNDROME: NUTRITIONAL FACTORS IN RECOGNITION AND ETIOLOGY. Phyllis F. Agran, Richard K. Mathis (Spon. by Beverly C. Morgan), Coll. of Med., Univ. of Calif., Irvine, Dept. of Peds., Irvine, CA.

Nutritional failure is implicated in the etiology of intractable diarrhea syndrome (IDS) following an acute diarrheal illness. Eleven patients (6 wks to 31 mths.) developing IDS were evaluated by history, nutritional assessment, stool studies, stool volumes, electrolytes, small intestinal biopsy. Mean number of days (outpatient plus inpatient) between onset of illness and provision of caloric intake greater than 100 kcal/kg was 26. Nutritional deficiency was identified in 91% of the patients. The serum albumin was less than 3.0 mg% in 50% and less than 3.5 mg% in 80%. Mean stool volume was 78 gm/kg/24 hr; mean stool sodium was 93 mg/L. Stool studies for pathogens were negative. 100% had a moderate to severe non-inflammatory villous-crypt lesion. Nutritional correction was the primary mode of therapy; greater than 100 kcal/kg/24 hr was required for a mean of 25 days. Refeeding was successful in 100% using an elemental formula by continuous nasogastric infusion. Factors have been identified which place patients at increased risk for the development of IDS: 1) prolonged history of illness with inadequate caloric and protein intake; 2) ratio of actual:ideal weight <.09; 3) serum albumin less than 3.5%; 4) fasting stool volume greater than 35 gm/kg/24 hr and stool sodium greater than 65 meq/L. Nutritional failure following acute diarrhea was the major identified cause of IDS. Early identification employing these risk factors and nutritional management should interrupt the cycle of progressive malnutrition and diarrhea and should decrease duration of illness.

461 SUPPRESSOR/HELPER T-CELLS IN CHILDHOOD LIVER DISEASE. Joel M. Andres and Douglas J. Barrett (Spon. by Martin L. Schulkind). University of Florida College of Medicine, Department of Pediatrics, Gainesville.

Abnormal immunoregulation may contribute to the pathogenesis and progression of liver disease in children. Utilizing a pokeweed mitogen (PWM)-driven lymphocyte culture technique we evaluated suppressor and helper T-cell regulation of B-cell function in children with various forms of liver disease. Different combinations of B-cells and T-cells from patients and controls were co-cultured in the presence of PWM and the cell culture supernatents were harvested and assayed for IgG. Lymphocytes from 4 patients with hepatocellular cholestasis were evaluated; two of the 4 showed suppression of IgG at 40 and 25% of expected IgG production (BnTnTp)* compared to normal controls of 132±77% (M±SD for $BnTn_1Tn_2$). Neither suppression nor enhancement of immunoglobulin synthesis occurred in the other 2 children. Three patients with hypoplasia or paucity of bile ducts showed normal T-cell function, but B-cells were unresponsive to normal regulatory influences with 60, 30, and 34% of expected IgG levels (BpTn-irradiated) compared to normals of 162±70% (M±SD for BnTn). Another patient in this ductal cholestasis group had biliary atresia and diminished T-helper function with only 26% IgG (BnTp) while one other infant with biliary atresia had normal B and T-cell function. The results suggest that host immunoregulatory mechanisms may be potentially important in the recovery from acute hepatitis and in the perpetuation of chronic liver disease in children.

*Bn = normal control B cell, To = patient T cell

462 INEFFICIENT DETOXIFICATION OF BILE ACIDS MAY PREDISPOSE TO CHOLESTASIS. William F. Balistreri, Linda A. Zimmer, Frederick J. Suchy, Kevin E. Bove. Children's Hospital Research Foundation, Cincinnati, Ohio.

Lithocholate is an hepatotoxic endogenous bile acid which may play a role in neonatal cholestasis. Our aim was to observe postnatal changes, as well as the effect of lithocholate administration, on the presumed detoxification pathway-sulfation via "sulfotransferase" (ST). Pregnant rats were fed a standard chow diet containing either 0% (control), 0.5% (LOW) or 2.5% (HIGH) lithocholate; the diet was continued after birth. Liver and serum was obtained from dams and pups (fetal-21st d, 1,2,3 and 4 wks old). In controls, there was a progressive increase in hepatic ST activity from fetal (4.5 ± 1.7 pmoles/mg prot/min, $\bar{x}$ ± SEM) to 3 wks of age (59.0 ± 4.2) followed by a decline to adult levels (38.1 ± 3.2). In rats > 3 wks old, ST was 2-3 times higher in females. There was no detectable (by RIA) sulfated lithocholate in control serum at any age. Administration of lithocholate caused dose-related alterations in intrahepatic bile ducts (cholangitis, ductular proliferation); lesions were much less prominent in fetuses. There was a concomitant dose-related elevation in sulfated lithocholate in serum (LOW = 0.3 μM in fetus, 0.8 μM in 4 wk old; HIGH = 1.2 μM in fetus, 7.0 μM in 4 wk old). Despite marked structural and functional alterations, there was no significant increase in ST at any age. Conclusions: 1) Age and sex-related differences in ST activity are unaltered by substrate ingestion; relative inefficiency of detoxification allows initiation of bile duct injury. 2) The fetal liver may be transiently protected from hepatic injury by placental transfer of bile acids.

463 ABNORMAL RECTAL AND SIGMOID SENSATION IN CHRONICALLY CONSTIPATED CHILDREN (PTS). Vera A. Loening-Baucke and M. Kabir Younoszai. The University of Iowa Hospitals and Clinics, Department of Pediatrics, Iowa City.

Chronic constipation may be caused by abnormal rectal (r) and sigmoid (s) sensation. R and s sensation were studied initially in 18 Pts and in 18 healthy children (C) 4-12 years old. At 1 year after initiation of treatment with milk of magnesia, 3 Pts did not comply and were not studied, 8 recovered (Rec), and 7 still required medication (ØRec). A latex balloon (2.5x3 cm) was placed 11 (r) and 20 (s) cm and the strain gauge 1 cm above the anal verge. We measured the smallest volume (ml) of r and s distension necessary to cause a passing sensation of balloon distension (SV) by transiently inflating the balloon, a constant relaxation of the internal anal sphincter (CR) and a persistent urge to defecate or pain by filling the balloon stepwise in increments of 30 ml/2 min (CV). Mean ± SD of SV, CR, and CVs are given below. Only CR and CVs were significantly lower in untreated Pts than in C ($p<0.05$)*. In the follow-up studies of the 8 Rec and the 7 ØRec, CR and CVs remained significantly lower. These findings suggest that in Pts a normal fecal bolus does not cause a sensory stimulus for defecation even in patients who recovered.

	rSV	rCR	rCV	sCV
C (18)	19±9	108±44	123±29	113±30
Pts: Initial (18)	23±16	158±67*	220±94*	210±95*
12 mo. Rec (8)	15±10	176±79*	185±54*	191±58*
12 mo. ØRec (7)	17±10	227±107*	253±64*	223±60*

464 PLASMA AND ERYTHROCYTE AMINO ACID LEVELS IN NEWBORN INFANTS RECEIVING PARENTERAL SOLUTIONS WITH AND WITHOUT GLUTAMATE AND ASPARTATE. Edward F. Bell, Lewis D. Stegink and L.J. Filer, Jr. University of Iowa, Department of Pediatrics, Iowa City, Iowa.

Plasma, erythrocyte, and urine amino acid levels and nitrogen balance were measured in 8 infants (age 1-63 d, wt 1.2-2.8 kg) receiving no enteral feedings, while on 3 different parenteral feeding regimens. Each infant was studied after 3 days on each regimen: dextrose only (D); dextrose, lipid emulsion, and Travasol[R] (T); and dextrose, lipid emulsion, and Neopham[TM] (N). Neopham[TM] (Cutter) is a new amino acid solution containing glutamate (7.1 g/L), aspartate (4.1 g/L) and cystine (1.0 g/L), in addition to the other amino acids present in Travasol[R]. Free amino acid levels in plasma, erythrocytes, and urine generally reflected the composition of the solutions. Of particular interest were these results (mean, *P<0.05 T vs N):

	Plasma (μmol/dl)			Erythrocytes (μmol/dg)		
	glutamate	aspartate	glycine	glutamate	aspartate	glycine
D	5.0	1.9	26.7	43.4	11.9	47.5
T	6.7*	2.7	66.0*	52.6	16.1	96.3*
N	8.7	3.4	29.8	60.8	18.2	61.1

Although amino acid intake was the same (2.0 g/kg/d), nitrogen intake was higher on T (758 vs 661 mg/d). Nitrogen balance (intake - urine excretion) was higher on T (430 mg/d) than on N (347 mg/d), but nitrogen retention (balance/intake) was similar; T 58%, N 52%. The glutamate and aspartate provided by Neopham[TM] did not produce levels of plasma or erythrocyte free amino acids in excess of postprandial values in these infants.

● **465** HEPATIC DEVELOPMENT AND THE ^{14}C-AMINOPYRINE AND ^{14}C-METHACETIN BREATH TESTS. Stuart Berezin, Saidee Ling, John B. Watkins, Peter D. Klein. Div. of Gastroenterology and Nutrition and Div. of Pharmacology, Dept. of Ped., Univ. of Pa., Sch. of Med., Phila., PA and Stable Isotope Laboratory, Baylor School of Medicine, Houston, TX.

Hepatic function, assessed by the N-Demethylation of aminopyrine (AP) and methacetin (ME) may now be accomplished at high precision without radiation hazard, using non-invasive breath tests and ^{13}C isotopically-labelled, stable substrates. To extend these diagnostic capabilities to infants and children, we have studied in the rabbit the influence of postnatal age on hepatic function, using a closed system for quantitatively trapping $^{14}CO_2$ after an IV or IP dose of ^{14}C-AP or ^{14}C-ME. The dose-response was determined for 0.5 to 5mg/kg at 0-10, 11-23, 24-30 and> 30 days of age; the linear response was exhibited at 2mg/kg ME and 5mg/kg AP. A steplike increase in metabolism of both AP and ME was seen, showing earlier and higher $^{14}CO_2$ peak values and a 10-fold increase in the percent dose excreted at 40min. occurred for both ME and AP at weaning (≅ 23 days). N-demethylation of ME and AP exhibit developmentally-related increases with marked changes at the time of weaning. Thus, quantification of hepatic function in children must include consideration of developmental changes. This may be safely facilitated by the use of non-radioactive ^{13}C-tracers in normal children as well as those with liver disease.

466 PARENTERAL NUTRITION PROMOTES RISK OF CHOLELITHIASIS IN CHILDREN. William E. Berquist, Henry A. Pitt, Linda L. Mann, Marvin E. Ament, Hooshang N. Kangarloo, Lawrence N. DenBesten. UCLA Departments of Pediatrics, Surgery and Radiology, Los Angeles.

Increasing rates of acalculous cholecystitis and cholelithiasis have been observed in adults on prolonged total parenteral nutrition (TPN). From our patients receiving prolonged parenteral nutrition we evaluated 18 children (10 males) age 4 to 90 months for the presence of gallstones (GS) by abdominal ultrasound (17/18) or at laparotomy (1/18). Their diagnosis at time of gallbladder evaluation included severe short bowel syndrome (9/18), chronic idiopathic pseudo-obstruction syndrome (CIPS) (5/18), or intractable diarrhea (4/18). The duration of parenteral nutrition prior to evaluation varied from 4 to 79 months with mean of 24 months. Mean SGPT value at evaluation was 97±17 IU/L (mean ± SE), normal (N) < 45, alkaline phosphatase was 422±65 IU/L (N < 210) and total bilirubin was 1.6±.5 mg/dl (N < 0.8). 6/18 (33%) of children were found to have GS compared to 0.1% of an autopsy age and sex matched incidence of GS. Of the children with GS, 2 were female with CIPS on TPN for greater than 4 years each and 4 were male with SBS all on TPN greater than 10 months. One patient was found to have calcium bilirubinate stones at cholecystectomy. Of four autopsied children (three male) age 5 to 23 months on TPN 5 to 21 months, one was found to have GS. These findings indicate the need for periodic screening for GS by ultrasound of patients requiring prolonged TPN. Presence of GS may result from prolonged fasting or the primary illness requiring TPN and may contribute to TPN related liver disease.

● **467** ROLE OF ENDOGENOUS GASTRIN IN MEDIATING COLOSTRUM-STIMULATED GUT GROWTH. Carol Lynn Berseth, Lenard M. Lichtenberger, Henry S. Bayley, and Frank H. Morriss. Univ. of Tx. Med. Sch. at Houston, Depts. of Ped. and Physiol., Houston, and Univ. of Guelph, Dept. of Nutr., Guelph, Ont.

Suckled newborn animals experience more rapid postnatal growth of small intestine mucosa than do control animals fed water, formula, or mature milk. Investigations with fibroblast cell cultures suggest that this effect is produced by epidermal growth factor in colostrum. To determine whether endogenous gastrin, a hormone known to be important in GI growth, is involved in colostrum-induced small intestine growth, we measured serum gastrin concentrations and antral and duodenal tissue gastrin concentrations in littermate newborn dogs that were suckled (S), hand-fed expressed bitch colostrum (C), or hand-fed Esbilac[R], a synthetic formula (E), from birth to sacrifice at 48 hr. Results:

Regimen	Serum Gastrin, fm/ml			Gastrin, μg/g, @48hr		Wt. Sm. Intest, g
	(n)	Birth	24 hr	48 hr	Antrum	Duodenum	
S	(8)	45±7*	279±83	136±39	-	-	-
C	(9)	32±7	362±35	147±59	2.91±0.47	0.30±0.09	15.3±0.8
E	(12)	27±3	49±16	37±8	2.80±0.34	0.26±0.07	10.7±0.5
p (CvsE)		NS	<0.005	<0.025	NS	NS	<0.005

Conclusions: (1) Postnatal hypergastrinemia requires colostrum feedings. (2) Colostrum promotes 6-fold greater serum gastrin levels of synthetic formula in the first 48 hr; gastrin levels in the tissues of origin are not different, suggesting increased production and release of gastrin. (3) Colostrum-stimulated small intestine growth involves enhanced endogenous serum gastrin levels. (Supported by P01 HD 13021 and R01 AM 20686). *$\bar{x}$±SE

468 RIBOFLAVIN-INDUCED PHOTODEGRADATION OF AMINO ACIDS (AA) IN PARENTERAL SOLUTIONS. Jatinder Bhatia, L.D. Stegink and Ekhard E. Ziegler. University of Iowa, Department of Pediatrics, Iowa City, Iowa 52242.

Previous studies have suggested that phototherapy decreases AA concentrations when vitamins are present. Riboflavin (R) is a known photosensitizer. The effect of phototherapy on AA concentrations in the presence and absence of added R was determined in parenteral solutions under simulated clinical conditions. The parenteral solutions (n=6; 2 g AA and 10 g glucose/dl), with and without added R (1 mg/dl), were infused for 24 hours through IV tubing placed in a heated incubator exposed to phototherapy and collected into light-shielded bottles. The infusion rate used (4 ml/hr) would provide a 1 kg infant with 1.92 g AA and 1 mg R per day. Phototherapy, delivered via day light bulbs, provided a mean irradiance of 5.1 $\mu W/cm^2/nm$ at the level of the tubing in the incubator. The mean (±SD) AA concentrations were:

AA Conc. (mM)	CONTROL (-R) PRE	CONTROL (-R) POST	EXPERIMENTAL (+R) PRE	EXPERIMENTAL (+R) POST
Methionine	5.48 ± 0.60	5.20 ± 0.61	5.69 ± 0.83	4.33 ± 0.76*
Tryptophan	1.71 ± 0.14	1.62 ± 0.13	1.40 ± 0.26	0.96 ± 0.11*
Tyrosine	0.69 ± 0.15	0.67 ± 0.07	0.71 ± 0.14	0.60 ± 0.11*

*$p < 0.05$ between pre and post samples

Proline, glycine, valine and R concentrations were also significantly reduced after exposure to phototherapy (+R). No significant change in pH was noted. The data suggest intravenous solutions of amino acids containing R should be protected from phototherapy light.

469 IS ENDOSCOPY OF BENEFIT IN THE DIAGNOSIS OF ESOPHAGITIS IN CHILDREN?

J. Biller, H. Winter, R. Grand. Harvard Medical School, Children's Hospital Medical Center, Division of Gastroenterology, Boston, MA

Previous studies in adults have reported a correlation between endoscopic appearance of the esophagus and biopsy proven esophagitis; a similar relationship has not been established for pediatric patients. Accordingly, we compared results of esophagoscopies and biopsies in 114 patients, ages 8 mos to 18 yrs (mean, 12 yrs, 61 males and 53 females) evaluated for acid reflux. Endoscopic diagnosis of esophagitis depended upon presence of erythema, granularity, friability, ulceration, pallor, edema or plaques. Esophagitis on biopsy was defined as presence of either intraepithelial eosinophils/neutrophils or basal zone hyperplasia.

RESULTS:

		Endoscopic Diagnosis	
		Normal	Esophagitis
Biopsy Diagnosis	Normal	20	44
	Esophagitis	7	43

Of 50 patients with biopsy-proven esophagitis, 43 had endoscopic abnormalities (sensitivity, 86%, p = 0.03). Of 64 patients with normal esophageal biopsies, only 20 were found to be normal on endoscopy (specificity, 31%). There were 69% false positives and 14% false negatives. Endoscopically, friability correlated best with biopsy-proven esophagitis ($p<0.05$); ulceration was an infrequent finding (11%). We conclude that endoscopic evaluation for esophagitis in children is not specific,and the diagnosis must be made histologically. Suction biopsies in conjunction with studies of acid clearance are therefore the most efficient approach to the diagnosis of esophageal inflammation in children.

470 ENCEPHALOPATHY IN CHILDREN WITH NORMAL HEPATIC FUNCTION AND PORTAL VEIN OBSTRUCTION

Mark C. Blaufuss, James P. Keating, Richard J. Bower, Blaise F. D. Bourgeois and Jessie L. Ternberg. Washington University School of Medicine, St. Louis Children's Hospital, Department of Pediatrics & Surgery, St. Louis, Missouri.

Portosystemic encephalopathy (PSE) may complicate portocaval shunt procedures in children with extrahepatic portal hypertension (EHPH) more frequently than is generally recognized. Reviews including over 400 children with EHPH fail to mention this complication.

We observed two children with EHPH who suffered recurrent episodes of severe variceal hemorrhage culminating in the creation of emergency surgical portocaval shunts (PCS) at seven years of age. Both patients developed an encephalopathy in the post-operative period. Agitated delerium, pupillary dilation, axterixis, hyperventilation and extensor posturing came and went in a sequence typical of PSE. By the fifth day after the creation of the shunts, after oral neomycin and purgation, the children recovered fully. Hyperammonemia was documented in both (273 & 314 ug/dl); blood ammonia prior to surgery and after surgery was normal ($<$ 60 ug/dl). Serum transaminase, bilirubin, albumin, liver biopsy and coagulation studies were normal in both patients on numerous occasions before, during and after the episodes of PSE. Serum glucose and arterial oxygen were normal.

Portosystemic encephalopathy should be anticipated in children undergoing PCS, even in the absence of cirrhosis. Voorhees has observed neuropsychiatric disturbances years after the creation of PCS in children with EHPH suggesting that a chronic form of PSE may also occur in such children.

471 TRACE MINERALS IN CHILDREN WITH BILIARY ATRESIA

Linda S. Book, Larry Eggert, Michael Matlak. (Spon. by Lowell Glasgow) University of Utah Medical School, University of Utah Medical Center, Department of Pediatrics, Salt Lake City.

Abnormal absorption, metabolism, or excretion of minerals may occur in cholestatic liver disease which could result in either mineral deficiency or excess. In 11 patients ages 6 months to 4 years who had had the Kasai procedure for biliary atresia, trace minerals were measured every 3 to 6 months. Plasma and red blood cell levels of magnesium (Mg), zinc (Zn), copper (Cu), manganese (Mn), were determined using atomic absorption spectrophotmetry. Values were compared to healthy age-matched controls.

	RBC level ± SD			Plasma level ± SD		
	Controls n=150	Patients n=11	P Value	Controls n=150	Patients n=11	P Value
Mg(mg/dl)	5.8±1.1	6.2±1.3	NS	2.3±.8	2.4±.6	NS
Cu(µg/dl)	100±15	89±31	NS	120±20	205±78	p<.001
Zn(µg/dl)	1200±100	898±265	p<.001	100±10	61±16	p<.001
Mn(µg/L)	9.7±4.7	14.2±10.5	p<.025	1.1±.9	6.3±3.4	p<.001

Zinc levels were significantly lower than controls and correlated with serum albumin (r=.61 p<.001); zinc levels correlated inversly with SGOT (r=.81 p<.001) and direct bilirubin (r=.89 p<.001). Manganese levels were significantly increased and correlated inversely with zinc levels. Zinc and manganese levels are strikingly abnormal in our population of biliary atresia patients who have had the Kasai procedure and appear to correlate with disease severity. The potential clinical significance of these observationsdeserve further investigation.

472 BONE DEMINERALIZATION IN CHILDREN WITH SHORT BOWEL SYNDROME

Linda S. Book, Gary Chan , Michael Matlak, (Spon. by Lowell Glasgow) University of Utah Medical School, University of Utah Medical Center, Department of Pediatrics, Salt Lake City.

Infants who have had small bowel resection may have malabsorption of minerals and vitamin D; therefore, bone mineralization could be impaired in these children. We evaluated 18 children two months to five years after they had had resection of 10 to 90% of their small intestine. Serial measurements were made of height, weight and bone mineral content and serum values determined for calcium, phosphorus, alkaline phosphatase and 25-OH vitamin D. Anthropometric parameters were within 2 SD of the mean of normals in 77% (14/18) of short bowel patients. However, bone mineral content was >2 SD below the mean of age-matched controls in 14 of 18 patients. The bone mineral content vs weight regression line was significantly lower for short bowel patients than for controls (F=6.6 P<.025). The amount of intestine remaining positively correlated with bone mineral content (r=.73 P<.01) in 15/18 children. Mean serum calcium was 9.8 mg/dl (8.6-11.3) and phosphorus 4.7 mg/dl (2.5-6.7). Serum alkaline phosphatase was increased in 5 of 16 and 25-OH vitamin D was normal (10-40 ng/ml) in all but one. Impairment in bone mineralization was proportionate to the percentage of small intestine removed in children with small bowel resection. Decreased bone mineral content was identified even when levels of 25-OH vitamin D, calcium and phosphorus were normal. This suggests there may be inadequate mineral absorption or utilization in children with short bowel syndrome.

473 EFFECT OF GESTATIONAL AND POSTPARTUM AGE ON THE NITROGEN COMPOSITION OF BREAST MILK.

D. Bouglé, G. Lepage, S. Melançon, S. Colin and C.C. Roy. Hôpital Ste-Justine, Department of Pediatrics, University of Montreal.

Several reports have shown the superiority of preterm (PT) over term (T) milk in terms of total nitrogen content but a progressive decrease has been noted with postpartum age and little is known about the effect of gestational age. Total nitrogen (TN) in PT milk obtained during the first 8 postpartum weeks was higher than in T milk. The highest TN and the lowest NPN/TN ratio was found in early PT milk.

	Preterm milk				Term
Days	1-7	8-14	15-28	> 28	8-14
	(n=9)	(n=12)	(n=11)	(n=10)	(n=6)
TN (mg/dl)	380±51	308±30	289±17	312±32	201±11
NPN/TN	.17±.01	.19±.01	.21±.01	.20±.01	.20±.01

TN concentration was 50% higher in milk obtained 2 to 4 weeks postpartum from mothers who delivered prematurely but did not change with the degree of prematurity.

	Gestational age		
Weeks	26-30	31-35	38-42
	(n=5)	(n=5)	(n=6)
TN (mg/dl)	301±19	301±6	201±11
NPN/TN	.19±.01	.20±.01	.20±.01

These data from full 24hr collections show that nitrogen composition of PT milk was different from that of T milk. Little change was seen between 26-35 weeks of gestation and the concentration of total nitrogen in PT milk showed no decrease after the first postpartum week. PT milk has a nutritional advantage which is independent of gestational and of postpartum age.

474 DEVELOPMENTAL PROFILE OF JEJUNAL LACTASE (LA) AND SUCRASE (SA) ACTIVITY ALONG THE VILLUS-CRYPT UNIT (VCU) IN THE RAT.

John T. Boyle, Mary Kokonos, Otakar Koldovsky. (Spon. by John B. Watkins) U. of Penn., Children's Hosp., Dept. Ped., and U. Arizona, Dept. Ped., Tucson, AZ.

Lactase and sucrase have distinctive developmental patterns in rat jejunum. The distribution of these enzymes along the VCU also varies with development, but previous studies separating cells along the VCU by the Weiser "washing" technique have yielded conflicting results. In this study, cryostat sectioning of frozen jejunum provided sequential histological separation of cells along the VCU, enabling comparison of distribution of enzyme activity at various heights of the VCU during development (Table). While total jejunal protein increased with age, the protein concentration along the VCU was constant at all ages tested.

PER CENT OF MAXIMAL (LA;SA) ENZYME ACTIVITY ALONG VCU

Histology/Age	14d	17d	21d	28d	120d
Apical Villus	97;0	99;0	93;55	100;88	94;90
Mid-Villus	99;0	100;0	100;78	84;97	89;100
Lower Villus	100;0	97;0	92;100	57;100	57;95
Mix-V-C	78;0	81;100	71;99	39;64	20;74
Crypt	46;0	48;61	23;54	13;22	12;6

Conclusions: 1) There is a definite evolutional pattern of distribution of LA and SA along the VCU. An apical shift of LA with loss of activity from the crypt correlates with dietary transition following weaning (21d). SA,in contrast, is initiated in the crypts and progresses gradually to uniform distribution along the villus following weaning. 2) The adult distribution for both enzymes is approximated by 28d. 3) The adult pattern of SA approximates the pattern of LA in the suckling.

475 VITAMIN E STABILITY AND AVAILABILITY DURING PARENTERAL ALIMENTATION. Mary Ellen A. Bozynski (Sponsored by Joseph R. Christian), Rush Medical College, Rush Presbyterian St. Luke's Medical Center, Department of Pediatrics, Chicago and Mohammed Mazharuddin, William Boyle, Steve T. Koeff, Daisy S. McCann, University of Michigan, School of Medicine, Wayne County General Hospital, Department of Pediatrics and Medicine, Wayne, Michigan.

Vitamin E may be important in the prevention of hemolytic anemia and amelioration of retrolental fibroplasia and bronchopulmonary dysplasia in the premature. Prematures are thought to be relatively Vitamin E deficient. They often receive parenteral nutrition for prolonged periods. Vitamins during parenteral nutrition are often administered using multi-vitamin infusion (MVI^R) containing tocopherol acetate as the Vitamin E supplement. Fat soluble vitamins may absorb to glass and intravenous administration sets. This has been reported for Vitamin A. Parenteral alimentation fluid was prepared for a theoretical 1/kg. neonate containing 1 cc MVI^R (1 mgm Vitamin E acetate). The solution was run through an intravenous administration set. Aliquots were collected at t=0, 2, 4, 6 and 24 hours and Vitamin E was measured by high performance liquid chromatography. This was repeated under conditions similating exposure of the system during phototherapy. Recovery from the multi-vitamin preparation was 60%. There was no loss from initial concentration over time. Passage through the administration set and phototherapy did not result in any change in recovery. Vitamin E appears to be stable in solution and available to the neonate under usual clinical conditions.

476 THYROXIN EVOKED INCREASE OF SUCRASE ACTIVITY IN LOWER VILLUS CELLS IN THE JEJUNUM OF SUCKLING RATS. Sergio Bustamante, Darren Neal, and Otakar Koldovský. Departments of Pediatrics and Physiology, University of Arizona College of Medicine, Tucson, Arizona.

Intestinal sucrase activity (SA), absent in the suckling rat, is evoked precociously by thyroid hormones. Since enterocytes migrate from crypt to villus tip the question arises: at which level of the villus-crypt columns (VCC) do the enterocytes respond with an increase of SA to thyroxin (T_4).

Suckling rats (11-day-old) were injected daily s.c. with T_4 (2µg/g B.W./day). They were sacrificed 1, 2 and 3 days later; SA was determined in homogenates of entire jejunal wall and in serial homogenates of VCC using cryostat sectioning. Maximal increase of SA was seen after 3 days in the lower villus. This resembled the effect of glucocorticoids (Biochem. J. 126:471, 1972). To exclude the effect via precocious maturation of adrenal cortex, same experiments were repeated using rats adrenalectomized on day 10. The SA in the mid-third of the jejunoileum two and three days after the 1st injection was [µmol/mg prot/hr (mean ± SEM:N) * = significant from uninjected controls] :

	VILLUS - CRYPT COLUMNS			
DAYS	Tip	Middle	Lower	V-C Mix
2	.06 ±.02;20	.05 ±.02	.07 ±.02*	.12 ±.03*
3	.10 ±.04;16*	.18 ±.04*	.29 ±.06*	.37 ±.08*

Conclusion: Enterocytes nearest the villus-crypt junction respond to T_4 with the highest increase of sucrase activity. T_4 effect is independent of adrenal glands.

477 SERUM GASTRIN CONCENTRATIONS IN CHILDREN WITH RENAL DISEASE. William J. Byrne, and Watson C. Arnold (sponsored by Donald E. Hill). Arkansas Children's Hospital, Little Rock, Arkansas.

Hypergastrinemia has been documented in adults with chronic renal failure (CRF). Its role in the increased incidence of peptic ulcer disease in renal patients is unclear. Radioimmunoassays using region specific antisera were employed to examine total serum gastrin (TG) and G-17 concentrations in 4 groups of children: those with acute renal failure (ARF), nephrotic syndrome without renal failure (NS), chronic renal failure (CRF), and stable end stage renal disease on hemodialysis (HD). Specimens were obtained following a 6 hour fast. Simultaneous serum creatinine (Cr) determinations were also performed. Results are presented below:

	Normal Cr<1.0 (n=10)	ARF Cr 2.8-9.8 (n=5)	NS Cr < 1.0 (n=4)	CRF Cr 2.8-9.2 (n=5)	HD (n=4)
TG (pm)	13 ± 2	49 ± 22	12 ± 2	45 ± 19	16 ± 5
G-17 (pm)	9 ± 1	8 ± 2	9 ± 5	13 ± 10	14 ± 3

Compared to normal children significant elevations in TG were found only in those patients with ARF ($p < 0.05$) and CRF ($p < 0.01$). However statistically significant differences were not obtained for G-17 between normals and any of the four groups including those with ARF ($p > 0.05$) or CRF ($p > 0.05$). These studies show that TG but not G-17 is elevated in children with ARF and CRF. G-34 is therefore the predominant gastrin molecule. Since it is 1/6 as potent as G-17 as a secretogogue, it is unlikely that gastrin plays a significant role in the etiology of peptic ulcer disease.

478 FASTING BREATH HYDROGEN (H_2) IN CYSTIC FIBROSIS. Ricardo O. Castillo, Jay A. Perman, Kon-Taik Khaw, Chris Landon, Richard J. Grand, (Spon. by M.M. Thaler) University of California San Francisco and Harvard Medical School, Boston, Departments of Pediatrics.

Excretion of H_2 in breath commonly persists despite an overnight fast. While elevation of H_2 above the fasting value (FH_2 in ppm) after administration of a test sugar is evidence of carbohydrate malabsorption, the significance of FH_2 is unknown. FH_2 was measured in randomly selected patients with cystic fibrosis (CF) maintained on 1 or more oral antibiotics, normal subjects (N), and subjects with lactose malabsorption (LM). All were >2 years old. Results of FH_2:

	Patients	Patients>30ppm(%)	Mean±SD	Range
CF	26	14(54)	37±31	5-241
N	12	0(0)	12±9	0-30
LM	48	4(8)	11±13	0-53

FH_2 in CF differed from N ($p<.007$) and LM ($p<.001$). FH_2 was >30 in 3/5 CF subjects studied repeatedly. Since sulfa-containing antibiotics were used most frequently in CF subjects, the effect of sulfa on H_2 production from glucose by fecal homogenates from 3 normal adults was assessed in vitro. Sulfa increased H_2 production by 26% compared with sulfa-free controls. Conclusion: Fasting H_2 levels are frequently elevated in CF. Although impairment of pulmonary and intestinal function may influence FH_2, the present results are consistent with antibiotic-induced enhancement of degradation of carbohydrate and/or glycoproteins by intestinal bacteria.

479 MOLECULAR LOCALIZATION OF MANGANESE IN HUMAN BREAST MILK, BOVINE MILK AND INFANT FORMULA. Wai-Yee Chan, James M. Bates, Jr., and Owen M. Rennert. University of Oklahoma Health Sciences Center, Department of Pediatrics, Oklahoma City.

Recent studies demonstrated that the bioavailability of a trace mineral is greatly affected by its chemical environment and molecular form as evidenced by the fact that iron and zinc are more available in human than in cow's milk. Since cow's milk and infant formula have been used as human milk substitutes, it is desirable to study the molecular localization of minerals such as manganese (Mn) in these preparations because neonates are at greater risk to develop deficiency. Delipidized milk and formula samples after labelling with carrier-free Mn-54 were examined by Sephadex G-200 column chromatography. Labelled protein species were analyzed by DEAE Sephacel ion exchange chromatography. Human milk contained at least 2 Mn binding proteins, the major one of M_r 340,000 and the minor one of M_r 80,000. The 340 k protein was homogeneous with respect to charge and molecular weight and had a Mn to protein ratio of 1:1. Cow's milk had at least 3 Mn binding species with M_r 234,000, 83,200 and <1000. The 234 k species was heterogeneous. Infant formula had no Mn-binding ligand with M_r >1000. This work indicates that Mn is bound by different ligands in human milk, cow's milk and formula. Whether this difference in Mn-binding molecular species has any effect on its bioavailability is under investigation.

480 ADAPTATION TO ALTERED DIETARY INTAKE OF AMINO ACIDS OCCURS AT THE BRUSH BORDER MEMBRANE. Russell W. Chesney, Aaron L. Friedman, Naomi Gusowski, Mary Theissen, Univ. of Wisconsin Hospitals, Dept. of Pediatrics, Madison, WI.

Our previous studies have shown that taurine (T), a ß-amino acid, is conserved in the kidney of rats fed a low-sulfur amino acid, but normal protein-containing, diet. Urinary T falls by 90% and uptake by isolated tubule segments increases by 60% (Life Sci 23:2415, 1981). Using renal brush border membranes (BBM) prepared by a double $CaCl_2$ precipitation method, the uptake of T was found to be Na^+-dependent. A typical T overshoot is found with $Na_{out} > Na_{in}$. Mannitol, K and Li do not support this uptake. Only other ß-amino acids inhibit uptake and do so in a competitive fashion. BBM were prepared from rats fed a high (HTD), normal (NTD) and Low (LTD) sulfur amino acid diet for 14 days. Both the initial rate of uptake (30 sec) and peak uptake (7 min) indicated that T is accumulated LTD > NTD > HTD. The enhanced and blunted accumulation in relation to diet occurs over a wide range of concentrations (10-2500 µM) and throughout the time course of uptake. The Km of uptake, 150 µM, is unaltered by dietary change, but the Vmax is 182 pmole/30 sec/mg BBM protein for LTD animals, 140 pmole for NTD animals and 91 pmole for HTD animals. These findings indicate that alterations in dietary sulfur amino acid intake lead to changes in the Na-dependent uptake process for ß-amino acids and that the affinity for the substance is unaltered, but the rate of uptake varies according to dietary load. Moreover, the findings in the BBM parallel the changes in vivo and in tubules. Organic solutes may be conserved by such a process in nutritional disorders.

481 HUMAN MILK SIMULATES THE QUALITY OF FETAL GROWTH IN PRETERM INFANTS. Philippe Chessex, Brian Reichman, Gaston Verellen, Guy Putet, John Smith, Tibor Heim, Paul Swyer. Dept Paeds & Med Eng., U of Toronto, Res Inst, Hosp for Sick Children, Toronto.

The macronutrient adequacy of own mothers' milk (OMM) for feeding very low birthweight preterm infants was evaluated using nutrient balance,open-circuit indirect calorimetry & anthropometry. 15 studies were performed in 11 growing infants (M ± SE: gest age 30 ± 0.4wks; birthweight 1.16 ± 0.04kg; study age 21 ± 2d; study wt 1.27 ± 0.06kg). The infants were gaining weight (15.2g/kg.d), length (0.98cm/wk) & head circ (0.76cm/wk) at approximately intrauterine growth rates. The infants received 172 ± 4ml/kg.d of OMM containing 64.8 ± 7kcal/dl.

RESULTS

(M ± SE)	Energy (kcal/kg.d)	Protein (g/kg.d)	Fat (g/kg.d)	CHO (g/kg.d)
Intake	111 ± 4	3.02 ± 0.1	4.74 ± 0.3	12.6 ± 0.4
Losses	11 ± 2	0.37 ± 0.01	0.86 ± 0.2	0.2 ± 0.02
Oxidation	56 ± 1	0.68 ± 0.07	1.63 ± 0.3	9.5 ± 0.7
Storage	44 ± 4	1.97 ± 0.1	2.25 ± 0.5	2.9 ± 0.9

The energy cost of wt gain was 3.66kcal/g comprising 3.09kcal/g as stored energy & 0.57kcal/g as the energy cost of tissue synthesis. The accretion rates of protein & fat & proportional composition of the daily wt gain(fat 16.6%; protein 13.4%)were comparable to those reported for the 3rd trimester fetus[1], suggesting that 172ml/kg.d of OMM provided a source of energy & macronutrients sufficient to promote growth in the preterm infant of similar quality to that of the fetus.

1) Widdowson E, Scien Fdn Peds, Heineman, Lond, 1974, p.44 & 153.

482 LOCALIZATION OF IRON ACCUMULATION IN THE SKELETAL MUSCLE OF VITAMIN E DEFICIENT RABBITS. Jen-Yih Chu, Daphne deMello, Phitsamai Kanjananggulpan, & Coy D. Fitch, St. Louis University, Cardinal Glennon Memorial Hospital, Department of Pediatrics, Pathology & Medicine, St. Louis, Missouri.

Vitamin E deficiency in young rabbits has been shown to induce changes characteristic of iron deficiency due to sequestration of iron in muscle. When iron dextran was injected parenterally, the increase in storage iron in the thigh muscles 6-8 days later was much greater in the deficient than in the control group. Even larger differences were noted when more iron was given.

Iron Injected		0	25mg	30mg	75mg
Control	TNHI	5.0±1.2(6)	6.2±0.9(3)	6.7±0.1(3)	11.7(1)
	SNHI	2.1±0.4(6)	2.6±0.2(3)	2.8±0.4(3)	3.8(1)
Deficient	TNHI	8.4±3.3(6)	12.1 (2)	21.0±5.8(3)	135.0(1)
	SNHI	4.3±1.4(6)	8.8 (2)	12.8±4.4(3)	54.0(1)

The mean ± S.D. & the number of determinations are shown for TNHI (total nonheme iron) & SNHI (soluble nonheme iron) measured as µg of iron per g wet weight of tissue. Histological examination revealed muscle degeneration with infiltration of inflammatory cells in the deficient group. Stainable iron was noted only in a few scattered mononuclear cells of control rabbits regardless of iron supplement, but it appeared in clumps of mononuclear cells & between myofibrils of the most severely degenerated muscle of the deficient group. With injection of iron dextran, more iron was located in the mononuclear cells of the deficient muscle. (Partly supported by a grant from the U.S. Department of Agriculture & Fleur de lis Fund).

483 VARIABILITY OF NEWBORN BREATH HYDROGEN. Ronald S. Cohen, David K. Stevenson, Susan M. Shahin, Clinton R. Ostrander, John A. Kerner, and John D. Johnson, Depts of Ped., Stanford Univ. Sch. of Med., Stanford, CA and Univ. of New Mexico Sch. of Med., Albuquerque, NM.

We analyzed paired end-tidal (ET) breath samples from 52 neonates for both CO and H_2. The ETCO values were more reproducible than the ETH_2 results; the mean coefficients of variation were 2.25 ± 2.44 (range 0-11.2) for the ETCO, and 13.4 ± 18.7 (range 0-102.5) for the ETH_2 ($p<.001$). The coefficient of variation of the paired ETH_2 samples was greater than that for the corresponding ETCO samples for 46 of the 52 patients ($p<.001$). With CO as an "internal control," this indicates that despite reliable sampling, short-term variability in breath H_2 can occur. The causes of this variability are uncertain, but potentially include changes in respiratory function, gut perfusion, gut gas content, and gut surface area for diffusion. Based on 28 paired, simultaneous determinations of the pulmonary excretion rate of H_2 (VeH_2) and ETH_2 in 5 neonates studied repeatedly over a 3-hour postprandial period, the mean difference between individual ETH_2 and VeH_2 values standardized to each infant's respective means was .007 ± .140 (range -.273 to +.287). Simultaneous measurements of ETH_2 and VeH_2 were performed on 34 additional infants at a single point in the postprandial interval. The ETH_2 and VeH_2 correlated over a wide range of H_2 elimination ($n=34$; $r=.63$; $p<.001$). Thus ETH_2 may reflect VeH_2 for a population of neonates, but lack of a better correlation is consistent with the finding that ETH_2 is subject to short-term variability, or the relationship of ETH_2 to VeH_2 may vary from patient to patient.

484 HAIR ZINC CHANGES DURING THE FIRST YEAR. Platon J. Collipp, Betty Kuo, Shang Y. Chen, Mariano Castro-Magana, Steven Salvatore. Nassau County Medical Center, Department of Pediatrics, East Meadow, New York.

Zinc concentration in normal full term infants was measured during the first year of life (10 infants at each month, 306 infants at birth) using atomic absorption spectrophotometry. At birth the concentration was 204 ug/gm, and this declined to 100 ug/gm between 5-9 months, and increased to 130 ug/gm at 12 months of age. Quantity of hair and extent of diaper rash were assessed from polaroid photographs. The two children with the most hair at each month of age (24 children total) had mean hair zinc 133 ug/gm, and the two with the least hair had 108 ug/gm zinc ($p < 0.01$). Diaper rash occurred significantly more frequently in children with lower hair zinc, and in children with significantly less hair. Diaper rash cleared up promptly in all children given 10 mg daily oral zinc supplements. Breast fed infants had higher hair zinc than formula fed infants. This remarkable fall in hair zinc concentration during the first year of life is apparently related to some of the features we have considered to be normal characteristics of infants.

485 HAIR MANGANESE INCREASE IN LEARNING DISABLED CHILDREN'S POSSIBLE RELATIONSHIP TO INFANT FORMULA FEEDING. Platon J. Collipp, Shang Y. Chen, Steven Maitinsky, Brad Katchen, Steven M. Hollenberg, James K. Yeh. Dept. of Pediatrics, Nassau County Medical Center, E. Meadow,NY 11554.

Manganese has been determined in hair specimens using atomic absorption spectrophotometry. Concentration was increased $p<0.05$ (0.405 ug/gm) in hair from 16 children (average age 8 years) with hyperkinetic learning disability followed in our Child Development Center compared to 44 age-matched healthy controls (0.268 ug/gm) followed at a nearby HIP group. Elevated hair manganese in LD children was previously reported by Barlow. Hair manganese was measured in children at different ages:

#	Age	Wks Formula-fed	Hair Manganese (ug/gm)
10	0	0	0.19
10	6 wks	6 wks	0.965
10	16 wks	16 wks	0.685
20	9 mos	33 wks	0.587
10	3 yr	24 wks	0.398
44	8 yr	32 wks	0.268
10	3-24 mos	breast-fed	0.330

Since infant formula contains much greater quantities of manganese than human or cow's milk, it is likely the formula is the source of the significant increase we observed in hair manganese which occurs after birth. Because manganese has been reported to cause CNS toxicity in animals and humans, it may play a role in learning disabled children.

486 EFFECT OF RECTAL AND AXILLARY TEMPERATURE MEASUREMENT ON MECONIUM PASSAGE, PLASMA BILIRUBIN, AND HOSPITALIZATION COSTS. Barbara H. Cottrell & Gene C. Anderson, College of Nursing (spon. by John A. Mangos, Department of Pediatrics, College of Medicine), Univ. of Florida, Gainesville.

Physiologic jaundice (5-6 mg% bilirubin) is common and considered normal in newborn infants during the first week postbirth. Subtle forms of bilirubin toxicity may occur at these levels which are considered abnormal in older infants. Early meconium passage is associated with lower bilirubin concentrations. The rectal stimulation which occurs during rectal temperature measurement may aid passage of meconium containing potentially toxic, absorbable bilirubin. The effect of axillary versus rectal temperature measurement on time of first meconium, first yellow stool, total plasma bilirubin, and hospitalization costs was compared in 100 clinically normal newborns assigned randomly to rectal temperature or axillary temperature groups. Bilirubin was measured at the close of the study during metabolic screening at 48-80 hours postbirth (mean 68 hours in both groups). By this time 30 infants in the rectal group, but only 17 in the axillary group, had passed all-yellow stools. The rectal group had lower mean bilirubin (5.49 mg% vs. 6.50, $p < .05$); lower hospitalization costs ($207 vs. $219, $p < .05$); and a trend towards earlier first meconium (5.9 hours vs. 7.3, $p = .19$).

Conclusion: For infants in the first 48-80 hours postbirth, these data suggest that rectal stimulation with temperature monitoring (1) enhances intestinal bilirubin excretion because of more rapid meconium passage, and (2) significantly lowers hospitalization costs.

487 MONITORING THE USE OF INTRAVENOUS FAT (IVF) IN NEONATES. Arthur D'Harlingue, David K. Stevenson, Susan M. Shahin, Andrew O. Hopper, and John A. Kerner (Spon. by Philip Sunshine). Stanford Univ. Sch. of Med., Dept. of Ped., Stanford, CA.

Twenty-three infants in the neonatal ICN receiving IVF as Intralipid^{R} by continuous infusion (range 0.25-2.5 gm/kg/day) had simultaneous measurements of IVF levels by laser nephelometry (n=58, range 18-150 mg/dl), free fatty acid-albumin molar ratio (n=58, range 0-5.18), triglycerides (n=54, range 33-305 mg/dl), cholesterol (n=36, range 85-304 mg/dl), and serum turbidity (n=58). The purpose of this study was to determine whether IVF level as measured by laser nephelometry, a microtechnique, would be predictive of hyperlipidemia. A previous study found that keeping the IVF level below 100 mg/dl avoided hyperlipidemia, but this was not the finding in a subsequent study using a modified fluorometer.

We found a positive correlation between IVF level and triglycerides ($r=.406$, $p<.001$), but the IVF level did not reliably predict elevated triglycerides. Of 7 triglyceride determinations above 200 mg/dl, only 2 had elevated IVF levels. No correlation was found between IVF level and cholesterol or free fatty acid-albumin molar ratio. Serum turbidity was also a poor predictor of hyperlipidemia. Monitoring serum lipemia with either IVF levels or turbidity checks does not accurately provide information regarding hyperlipidemia, suggesting there are other important contributing factors to the development of hyperlipidemia than the clearance of the IVF chylomicron. It appears one must monitor triglycerides, cholesterol, and free fatty acids in the use of IVF in neonates.

488 FECAL BILIRUBIN EXCRETION AND SERUM BILIRUBIN CONCENTRATION IN BREAST (BR) AND BOTTLE (B) FED INFANTS. M. DeCarvalho, M. Klaus, S. Robertson, E. Rosenkranz, J. Ennever, W. Speck, University Hosp., CWRU, Cleveland, Ohio.

The role of the enterohepatic circulation of bilirubin in physiologic jaundice in BR and B fed infants remains controversial. To evaluate the reabsorption of bilirubin from meconium we studied the fecal excretion of bilirubin and its relationship to increments of serum bilirubin in 10 healthy full term BR and 10 B fed infants in the first 3 days after birth. Maternal medication and type of delivery were not significantly different. The total number of stools for the first 3 days was not significantly different

	BIRTH WEIGHT(kg)	SERUM BILIRUBIN INCREMENT 1st TO 3rd DAY(mg%)	CUMULATIVE WEIGHT OF STOOLS 1st 3 DAYS (gm)	CUMULATIVE FECAL EXCRETION OF BILIRUBIN 1st 3 DAYS (mg)
BREAST	3.3 ± 0.4	4.2 ± 3.5	57 ± 13	16 ± 3.3
BOTTLE	3.0 ± 0.2†	1.3 ± 2.1*	81 ± 20**	25 ± .2*

mean ± SD *p<.05 **p<.01 † not significant

between groups (range 5-24 stools). However, B infants had significantly greater weight of stools, excreted significantly more bilirubin in the stools and had significantly lower serum bilirubin increments. Although BR fed infants lost significantly more weight over the first 3 days(232 vs 72 gm, $p<.01$),weight loss was not correlated with serum bilirubin increments. These data suggest that in BR fed infants the slower excretion of fecal bilirubin together with enhanced enterohepatic circulation may explain the increased incidence of hyperbilirubinemia.

489 FREQUENT BREASTFEEDING IMPROVES MILK PRODUCTION AND INFANT WEIGHT GAIN. M.DeCarvalho, M.Klaus, S. Robertson, E. Neils, A. Friedman, R.Merkatz. Rainbow Babies & Childrens & Mt. Sinai Med. Ctr., CWRU, Cleveland, OH

Although the incidence of breastfeeding has increased in recent years, the major cause of lactation failure continues to be insufficient milk production. To assess the effect of frequency of breastfeeding on milk production, infant weight gain and serum prolactin, we studied two gropus of mother-infant pairs during the first 2 weeks after delivery. Assignment to groups was determined by day of delivery. Mothers in the low frequency group (n=24) nursed on a routine 3-4 hour schedule, while the high frequency group (n=20) were encouraged to nurse frequently. Mothers recorded the time and duration of each feeding during the first 14 days. We measured 24 hour milk production, infant weight gain and serum prolactin on the 15th day. As shown in the Table, mothers in the high frequency group produced significantly more milk, and their infants gained significantly more weight. Serum prolactin levels were not correlated with milk output. Although the frequency of feeding differed significantly, the total duration of feeding was remarkably similar in the two groups. These data demonstrate

	FEEDING FREQUENCY (feeds/24h)	DURATION OF FEEDING (min/24h)	MILK OUTPUT (ml/24h)	WEIGHT GAIN FROM BIRTH (gm)	SERUM PROLACTIN (ng/ml)
LOW	7.3 ± 1.4	137 ± 38	502 ± 185	347 ± 331	271 ± 236
HIGH	10 ± 1.9***	138 ± 50	724 ± 171**	560 ± 186*	212 ± 136

mean ± SD *p<.02 **p<.001 ***p<.0001

that milk production and infant weight gain are greater in mothers who breast feed more frequently.

490 BLOUNT'S DISEASE (TIBIA VARA): ANOTHER SKELETAL DISORDER ASSOCIATED WITH CHILDHOOD OBESITY. William H. Dietz, Wendy A. Gross, John A. Kirkpatrick. Harvard Medical School, Children's Hospital Medical Center, Department of Gastroenterology and Nutrition, Boston, MA.

Blount's disease is a skeletal disorder characterized by bowed legs, tibial torsion, and consistent radiographic changes in the affected extremities. Although the causes of Blount's disease are unknown, obesity has frequently been mentioned in association with the infantile type of the disease. Two cases of infantile onset Blount's disease were observed in massively obese children. In case 1, osteotomy followed by weight reduction halted progression of the deformity despite persistent radiographic abnormalities. In case 2, surgery was followed by unsuccessful weight reduction, and further surgery is now required. A review of 18 patients with Blount's disease seen at this institution in the last 10 years revealed obesity in 67%. Among the obese patients, highly significant correlations were observed between the % ideal body weight (IBW) and the femoral: tibial shaft angle ($r=0.92$, $p<.001$) and % IBW and the femoral condyles: tibial shaft angle ($r=0.90$, $p<.001$). The 12 obese patients required 26 osteotomies to correct their deformities whereas the 6 non-obese patients required 8. The occurrence of Blount's disease in non-obese children, resolution of obesity despite persistence of Blount's disease, and progression of Blount's disease without obesity suggest that the onset of Blount's disease, but not its course, isindependent of obesity. Weight reduction may be as important as surgery in the treatment of Blount's disease occurring in obese children.

491 COPPER AND ZINC CONCENTRATIONS IN HUMAN MILK FROM MOTHERS OF PREMATURE INFANTS. J. Donlen, S. Bartosh, E.E. Tyrala, Temple University School of Medicine, St. Christopher's Hospital for Children, Philadelphia, Pa. (Sponsored by V.H. Auerbach)

Weekly milk specimens were collected for analysis for copper and zinc from 5 mothers of premature infants from the end of the first week, to an average of 5 weeks following delivery. The average gestational period was 32 weeks (range 31-35). The mothers were instructed in proper milk collection technique. Samples were stored in plastic bags and frozen until time of analysis.

	Weeks After Birth				
	2	3	4	5	7
Cu (μg/dl)	.76	.74	.64	.47	.49
Zn (μg/dl)	5.5	4.8	3.5	3.3	2.2

Cu and Zn concentrations in the 2nd week's specimens were slightly higher than that which has been found in milk from mothers of full-term infants. The concentrations of both Cu and Zn progressively fall, however, and at 7 weeks of lactation are similar to concentrations from mothers of full-term infants at the same stage of lactation.

The concentrations of Cu and Zn in the milk of mothers of premature infants, although slightly higher than that seen in mothers of full-term infants, may still be too low to meet the needs of the growing premature infant.

● **492** THE SIGNIFICANCE OF TRYPSIN-PROTEASE INHIBITOR BOUND COMPLEXES IN ACUTE PANCREATITIS. Peter R.Durie, Kevin J.Gaskin, Corey Largman, Charles R.Smith, Janet E. Ogilvie. (Spon. by J.R. Hamilton) The Hospital for Sick Children, Toronto, Canada, The Enzymology Research Lab., VA Medical Center, Martinez, Calif., and UC Davis School of Medicine, Davis, Calif.

The immunoreactive forms of plasma cationic trypsin (CATRYP) were determined by radioimmunoassay (RIA) in 5 patients with acute pancreatitis. During the course of their disease we obtained daily plasma samples; these were subjected to gel filtration to separate α_2-macroglobulin trypsin complexes (α_2M-CATRYP), α_1-antitrypsin bound trypsin (α_1AT-CATRYP) and trypsinogen, followed by RIA of the column fractions. In 2 patients, early samples contained only increased trypsinogen but after 2 days there was progressive conversion of the zymogen to active trypsin bound to protease inhibitors (α_2M-CATRYP, α_1AT-CATRYP). At autopsy both patients had severe, hemorrhagic pancreatitis. In contrast, only elevated trypsinogen could be detected in 3 patients, with little or no conversion to inhibitor bound trypsin (α_2M-CATRYP, α_1AT-CATRYP) with disease progression. Two of these patients died of complications unrelated to pancreatitis and at autopsy mild, focal, edematous pancreatitis was present. The remaining patient recovered uneventfully. We suggest that the severity of pancreatitis may be reflected by the degree of conversion of trypsinogen to α_2M-CATRYP and α_1AT-CATRYP. Furthermore, since α_2M-CATRYP remains active towards some polypeptides (Parathyroid hormone, Angiotensin, Pro-insulin etc.) the presence of circulating α_2M-CATRYP may produce many systemic complications of this disease.

493 COMPARATIVE PROTEIN EFFICIENCY OF PRETERM HUMAN MILK (PTHM), FORTIFIED-PTHM, AND FORMULA. Richard A. Ehrenkranz, Barbara A. Ackerman, and Catherine M. Nelli (spon. by J.B. Warshaw). Yale Univ. Sch. of Med., Yale-New Haven Hospital, Dept. of Pediatrics, New Haven, Connecticut.

Nineteen AGA premature infants, BW≤1250 gm, were studied from the time that full volume gavage feedings were tolerated until about 1750 gm. 7 infants received a whey predominant premature formula; the other 12 infants were randomized between their own mother's milk (6) and fortified-PTHM (6), a 1:1 (v/v) mixture of the premature formula and their own mother's milk. The ave daily intake was isocaloric. PTHM was used in the order in which it was expressed and was kept frozen until needed. N_2-balance studies were performed when the infants had gained at least 10 gm/kg/d for 7 days and/or weighed 1500 gms. Findings (mean ± SE) are shown in the table. Formula resulted in a larger daily wt gain ($p < 0.01$) and N_2-balance ($p < 0.05$) when compared to PTHM. However, the protein efficiency ratio (PER; a ratio of ave daily wt gain to ave daily protein intake/kg) for PTHM was similar to that of formula. Compared to PTHM and formula, fortified-PTHM resulted in a similar daily wt gain and PER, but intermediate N_2-balance values. Each type of feeding provides similar nutritional support of wt gain.

Diet	Average daily intake cc/kg	gm prot/kg	Ave daily wt gain (gm)	PER
PTHM	168 ± 1.7	3.20 ± 0.28	19.5 ± 1.1	6.4 ± 0.8
Fortified-PTHM	160 ± 4.7	3.12 ± 0.14	22.6 ± 1.5	7.2 ± 0.4
Formula	147 ± 6.5	3.51 ± 0.07	24.3 ± 1.2	7.1 ± 0.3

494 CHEMILUMINESCENCE OF NEUTROPHILS AS A NEW INDEX OF DISEASE ACTIVITY IN INFLAMMATORY BOWEL DISEASE (IBD) Howard S. Faden, Thomas M. Rossi. State University of New York at Buffalo, Children's Hospital of Buffalo, Department of Pediatrics, Buffalo, N.Y.

Laboratory evidence of active inflammation in 11 patients with IBD (Crohn's D. 8, ulcerative colitis 3) was determined by comparing the luminol-dependent chemiluminescent response of ficoll-hypaque separated neutrophils with two standard tests, ESR and WBC. Eight patients had active disease, and 3 had inactive disease according to clinical evaluation. Drug therapy consisted of prednisone (P), and asulfidine (A) in 4, P alone in 3, A alone in 3, and neither in 1. The chemiluminescent response of resting neutrophils from patients was significantly greater than controls (1783 vs 1155 counts/0.2 minute, $p<.05$) as was the response of stimulated neutrophils (265,115 vs 80,000 counts/0.2 minute, $p<.001$). In contrast, the ESR and WBC were normal in 9 and 8 patients, respectively. Incubation of neutrophils from patients in sera from controls did not lower the chemiluminescent response to normal; similarly, incubation of neutrophils from controls in sera from patients did not elevate the chemiluminescent response. These data demonstrate that neutrophils from patients with IBD exhibit markedly increased metabolic activity although clinical and standard laboratory tests may be normal. Chemiluminescence of neutrophils can be useful as an index of disease activity in IBD.

495 SHORT-TERM NASOGASTRIC FEEDING AS AN ALTERNATIVE TO SURGERY IN INFANTS WITH SEVERE GASTROESOPHAGEAL REFLUX (GER) AND GROWTH FAILURE. George D Ferry, Maija Selby, and Timothy J Pietro (Spon by Ralph D Feigin). Baylor College of Medicine, Texas Children's Hospital, Dept of Pediatrics, Houston.

Fundoplication usually is recommended for infants when upright positioning and thickened feedings have failed to reverse growth failure caused by severe GER. We used an alternative approach of 6 to 21 days of continuous-drip nasogastric (NG) feedings in 10 infants with GER who did not respond to medical management and were candidates for surgery. All had GER documented by 24-h pH monitoring, barium esophogram, and/or esophagoscopy. All had net wt loss for 1 mo or longer, wt-for-ht deficit of 10-25%, and/or an arm/FOC ratio≦.28. Five infants (50%) experienced immediate and sustained resolution of vomiting with return to a normal growth pattern as shown by long-term follow-up (mean 6 mo). These treatment successes had a higher mean daily wt gain on NG feedings than did treatment failures (62±20 vs 14±20 g, p=.007). Presence of other medical problems (pulmonary disease, cerebral palsy, malabsorption, and laryngomalacia) was associated with poor long-term outcome; 4 of 5 failures had other medical problems while none of 5 successes did (p=.024). One NG treatment failure had resolution of both growth failure and vomiting after hyperalimentation. Four failures who had fundoplication continued to grow poorly after surgery.

Short-term continuous-drip NG feeding may be an appropriate alternative to surgery in patients with growth failure and GER uncomplicated by other medical problems.

496 SODIUM CHLORIDE DEFICIENT GROWTH RETARDATION IN RATS Burton P. Fine, Antonia Ty, Nancy Blasucci, J.Alberto Bastidas, and O. Robert Levine, New Jersey Medical School, Newark, New Jersey

NaCl has long been recognized as an essential nutrient for growth; yet, the mechanism for salt deficient growth failure is unknown. This study was designed to investigate the minimum dose of Na required for optimum growth, whether decreased growth rates were proportionate to Na intake, and whether the growth retardation was caused by decreased food intake. 40 weanling rats were fed a low NaCl diet containing 4.1Kcal/gm, protein 20%, fat 7%, carbohydrates 67%, with adequate minerals and vitamins. The rats were randomly divided into five groups and housed in individual cages for five weeks. The designated dose of NaCl was given in the daytime ration of drinking water. Food was offered ad-libitum to all the groups. (Results = $\bar{x}$ ± SEM)

NaCl meq/day	wt.gain gms.	^{24}Na space (ECF%BW)	Serum Conc. in meq/l (Na)	(K)	food(gm) wt.gain(gm)
0.030	64±3.0	26.6±1.3	141±1.9	4.9±0.2	7.0±0.34
0.150	153±2.9	28.5±0.9	137±1.9	4.9±0.26	3.5±0.06
0.300	212±4.6	28.1±0.6	140±1.6	4.7±0.29	3.0±0.04
0.600	210±6.0	30.5±1.2	140±1.6	5.2±0.23	3.0±0.06
0.900	224±4.1	29.5±1.0	140±1.7	4.7±0.16	2.8±0.03
ANOV	P< .001	n.s.	n.s.	n.s.	P< .001

Weight gain was related to the dose of Na in the groups receiving minimum and subminimum requirements ($Y=1.56\pm0.16x$ $r=0.98$ $P<0.001$). The quantity of food eaten per kg body weight was similar in all groups. We conclude that the minimum daily Na requirement is constant at 0.300 meq (approx. 0.05 meq/gm of wt. gain) and does not increase with body weight, and that suboptimum doses of Na result in a graded retardation of the growth rate caused by poor utilization of food and not decreased intake.

497 SELECTIVE FETAL MALNUTRITION IN THE NON-HUMAN PRIMATE Stanley E Fisher, Mark Atkinson (Spon. by F. Lifshitz) Department of Pediatrics, Cornell University Medical College and North Shore University Hospital, Manhasset, NY

Animal studies have implicated ethanol(E)-induced placental injury in the pathogenesis of the fetal alcohol syndrome (FAS). In vitro work with human placentae has given contrary results. Since the primate placenta is very similar to the human, we studied the uptake of α-amino isobutyric acid(AIB) and valine(VAL) by placental slices from 4 M.fascicularis monkeys: Control(C); Chronic high(CHD) and low(CLD) dose E exposure prior to and throughout pregnancy; E exposure during the last trimester(LT). C and LT were pair-fed with CHD using a liquid diet. CLD was chow-fed with E in the drinking water. Blood E(4 hr post prandial) ranged: CHD 46-75 mg/dl; CLD 0-66 mg/dl; LT 28-46 mg/dl. Placental slices were incubated in 6 replicates each with ^{3}H-AIB or ^{3}H-VAL. Consistent depression of uptake (C_i/C_o) was seen with the CHD placenta, although 45 min C_i/C_o of AIB was depressed for CLD and LT as well.

C_i/C_o * p<0.05 **p<0.01

	45 min AIB	45 min VAL	90 min AIB	90 min VAL
C (mean±SE)	3.98±.23	2.54±.13	5.10±.33	4.05±.26
CHD	1.43±.12**	1.54±.14**	2.34±.36**	2.80±.25**
CLD	3.14±.29*	2.56±.37	4.61±.33	3.66±.22
LT	2.93±.30*	2.90±.28	4.50±.28	4.06±.35

CONCLUSION: Exposure to E throughout pregnancy, consistently raising blood E levels above 50 mg/dl, may impair placental delivery of essential nutrients in man. This selective fetal malnutrition may contribute to the pathogenesis of the FAS.

● **498** IN SITU CHARACTERIZATION OF T CELL SUBPOPULATIONS IN GLUTEN SENSITIVE ENTEROPATHY (GSE). A.F. Flores, H.S. Winter, A.K. Bhan, Harvard Med. Sch., Children's Hosp. Med. Ctr., Div. of Gastroenterology; Mass. Gen. Hosp., Dept. of Path., Boston, MA 02115 (Spon. by R.J. Grand).

Aberrations in local immunoregulation are suspected to be important in injury of epithelial cells in patients with GSE. We characterized the immunological nature of the intraepithelial (IEL) and lamina propria lymphocytes (LPL) in patients with GSE (7 patients, 7 mos - 8 yrs, $\bar{x}$: 3.4 ± 2.4 yrs) as proven by biopsy before and after gluten challenge. The control group consisted of 7 patients (11 mos-19 yrs, $\bar{x}$:5.6±6.8 yrs) with chronic diarrhea and normal histology. Frozen tissue sections of jejunal biopsies were stained with a series of monoclonal antibodies by means of an immunoperoxidase technique. Most IEL were T8(+)(suppressor/cytotoxic), whereas predominant LPL were T4(+)(helper/inducer). T8(+)lymphocytes per 100 epithelial cells in patients with GSE averaged 37.6±21.8 compared to 11.3±12.7 in controls ($p<0.02$). There was a significant difference in the ratios of T8(+)IEL/T4(+)IEL between GSE patients and controls. No significant difference was found in the ratios of T8(+)LPL/T4(+)LPL between the groups. The data demonstrate that: 1) the suppressor/cytotoxic lymphocytes are the most common T cell subset in the surface epithelium of the jejunum, whereas helper/inducer cells are the predominant subset in the lamina propria; 2) patients with GSE have increased suppressor/cytotoxic lymphocytes in the surface epithelium as compared to controls. The intraepithelial suppressor/cytotoxic cell(T8+)may be responsible for epithelial injury in gluten sensitive enteropathy.

● **499** LONG-TERM SIGNIFICANCE OF INTRAEPITHELIAL EOSINOPHILS (IE) IN CHILDREN WITH ABNORMAL ESOPHAGEAL ACID CLEARANCE. A.F. Flores, H.S. Winter, R.J. Grand. Harvard Med. Sch., Child. Hosp. Med. Ctr., Div. of Gastroenterology, Boston, MA

The outcome in children with IE, a new histologic marker in the esophagus for acid reflux, is not known. IE in the esophagus has recently been identified as an early histologic marker of pathologic acid reflux which precedes basal zone hyperplasia. We evaluated 14 children (mean age 7.5±5.3 yrs) with pathologic acid reflux defined by continuous intraesophageal pH probe (CIPH) using established criteria. All had IE at initial evaluation. For comparison, 8 children (mean age 5.9±4.7 yrs) with abnormal CIPH tests but without IE were studied. There was no difference between features of esophageal acid clearance (number of refluxes, duration of reflux, % time pH<4) between the 2 groups. All 22 patients were evaluated subsequently (13±8 mos) using CIPH and esophageal biopsy. Of the 14 with IE, 11 were treated medically (antacids & cimetidine) and 3 had fundoplication. Esophagitis persisted in 8 patients (57%) including 2 of 3 post-op patients and 6 of 11 treated medically. The persistence of IE correlated with ongoing reflux. Of the 8 patients lacking histologic evidence of esophagitis initially, 2 (25%) developed esophagitis (IE) in the follow-up period despite medical antireflux therapy. Conclusions: Following either medical or surgical therapy, no feature of the pH probe test will predict which patients will continue to have IE. A significant number of patients with abnormal acid clearance developed IE after 1 yr. follow-up. The presence of IE is more reflective of duration of disease than severity of reflux.

500 METABOLIC STUDIES IN ANOREXIA NERVOSA. Gilbert B. Forbes, Barbara Lipinski, Richard E. Kreipe. University of Rochester, Department of Pediatrics, Rochester, NY 14642

High protein diets are often advocated for the treatment of undernutrition. As a test of the validity of this custom, we treated 4 patients with a high protein diet (20% protein cals) and 4 with a low protein diet (10% protein cals) on the Clinical Research Center. All had metabolic balances of N, K, Ca, and P, sequential K-40 counts, BMR and routine lab studies.

The high protein diet did produce higher values for BUN and for urinary Ca; and a slight rise in serum albumin, whereas the low protein patients showed no change (none had subnormal values at any time).

The high protein diet did not augment weight gain, % of gain due to LBM (av. 76%), N retention per unit weight gain, the rise in BMR, or the sense of wellbeing. It did not hasten the recovery from leukopenia, nor did it prevent the slight drop in hematocrit so often seen during recovery in these patients. The caloric cost of weight gain (av. 6.4 k cal/gm gain) was the same for both diets.

Additional findings of interest were 1) the high % of weight gain attributable to lean weight; 2) K balance exceeded K retention by K-40 counting by 2 to 16 meq/d.

We conclude that high protein diets offer no nutritional advantage in the rehabilitation of patients with anorexia nervosa.

501 IgE AND IgD ANTIBODIES TO COW MILK AND SOY PROTEIN IN DUODENAL FLUID (DF): ROLE OF PANCREOZYMIN (PZ-CCK) AND SECRETIN (S). Serem Freier, Miriam Freier, Praful C. Shah, Byung H. Park, Ping-C Lee, and Emanuel Lebenthal. Department of Pediatrics, Children's Hospital, SUNY at Buffalo, Buffalo, N.Y.

We estimated the specificities and activities of IgE and IgD against α-casein, β-lactoglobulin A and soy agglutinin in DF. Four healthy adults and 13 children with diarrhea (8), malabsorption (1), pancreatic insufficiency (1), gastroschisis (2) and abdominal distention (1) were studied before and after injection of PZ-CCK and S. An ELISA technique capable of detecting 0.18 ng/ml IgE and 39 ng/ml IgD was used. In adults, resting DF contained no IgE or IgD antibodies specific to milk or soy proteins but they appeared 10 minutes after PZ-CCK stimulation. Following S, IgE specific antibodies appeared in 5 minutes, but no IgD antibodies. Of the patients, 6/12 had IgE and 5/12 had IgD antibodies in their resting DF. Secretin resulted in a further rise in antibody activity. No correlation existed between the disease, the intestinal biopsy appearance and the antibody activity. There was a close correlation between IgE and IgD antibody levels. In normal adults IgE and IgD antibodies specific to food appear following stimulation by PZ-CCK. These may play a role in the handling of food antigens in digestion. In children with GI disease, IgE and IgD antibodies specific to food are present in resting juice suggesting an increased translocation perhaps resulting from inflammation.

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● **502** INTESTINAL H_2O AND ELECTROLYTE TRANSPORT DURING MUCOSAL IgE MEDIATED REACTIONS. D.GRANT GALL AND MAY CHUNG UNIVERSITY OF CALGARY,G.I.RES.UNIT,CALGARY,ALBERTA

To assess the intestinal dysfunction caused by IgE mediated mucosal reactions we studied absorptive function in Hooded-Lister rats sensitized to egg albumin(Ag).Animals were studied 14 days after eliciting a primary IgE response by intraperitoneal injection of small doses of Ag.Mean weight of animals developing reagenic(IgE)titers ≥1:64 was significantly ($p<0.025$)less than with minimal(≤1:16)or no response(188±16g,X±SD vs 207±29).Net fluxes of H_2O and electrolytes were measured by *in vivo* perfusion.Experimental animals(≥1:64)were compared to sham-treated litter-mate controls.Fluxes were determined during two periods:when the perfusate was antigen-free(0-60min)and then after the addition of antigen(Ag,60-200min).During the Ag-free period net fluxes of H_2O,Na,K and Cl did not differ significantly between controls(6) and experimental animals(9).Intraluminal Ag challenge(10μg/mL)had no effect in controls but in the sensitized group caused a significant($p<0.01$)decrease in H_2O,Na,K and Cl absorption.Epithelial morphology as assessed by light microscopy was not altered.In a second series of experiments fluxes were measured during three periods:Ag-free(0-60min),Ag(60-160min)and Ag-free(160-260min).In the experimental group intraluminal Ag exposure again caused significant ($p<0.025$)reduction of H_2O,Na,K and Cl absorption and during the subsequent antigen-free period there was no evidence of recovery.The findings indicate that(i)animal weight is important in eliciting an IgE response and(ii)IgE reactions in the mucosa lead to abnormalities in H_2O and electrolyte transport which persist after Ag withdrawal.

503 TAURINE PROMOTES GROWTH OF CULTURED HUMAN CELLS. Gerald E. Gaull, Charles E. Wright, Leslie B. Schweitzer, and Harris H. Tallan. Dept. Hum. Devel. Nutr., NYS Inst. Basic Res. Devel. Disab., Staten Island, N.Y. 10314.

Taurine occurs in high concentrations in human milk (250-350 μM) but there is much less in bovine milk (10 μM) and in infant formulas (0-30 μM). We have previously demonstrated a dietary requirement for taurine in both preterm and term infants, and there is evidence that it is important in development and in certain physiological functions. It is an essential amino acid for the cat and monkey, but demonstrating that it is essential for man is difficult because of its dietary ubiquity and efficient mechanisms of conservation.

Over 50% of the free amino acid pool of human lymphoid cell lines is taurine. Effects of its depletion and supplementation on these cells was investigated using a taurine-free, chemically-defined medium. RPMI 1640 supplemented with insulin, transferrin, $CuSO_4$, and $FeSO_4$ will support the perpetual growth of such lines without changing its karotype or ability to synthesize immunoglobulins. Taurine-depleted cells growing on such medium were transferred to RPMI 1640 with (1) 16% fetal bovine serum (FBS), (2) 16% dialyzed FBS, (3) 16% dialyzed FBS supplemented with 29 μM taurine and, (4) defined medium with 0-116 μM taurine. In all taurine-supplemented media, cell proliferation was greater as measured by viable and total cell count and there was a dose response to taurine.

These data establish taurine's importance in the growth of human cells; chemically-defined culture provides a useful system in which to demonstrate nutrient requirements of human cells.

504 SHORT TERM METRONIDAZOLE IN THE TREATMENT OF ANO-RECTAL CROHN'S DISEASE IN ADOLESCENTS. Donald E. George and Joel M. Andres (Spon. by John A. Mangos). University of Florida College of Medicine, Department of Pediatrics, Gainesville.

Ano-rectal involvement is a frequent complication in patients with Crohn's Disease (CD) and contributes to significant morbidity even when intestinal disease is well controlled. Also, ano-rectal disease is often refractory to treatment including surgery, Prednisone, Azulfidine and local therapy. We studied 4 adolescents, ages 13-17 years, with severe ano-rectal involvement of CD. Diagnosis was established by biopsy demonstration of granulomata. The average duration of CD was 2.5 years (range 8 mos-6 yrs) and that of ano-rectal disease 1.2 years (range 8 mos-2 yrs). Two patients had involvement of the colon only and two had ileocolonic disease. In the latter 2 patients, intestinal disease was quiescent at the time of presentation despite the ano-rectal complications. Informed consent was obtained prior to therapy with Metronidazole (20 mg/kg/day) which was given for 1.5 to 7 weeks. All patients significantly improved as manifested by a decrease in ano-rectal pain, induration, erythema and abscess drainage. Three patients with sinus tracts showed complete healing. Two of the 4 experienced gastrointestinal upset, and in one treatment was interrupted for 4 weeks. Time of followup ranged from 3 months to 2 years during which no recurrences were noted. Conclusion: Short term treatment with Metronidazole may be beneficial in the management of refractory ano-rectal CD in adolescents.

505 TRANSENDOSCOPIC INJECTION SCLEROTHERAPY IN THE TREATMENT OF ESOPHAGEAL VARICES IN CHILDREN WITH IDIOPATHIC PORTAL HYPERTENSION Wallace A. Gleason, Jr., Ernesto Guerra, James E. Gray (Spons. by Myung K. Park) Univ. of Texas Health Science Center, Depts. of Pediatrics and Medicine, San Antonio, Texas.

To establish the feasibility of management of bleeding esophageal varices in patients with extrahepatic portal hypertension by injection of a sclerosing agent at esophagoscopy, thirty such injections were carried out during ten fiberoptic esophagoscopy procedures in three children with frequently bleeding esophageal varices as a result of cavernous transformation of the portal vein. The Olympus JIT endoscope was passed after heavy sedation (meperidine, 2 mg/kgm, promethazine, 1 mg/kgm, and chlorpromazine, 1 mg/kgm), Atropine, .01 mg/kgm and topical cetacaine anesthesia. Balloon tamponade was used to occlude the varices, prevent cephalad flow of the sclerosing agent and stabilize the position of the endoscope. A flexible endoscopic injector was passed through the endoscope and into each varix following which sodium morrhuate was injected until the varix was distended (1-4 ml). 3-4 injections were made at each esophagoscopy and repeat esophagoscopy was carried out 1 week later to assess progress or complications. Significant bleeding occured on only one injection and stopped promptly. No other complications were encountered. Our limited experience and short follow-up does not allow us to assess the contribution of this technique to the long term prognosis of children with portal hypertension, but indicates that it is safe, applicable to children, and may be an important alternative to portal systemic shunt procedures in pediatric patients.

506 MIDARM/HEAD CIRCUMFERENCE (MHC/FOC) RATIO: SIMPLE, RELIABLE INDEX OF NUTRITIONAL STATUS. G.S. Gopalakrishna, Donald C. Anderson, E. O'Brian Smith, and Buford L. Nichols. USDA/ARS, Children's Nutrition Research Center, Baylor College of Medicine, Houston.

A need exists for a practical measurement of nutritional status which does not require complex equipment. Kanawati and McLaren (Nature 228:573, 1970) described the MHC/FOC ratio which can be obtained with only a tape measurement. This index of nutritional status has been tested in 27 children (11 female, 16 male) of differing ethnic backgrounds with an age range of 1 to 36 months. Other anthropometric and biochemical measurements included weight, height, triceps, skinfold thickness, albumin and prealbumin concentrations. MHC/FOC ratio correlated well with weight/height and weight/height Z scores with an r value of 0.74. The correlation with skinfold thickness was 0.74. The relationship to serum albumin concentration was 0.58. The MHC/FOC ratio did not correlate with weight/age, height/age, or the prealbumin measurements. Conclusions: 1) The MHC/FOC ratio is a simple and reliable measure of nutritional wasting (reduced weight/height). 2) It is largely a function of skinfold thickness (subcutaneous fat deposits). 3) It is independent of age, sex, ethnicity, or stunting of height (height/age). 4) It is insensitive to decreased prealbumin and relatively insensitive to decreased albumin. The ratio proved to be a sensitive index of nutritional recovery in the longitudinal evaluation of these patients. MHC/FOC ratio is a practical tool for detecting nutritional wasting in infants. It is obtained easily during physical examination of the infant. (Supported by USDA/ARS).

507 FLUORESCENCE POLARIZATION (FP) STUDIES IN MICROVILLUS MEMBRANES (MVM) OF DIABETIC RATS, Glenn R. Gourley, Ward A. Olsen, Helen Korsmo, Univ. of Wisconsin, Dept. of Pediatrics; VA Hospital, Dept. of Medicine, Madison, WI.

FP studies were conducted with the fluorophore DPH in intestinal MVM from control and streptozotocin-induced diabetic rats. 1,2 and 3-phase linear and quadratic models were fitted to plots of the log-FP as a function of $^{o}Kelvin^{-1}$. Model adequacy, examined using residual plots, showed only the 3-phase and quadratic models to have random residuals. The residual sum of squares (RSS) was lowest for the 3-phase model in 38/40 plots. The quadratic model had the second lowest RSS except in 2 cases when it was lowest. The 2-phase was a significantly better fit than the linear model, and the 3-phase was significantly better than the 2-phase model on the basis of F-tests. Breakpoints (BP) and anisotrophy parameters $\{(r^{o}/r)-1\}^{-1}$ in the 2-phase (A) and 3-phase (B) models are shown below.

	Control		Diabetic	
n	5*	4§	6*	5§
A: BP (^{o}C)	22.7±2.1	24.3±1.2	23.7±1.4	23.8±0.6
$\{(r^{o}/r)-1\}^{-1}$ (37°)	1.70±.06	1.72±.09	1.70±.08	1.71±.12
B: BP#1 (^{o}C)	27.8±4.1	28.2±1.7	28.2±2.2	28.4±2.5
BP#2 (^{o}C)	15.7±5.8	17.9±2.3	17.1±2.9	17.6±2.4
$\{(r^{o}/r)-1\}^{-1}$ (37°)	1.69±.04	1.71±.09	1.70±.08	1.71±.12

(Values are mean ± SD; incubation time: *15 min; §one hour)

There is no significant difference in FP data between control and diabetic rat MVM preparations.

● **508** CHOLESTATIC EFFECT OF A SYNTHETIC PARENTERAL AMINO ACID MIXTURE: CORRELATION WITH NET AMINO ACID FLUXES. Martin F. Graham, Anthony S. Tavill, Thomas C. Halpin and Loizos N. Louis (Spon. by Harold M. Maurer). Case Western Reserve University, Depts. of Pediatrics and Medicine, Cleveland

Rat livers (10-12 g) were perfused in a recirculating system. A mixture of Na taurocholate (TC) and [^{14}C] TC was infused into the perfusate. Timed bile specimens were collected in 100 µl aliquots and perfusate was sampled at 35' and 90'. A 50 min primed-constant infusion of synthetic L-amino acids (Travasol, 8.5% w/v) was begun at 40' (amino N:1.7 mg prime dose, 0.27 mg/min infusion). Controls were infused with saline.

Results

Expt. (n)	Bile flow-90' (% steady state value)	TC excretion-90' (% steady state value)	40'-90' TC recovery (% infused TC)	
Control 9	88.3 ± 2.1	100.7 ± 0.8	101.7 ± 2.3	
AA 8	*69.6 ± 4.5	*97.2 ± 1.2	*95.3 ± 1.7	*p<0.05

Net uptake of AA was most marked for glycine and alanine (144 and 130 µmole/hr), modest for phenylalanine, arginine and methionine (35.4, 32 and 26.4 µmole/hr) and 0 for valine, leucine and isoleucine. Relative uptake (as % of AA infused) was maximal for phenylalanine and tryptophan (84 and 60%). Post-infusion levels of glycine and arginine were markedly increased (5x and 3x) over post-prandial levels reported in the intact rat. Conclusions L amino acids administered to the perfused liver reduce bile flow and to a lesser degree TC excretion. These changes may be related to an increase in the ambient concentrations of specific AA and/or to an increase in the uptake of specific AA, and may be relevant to the cholestasis associated with parenteral alimentation.

509 AN IMPROVED TECHNIQUE FOR ACCURATE DETERMINATION OF BONE MINERAL CONTENT (BMC) AND IDENTIFYING DISORDERS OF BONE MINERAL METABOLISM IN LOW-BIRTH-WEIGHT INFANTS. F. Greer, J. Lane, S. Weiner, R. Mazess (Sponsored by R. Chesney), University of Wisconsin, Madison, Wisconsin.

A microcomputer-based system using ^{125}I absorptiometry for determination of BMC and bone width (BW) in infants was designed to allow: a) high accuracy and precision, b) high reproducibility, c) automatic data calibration with direct readout, and d) use of a low activity source (50mCi). The system accurately determined BMC on 9 small bone sections (range 29-212 mg/cm) confirmed by ashing of the bone sections (r=.99, S.E.E.=2.1 mg/cm). The regression line derived from weight of ashed bones and measured BMC was used to calibrate a bone phantom used in daily calibration. Long-term precision (months) of the phantom demonstrated a C.V. of 2.0%. Measurements of BMC, BW and BMC/BW were made on the radius of 100 appropriate-for-gestational age infants from 22-42 weeks gestation. A series of 4-6 scans were done on each infant (C.V.=3.7%). The range of BMC measured was 21-127 mg/cm. In 78 infants, the arm was repositioned and the scan repeated immediately. The correlation between the two BMC determinations was high (r=0.96,S.E.E.=6.20mg/cm, p<.002). BMC correlated with gestational age (r=0.85, p<.002) and birth weight (r=0.87, p<.002). Four low-birth-weight infants with chronic lung disease were identified as having a disorder of bone mineral metabolism using this improved system. Though BW in these 4 infants increased with time, BMC was decreased and a graph of BMC vs BW shows that these infants fell consistently 2 S.D. below the expected values.

510 ESOPHAGEAL ACID CLEARANCE IN INFANTS WITH GASTROESOPHAGEAL REFLUX. Bruce B. Grill, Craig Hillemeier, Richard McCallum, Joyce D. Gryboski. Yale Univ. Sch. Med., Dept. of Pediatrics, New Haven, Connecticut.

Esophageal acid clearance may play an important role in infants with gastroesophageal reflux (GER). To investigate this we studied 20 infants (x̄ age 7.9 mo) with GER by esophageal manometry and prolonged pH probe studies. Acid clearance time (ACT) was defined as amount of time required for esophageal pH to rise 2 pH units after ingestion of 5 and 10 cc apple juice in sitting and supine position. Swallowing was encouraged by having the infant suck on a pacifier. In 12 patients with > 75% normal peristaltic sequences on esophageal manometry, x̄ ACT for 5 cc in the supine position was 1.57±0.26 S.E. min. In 8 patients with <75% normal peristalsis, ACT was 2.9±0.56 S.E. min. This difference is significant at the 0.05 level. 11 patients had AC both in sitting and supine positions using similar volumes of apple juice (pH=4.0).

	5 cc		ACT, minutes	10 cc	
	supine	sitting		supine	sitting
N=11	*3.21±0.6	*4.96±0.62		4.78±0.8	6.1±1.36

*p < 0.001

We conclude: 1) Abnormal peristaltic activity is correlated with delayed acid clearance 2) ACT is significantly delayed in sitting vs. supine position. We speculate that abnormal peristaltic activity may be important in the pathogenesis of GER and that the traditional chalasia chair may result in delayed acid clearance.

511 INTESTINAL CLEARANCE OF ALPHA-1-ANTITRYPSIN (CA-1-AT) IN RELATION TO ENTERIC BLOOD LOSS. Bruce B. Grill, Thomas Tinghitella, Craig Hillemeier, Joyce Gryboski. Yale Univ. Sch. Med. Dept. Pediatrics, New Haven, Connecticut.

In a 12 month period we studied 25 patients (3 mo-17 yr) with a variety of gastrointestinal complaints. After clinical and laboratory evaluation, CA-1-AT was performed on 72 hour stool collections with serum A-1-AT obtained on day 1. Stool and serum A-1-AT values were determined by radial immunodiffusion against standard anti-sera. CA-1-AT was calculated: CA-1-AT = S x V/P (cc/day) S=stool A-1-AT concentration (mgm/gm); V=stool volume (gm/day); P=serum A-1-AT concentration (mgm%). Ten controls (functional abdominal pain, psychosocial FTT, chronic non-specific diarrhea) with normal albumin values, had a mean CA-1-AT of 2.35±1.77 cc/day. 9 patients with IBD and/or a history suggesting protein-losing enteropathy (PLE) were divided into those with and without blood loss (defined as any gross blood or guaiac + stools within one month of the A-1-AT determination).

Blood Loss			No Blood Loss		
Dx	Alb	CA-1-AT	Dx	Alb	CA-1-AT
Colitis	4.1	0.2	Crohns ds.	4.0	1.9
U.colitis	4.8	0.3	CD	2.8	71.2
Colitis	4.5	3.76	CD	3.1	55.8
Polyps, PLE	2.8	100.8	CD	3.1	11.3
PLE	2.2	277.0			

Patients with blood loss had CA-1-AT > $\bar{x}$ 2 SD of the controls only if PLE was present. 3/4 with CD and no blood loss had CA-1-AT > $\bar{x}$ + 2 SD. Blood loss alone was not sufficient to produce an elevated CA-1-AT.

512 AMINOSUGAR CONTENT IN STOOLS OF NEWBORNS. Lawrence J. Grylack, Dilbagh Sidhu, and Margit Hamosh. (Spon. by John W. Scanlon). Columbia Hospital for Women and Georgetown University Department of Pediatrics, Washington, D.C.

The amounts of the aminosugars glucosamine and galactosamine were measured in the stools of 20 human newborns in an attempt to assess the effects of asphyxia and maturity on gastrointestinal function. Birthweight was 3144 ± 1141 g (Mean ± S.D.), and gestational age was 35.7 ± 5.9 weeks. Ten babies had perinatal asphyxia on the basis of a one-minute Apgar score of ≤6, or a cord pH<7.25. Two successive stools collected from all babies after birth underwent acid hydrolysis and precipitation with ethanol and Ehrlich's reagent. The aminosugar content was determined by absorbance colorimetry in comparison to standard solutions.

	ASPHYXIA	CONTROL
AMINOSUGAR CONCENTRATION (micrograms/10 g stool)	1st stool 10.40±2.94mcg	8.97±2.08mcg
	2nd stool 10.17±3.67mcg	10.93±2.46mcg

Comparison of the measurements in the first and second stools of both groups showed no significant differences. The second stool of the control group contained a greater aminosugar concentration than the first stool ($p<.10$). Gestational age was inversely correlated with the aminosugar concentration of the first stool ($p<.01$), and the second stool ($p<.05$). The results indicate that stool mucous aminosugars can be measured in a consistent manner and that these measurements show a correlation with gestational and postnatal age.

● **513** SERUM VITAMIN E RELATIVE TO NEUROMUSCULAR DISEASE IN CHILDREN WITH CHOLESTASIS. Mary Anne Guggenheim, Virginia Jackson, John R. Lilly, and Arnold Silverman (Spon. by Frederick C. Battaglia), University of Colorado School of Medicine, Departments of Pediatrics and Surgery, Denver.

Strong evidence now exists that prolonged deficiency of vitamin E (E) can result in progressive neurologic disability characterized by ataxia, ophthalmoplegia, sensory loss, and areflexia in children with chronic cholestasis. Moreover, normalization of serum E levels, which usually requires intramuscular injection of alpha-tocopherol, can reverse the neurologic abnormalities (Rosenblum et al, NEJM 304:503, 1981; Guggenheim et al, J. Peds., in press). To further understand the development of this nutritionally-induced neurologic disease, we have prospectively evaluated serum E levels and neurologic status in 42 children with underlying cholestatic disease. We found that 34 (81%) have subnormal E levels ranging from less than 0.05-0.35 mg/dl (N=0.5-1.5 mg/dl). Only 2 patients were able to normalize serum E levels with high dose oral treatment. Correlation of the age of the child, the neurologic status, and serum E levels will be presented and supports the following hypotheses: 1) clinically apparent neurologic abnormalities do not become manifest until 4 years or more of an E-deficient state; 2) 6 years or more of an E-deficient state result in a 90% probability of clinical disease; and 3) areflexia is the initial neurologic finding. Parenteral administration of alpha-tocopherol, which currently requires an experimental protocol, may be indicated in the majority of children with congenital biliary atresia or other cholestatic syndromes.

514 REYE'S SYNDROME MODEL IN RATS WITH PHOSPHORUS (P_4) Mina Gurevitz, Geoffrey C. Tombaugh and Kathleen B. Schwarz (Spon. by P. Monteleone) St. Louis Univ. School of Medicine, Cardinal Glennon Mem. Hospital for Children, Department of Pediatrics, St. Louis, Missouri.

P_4, widely used in industrial chemical manufacturing, was chosen for our RS model because in P_4 poisoning (P_4P) and RS there are many clinical, biochemical, histological, histochemical and ultrastructural similarities. Male Sprague-Dawley rats 90-180gr were given 0.55-0.75mg P_4/100gr rat by orogastric tube and killed at intervals. Ultrastructural studies showed progressive increases in endoplasmic reticulum, fat droplets and mitochondrial size confirmed by point analysis. Hepatic triglyceride (TG) and muscle Pi were:

Liver	Rat	6 Hours	12 Hours	24 Hours
wt. (gr)	P_4	4.2±0.4	4.1±0.1	4.5±0.2
100 gr rat	Control	2.9±0.1	3.2±0.3	3.2±0.1
TG mg	P_4	58±22	63±16	62±37
100 gr rat	Control	21±2	24±5	10±4
Mitochon. Vol	P_4/Control	1.69/1	1.30/1	1.15/1
Muscle				
Inorganic Pi	P_4	3.7±0.8	2.6±0.4	4.5±0.6
ng/µg protein	Control	1.1±0.2	1.5±0.4	1.3±0.2
Total Pi	P_4	17.8±3.8	31.4±6.1	31.1±4.0
ng/µg protein	Control	19.0±1.4	16.3±4.2	14.5±4.2

Summary: P_4 can be used for a rat model of RS as a basis to test synergistic effects of viruses. We suggest that a possible etiologic role for P_4 or related compounds be investigated in patients with RS.

515 MYOINOSITOL (INO) - IMPORTANT NUTRIENT DURING PERINATAL PERIOD? Mikko Hallman, Patricia I. Bromberger, Richard Porreco, Benita L. Epstein. University of Calif., S.D., Department of Pediatrics, La Jolla, California.

Fetuses and premature newborns have high serum INO. Excess INO prevents surfactant phosphatidylglycerol synthesis, and decreases the capacity of surfactant to stabilize airways at birth. The importance of high INO is not known. Previous studies suggest that INO is synthesized in the fetus. In the present study we measured INO in 1) fetal serum during elective cesarean section at term; 2) infant feedings; 3) serum from premature infants. 1) INO in sera from umbilical artery (UA) and umbilical vein (UV) were as follows (n=8):

	INO in UA	INO in UV	UV-UA	Gestational age
INO (mM; mean±SEM)	0.11±0.01	0.16±0.03	0.05±0.01	40±1 weeks

2) Dietary INO concentrations were as follows: Breast milk 2.5 (range 0.6-5.6)mM (n=22); Infant formulas 0.3 (0.0-0.5)mM (n=4); parenteral nutrition 0.2 (0.0-0.3)mM (n=4). 3) Premature infants were fed with breast milk (BM), formula (IF), or were on parenteral nutrition (PN). Serum INO(mM) after 1st neonatal week were:

Diet/Age*/n	BM	Age	n	IF	Age	n	PN	Age	n
INO/weeks/n	.59±0.8+	33±1	8	.16±.03	34±1	3	.31±.04	33±1	9

*Weeks from conception. +P<.01 as compared to IF and PN.

Term fetus seems to receive INO from placenta, and dietary INO contributes to high serum INO in the newborn. Experimental studies indicate that healing of lung damage improves during INO supplementation, and deteriorates during INO deficiency. Therefore, adequate INO may prove to be important in dietary management of sick newborns. Supported by NIH Grant No. HD 10622.

516 HUMAN MILK IN CYSTIC FIBROSIS: (CF) COMPOSITION AND ENZYME CONTENT. Margit Hamosh, Joel Bitman, D. Larry Wood, Nitin R. Mehta, Michael J. Welch, Alan B. Osher, Jay B. Jones and Paul Hamosh. Georgetown University Medical Center, Washington, D.C.; UCLA Med. Sch., Los Angeles and USDA, Beltsville, MD. (Spon. by J.W. Scanlon.)

In order to assess whether mammary gland function is normal in CF we have analyzed milk specimens obtained from a 20 year-old woman with CF at 3 days, 7 and 10 wks of lactation.

	CYSTIC FIBROSIS			CONTROL		
	Colostrum	7 wks	10 wks	Col.	6 wks	12wks
Protein g/dl	2.0	1.34	1.0	2.50	1.62	1.20
Neutral fat g/dl	1.2	2.60	0.48	2.14	3.60	2.0
Phospholipid mg/dl	16.2	22.6	5.4	10.7	15.5	15.4
Cholesterol mg/dl	14.0	14.5	6.11	13.77	8.1	12.6

Analysis of fatty acid (FA) composition showed a twofold increase of $C_{12:0}$ and $C_{14:0}$ and a 30-50% decrease of $C_{18:1}$ and $C_{18:2}$, suggesting that FA synthesis within the mammary gland compensates for lower availability of dietary FA ($C_{18:1}$ and $C_{18:2}$). Bile salt stimulated lipase and esterase, lipoprotein lipase and α amylase were present in CF milk, although in lower concentration than in control milk obtained at similar stages of lactation. The data show that the milk produced by CF patients could provide adequate nutrition for the newborn during the first few weeks after birth. The marked decrease in total fat and protein content at 10 wks, suggests that prolonged lactation cannot be sustained in CF. (Support, NIH Grant AM 26641.)

517 IgA IMMUNE COMPLEX CLEARANCE DURING PREGNANCY: EFFECT OF HORMONAL ENVIRONMENT ON HEPATOBILIARY TRANSPORT OF POLYMERIC IgA (pIgA). Paul Harmatz, Ronald Kleinman, Daniel McClenathan, Bruce Bunnell, Kurt Bloch and W. Allan Walker, Harvard Medical School, Massachusetts General Hospital, Department of Pediatrics and Medicine, Boston, MA. 02114

Although hormonal changes of pregnancy and lactation appear to influence the transport of pIgA into breast milk, the effect of these hormones on transport of pIgA and IgA immune complexes across other epithelial surfaces has not been determined. In this study we examined whether the hormonal changes of pregnancy and lactation affect the hepatobiliary transport of pIgA in the form of IgA antibody-antigen complexes. After cannulation of the common bile duct, adult female Sprague-Dawley rats were examined at day 20 of pregnancy (P-20) or day 1 of lactation (L-1), and were compared to non-pregnant, non-lactating controls (C). pIgA-anti-dinitrophenyl (DNP) antibody was prepared from the ascitic fluid of mice bearing the MOPC-315 plasmacytoma. Antibody was injected intravenously immediately followed by the antigen, ^{125}I-DNP$_{10}$-bovine serum albumin. Timed serum and bile samples were analyzed for trichloracetic acid, ammonium sulfate and immunoprecipitable radioactivity. The clearance of IgA immune complexes from serum in P-20 and L-1 animals was significantly more rapid than in controls. The appearance of IgA immune complexes in bile was 7 to 15 fold higher in P-20 and L-1 animals than in controls. These observations in lactating and pregnant animals suggest that the hormonal milieu influences the hepatobiliary transport of pIgA and therefore may be an important modulator of the secretory component-mediated vesicular transport of secretory immunoglobulin.

518 IS MOTHER'S MILK NUTRITIONALLY ADEQUATE FOR HER PREMATURE INFANT? Janet K. Harnsberger, Linda S. Book, Gary Chan. (Spon. by Lowell Glasgow) University of Utah Medical School, University of Utah Medical Center, Department of Pediatrics, Salt Lake City.

There is controversy over feeding premature infants their own mother's milk. We studied the nutrient content of milk from 45 mothers delivering infants of 26-36 weeks gestation. Milk being fed to their infants during the first month of life was analyzed for phosphorous, calcium, protein, fat, and lactose. Caloric values were calculated.

		RANGE	MEAN	%meeting* R.N.I.
Phosphorous	mg/dl	3-14.5	7.8	0%
Calcium	mg/dl	15.4-47.4	26.6	0%
Protein	g/dl	1.23-3.83	2.06	72.7%
Fat	g/dl	0.75-15.4	5.7	91%
Lactose	g/dl	4.06-9.68	6.08	
Kcal/dl		38-180	85.5	

*American Academy of Pediatrics Recommended Nutrient Intake (RNI)

This human milk has a large variability of nutrient contents. Phosphorous and calcium were both strikingly below recommended levels in all samples. Using a minimum standard of 110 kcal/kg/d, if these infants were fed 150 cc/kg/d, 41% of the milks would not provide adequate calories. Over 50% of the milks analyzed did not meet AAP recommendations for three or more nutrients. If prematures infants are fed their own mother's milk, calories, phosphorous, calcium, protein, and fat as recommended by the American Academy of Pediatrics may be seriously deficient.

519 HUMAN MAMMARY AMYLASE: A POSSIBLE ALTERNATE PATHWAY OF CARBOHYDRATE DIGESTION IN INFANCY. Leo A. Heitlinger, Ping-C Lee, William Dillon, and Emanuel Lebenthal. Divisions of Gastroenterology and Obstetrics, Children's Hospital and SUNY at Buffalo, Buffalo, N.Y.

In the first few months of postnatal life, infants have little or no pancreatic amylase detectable in duodenal fluid, serum, or urine. Despite this physiologic deficiency, intolerance to dietary glucose polymers occurs in few infants. Human breast milk has amylase concentrations in the range of 10 to 100 times that of adult human serum, an amount far greater than reported in the saliva and duodenal fluid in early infancy. In order to evaluate the likelihood that a significant proportion of the activity would withstand passage through the stomach, purified and unpurified mammary amylase was exposed, in vitro, to acidity comparable to that found in the stomach of a young infant following a breast milk meal. More than one-half and one-third of the original activity was maintained for four and six hours respectively. Physiologic concentrations of pepsin did not affect any greater decay, despite a decrease in large molecular weight proteins, and an increase in amino acids and small peptides in the reaction medium. Purified mammary amylase decayed more rapidly; when albumin or breast milk proteins were present, the stability was comparable to that of whole, fresh frozen breast milk, incubated under the same conditions. Human mammary amylase may correct, in part, the physiologic pancreatic amylase deficiency of early infancy, and allow the infant to digest and absorb polymers of glucose.

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520 FACTORS CONTROLLING THE DEVELOPMENTAL APPEARANCE OF THE CIRCADIAN RHYTHM OF JEJUNAL SUCRASE ACTIVITY IN THE RAT. Susan J. Henning and Dolores M. Guerin, University of Houston, Department of Biology, Houston, TX 77004.

A circadian rhythm of jejunal sucrase activity has been shown previously to make its developmental appearance in the rat at the time of weaning (day 22). The process of weaning constitutes a complex environmental change for the intestinal tract because the diet changes in terms of: a) physical consistency (liquid → solid); b) relative proportions of carbohydrate (CHO) and fat (high fat/low CHO → low fat/high CHO; and c) nature of the CHO (predominantly lactose → starch, sucrose, etc.). There is also a significant change in the rhythmic pattern of ingestion. The aim of this work was to clarify the relative roles of the weanling diet per se and the timing of the feeding rhythm as cues for the appearance of the circadian rhythm of jejunal sucrase activity. We found that the rhythm was not present on day 23 if the onset of feeding was not coordinated with the onset of darkness. Conversely, the sucrase rhythm appeared precociously (day 19) in pups weaned onto chow on a schedule in which the onset of feeding was coordinated with the onset of the dark period. To determine whether the composition of the weanling diet is important, pups were weaned onto 3 different liquid diets: A = low CHO (glucose); B = high CHO (glucose); and C = high CHO (lactose). By day 19 a distinct sucrase rhythm was present in B pups, but no rhythm was present in A and C pups. It is concluded that nocturnal ingestion of a high-CHO diet is responsible for the developmental appearance of the circadian rhythm of jejunal sucrase activity.

This work was supported by NIH grant number HD 14094.

521 POSTNATAL DEVELOPMENT OF INTESTINAL BILE ACID TRANSPORT IN THE RAT. James E. Heubi, Janette L. Rigney, and Frederick J. Suchy, (Spon. by William F. Balistreri), Children's Hospital Research Foundation, Cincinnati, Ohio.

Impaired intestinal bile acid (BA) transport may be partially responsible for contracted BA pools and steatorrhea in term and preterm infants. We examined postnatal intestinal BA transport using the villus technique. Segments of jejunum and ileum from various age rats were incubated for 2 minutes in Krebs Ringer Bicarbonate buffer (pH 7.4) with glucose and taurocholate (TC) at 0.1, 0.25, 0.50, 1.0, 2.0 and 3.5 mM concentrations. Villi were isolated and villus uptake (μMol/mg(dry wt)/min) calculated. Jejunal uptake was linear with respect to incubation TC concentration at all ages. Ileal uptake was linear with TC concentration in 1 and 2-week (wk) rats, changing to a curvilinear relationship by 3 wks. The TC monomeric permeability coefficient (P_{app}(μMol/min/mg (dry wt)/mM)) was variable with age; ileal TC maximal transport velocity (V_{app}(μMol/min/mg(dry wt)) and Michaelis constant (K_m(mM)) were first apparent at 3 wks:

	1-wk(n=18)	2-wk(n=26)	3-wk(n=19)	4-wk(n=15)	adult(n=15)
P_{app}	.26	.27	.22	.27	.44
V_{app}	0	0	13.14	9.81	9.61
K_m	0	0	.37	.48	.46

Conclusions: 1) TC transport is exclusively passive in both ileum and jejunum of 1 and 2-wk rats. 2) Age-related differences in permeability do not facilitate BA recycling before the development of ileal active transport. 3) At the time of weaning, ileal active transport first appears and persists into adulthood. 4) The development of efficient enterohepatic cycling of BA in the rat in the first 3 wks coincides with pool expansion.

522 ACTION OF BETHANECHOL AND METOCLOPRAMIDE ON THE UPPER GASTROINTESTINAL TRACT IN THE KITTEN. Craig Hillemeier Robin Oertel, Richard McCallum, Joyce Gryboski. Yale Univ. Sch. Med., Dept. of Pediatrics, New Haven, Connecticut.

Metoclopramide (M) and Bethanechol (B) are being used to treat reflux of infancy but little is known of their mechanism of action on the developing intestinal tract. We examined their effects on esophageal peristaltic amplitude, lower esophageal sphincter pressure (LESP) and gastric emptying (GE) in 6 week old kittens. Amplitude and LESP were determined with double lumen perfusion catheters (1.1 mm O.D., rate of rise >800 mm Hg). Gastric emptying studies were performed by the instillation of 30 cc's/kg of 10% dextrose and a phenol red withdrawal technique. B at 80 mcg/kg or M at 200 mcg/kg were injected I.M. 30 min. prior to studies. LESP increased from 17.2 mm Hg to 32.8 mm Hg with B ($p < 0.001$) and from 16.2 to 19.3 mm Hg with M ($p < 0.05$). Peristaltic amplitude was unchanged with either B or M.

	Pre		M		B	
	5 min	10 min	5 min	10 min	5 min	10 min
%GE	33.6 ±3.4	57.2* ±3.8	38.8 ±5.0	72.0* ±7.9	36.4 ±4.6	50.4 ±5.7

*At 10 min. gastric emptying with M was significantly faster than the pre-treated state ($p < 0.05$). We conclude: B in the 6 week old kitten increases LESP but has no effect on esophageal peristaltic amplitude or GE; M increases LESP less than B, has no effect on esophageal peristaltic amplitude and significantly increases GE of a liquid meal. We postulate that M may be of significant value in infants with gastroesophageal reflux and delayed GE.

523 PHOSPHORUS DEFICIENCY IN INFANTS < 1200 GMS FED HUMAN MILK; RELATIONSHIP TO 25-HYDROXYVITAMIN D (25-OHD). L. Hillman, S. Salmons, and B. Fiore. Wash. U. Med. Sch., St. Louis Child. Hosp., Dept. Ped., St. Louis

10 premature infants of mean gestation 29.1 ± 1.5 weeks and mean birthweight 1049 ± 127 gms were fed their mothers breast milk. Serum and urine 25-OHD, calcium, phosphorus, and magnesium were monitored weekly. Over the first 8 weeks of life serum and urine phosphorus fell. Concomitantly urine calcium increased. Serum calcium transiently rose then fell to low levels. By 7 to 8 weeks the degree of these changes prompted therapeutic phosphorus supplementation in 5 of 10 infants. Mean serum 25-OHD fell. Analysis of individual 25-OHD patterns showed that the infants who did not require supplementation had sustained high 25-OHD concentrations or low 25-OHD concentrations which increased whereas infants requiring phosphorus supplementation had high 25-OHD concentrations which fell or persistently low 25-OHD. Breast milk feeding of very premature infants produces a progressive phosphorus deficiency because of the milk's low phosphorus content; however, this may be further exacerbated by 25-OHD insufficiency and both parameters require monitoring.

Week of Age (n)	2(6)	3(9)	4(7)	5(8)	6(10)	7(9)	8(8)
25-OHD ng/ml	22.	19.	15.	21.	27.	17.	17.
Serum Ca mg/dl	9.1	9.1	9.8	9.7	9.3	9.1	8.9
Serum P mg/dl	5.7	6.3	6.1	5.5	4.9	4.9	4.5
Serum Mg meq/L	1.8	1.8	1.7	1.7	1.7	1.8	1.7
Urine Ca mg/dl	3.7	5.7	6.8	17.1	7.7	5.2	19.
Urine P mg/dl	13.7	11.1	6.5	4.8	3.7	1.4	.8
Urine Mg meq/L	1.4	2.0	1.7	3.0	1.4	1.5	3.5

524 EVALUATION OF DIETHYL-IDA RATE CONSTANTS IN RAT MODELS SIMULATING NORMAL AND ATRETIC BILIARY FUNCTION. David C. Hitch, Joseph C. Leonard, Carl V. Manion, Roy B. Deal, Margaret King, Theodore J. Pysher, and Paul B. McCay (Spon. by William G. Thurman). Oklahoma Medical Research Foundation, University of Oklahoma Health Sciences Center, Oklahoma City.

Changes in hepatocellular function should be reflected in the distribution and elimination of compounds which are preferentially secreted into bile. Technetium 99^m labeled 2,6-diethylacetanilide-iminodiacetic acid (diethyl-IDA) is ideal. The present study was designed to quantify surgically and biochemically produced hepatic injury. A three compartment model with simultaneous elimination from two compartments described the elimination. Concurrent computer fitting of the cardiac and hepatic time-activity curves with the model quantified the rate constants. Sprague-Dawley male rats (200-400 gm.) were divided into three experimental groups: normal (n=13), bile duct ligated (n=6), and galactosamine treated (n=3, 400 mg./i.p./kg.). Bolus diethyl-IDA (250 mCi.) was injected. The observed rate constants (Table) reflect no hepatic elimination with surgically ligated bile ducts. Galactosamine produced a similar diminution in hepatic tracer elimination.

Rate Constants[a]	K12	K21	K13	K31	K10[b]	K20[c]
Normal	.196	.120	.113	.008	.070	.008
Bile Duct Ligated	.256	.048	.226	.238	.021	.000
Galactosamine	.442	.051	.183	.185	.120	.001

(a) mean values (b) renal (c) hepatic

It is concluded that the rate constants 1) are a function of the tracer distribution, 2) classify experimentally induced hepatic pathology, and 3) quantify relative elimination.

525 DIGESTION OF CORN SYRUP SUGARS IN NEONATES: IMPORTANCE OF SALIVARY AMYLASE AND GASTRIC HYDROLYSIS. Charles Hodge, Ping-C Lee, William Topper, and Emanuel Lebenthal. Children's Hospital, SUNY at Buffalo, Buffalo,N.Y.

Digestion of corn syrup sugars (CSS) in prematures has received attention only recently. Reports showed intolerance in some premature infants. To evaluate the digestive capacity of CSS in premature infants, we investigated the role of salivary amylase (A) in the initial degradation of these polymers of glucose. Samples of saliva and gastric fluid from fed and fasting infants 30 to 42 weeks of gestation were assayed for A activity. The A in the gastric fluid was further analyzed by polyacrylamide gel electrophoresis. In addition, degradation products of CSS in the gastric fluid were analyzed by thin layer chromatography (TLC). Activity of A was detected in the saliva of infants as early as 29 to 30 weeks of gestation. The level of A did not change from 29 to 42 weeks and seemed to relate to the secretory activity of the salivary glands. The majority of gastric fluids was shown to contain A with electrophoretic mobility identical to salivary A. The presence of A activity was pH dependent and was invariably present at a pH>3.5. The activity of gastric aspirates was shown to be related to feeding. Up to 90 min. after a gavage feeding, the pH of the gastric fluid remained above 3.5. TLC of gastric fluid containing CSS did not reveal significant degradation. The results suggested that the salivary A was present in premature infants. Thus A could survive the gastric environment in these infants and may be important as an amylolytic agent in the small intestine where the conditions are optimal for its activity.

Supported in part by NIH Grant #12586.

526 HYDROXY-METHYLGLUTARYL CoA LYASE: DEFICIENT ACTIVITY OF LIVER AND FIBROBLASTS AND HEPATIC STEATOSIS IN COUSINS WITH TOM CAT ODOR. George Hug, Evelyn Landrigan, Frederick J. Suchy, Shirley Soukup and Helen Berry. Department of Pediatrics, University of Cincinnati, Cincinnati, Ohio 45229.

Two children of brothers married to unrelated women, a girl age 12 months and a boy age 8 months, had vomiting, lethargy, coma, hepatomegaly, hyperammonemia, elevation of serum transaminases and "Tom cat" odor. Diagnostic considerations included: Reye's syndrome, carnitine deficiency, urea cycle defect, glycogenosis and deficient hydroxy-methylglutaryl CoA (HMG-CoA) lyase. Skin fibroblast cultures and needle biopsy specimens of liver and muscle were studied biochemically and by light- and electron-microscopy (EM). Tissue concentration of glycogen and carnitine was normal as was liver urea cycle activity. EM of liver showed normal mitochondria but marked micro- and macrovesicular fatty infiltration. EM of muscle showed large mitochondria with tightly packed cristae, increased numbers of lipid droplets (= non-specific changes). HMG-CoA lyase activity in fibroblast cultures was not detectable; HMG-CoA lyase activity in liver was (in μm acetoacetate/min/g): 0.26; 0.32 in the patients and 3.52 ± 1.28 in 16 controls.

We conclude that the initial differential diagnostic dilemma that has been reported repeatedly in the literature can easily be resolved by the described analysis of a needle liver biopsy specimen.

527 MATURATION OF GASTRIC ACID SECRETORY FUNCTION IN PRETERM INFANTS. Paul E. Hyman, Susan Everett, Barbara Nygard, Diana Stewart, and John D. Walsh. Sponsored by Rosemary D. Leake, UCLA School of Medicine, Department of Pediatrics, Harbor-UCLA Medical Center, Torrance.

Pentagastrin (PG), the C-terminal tetrapeptide of gastrin, is a gastric acid secretogogue. Term infants do not respond to administration of pentagastrin in the first two days of life. In order to describe the maturation of acid secretory function in healthy preterm infants, we measured fasting serum gastrin (SG), basal gastric acid secretion (BAO), and PG stimulated maximal acid secretion (MAO). Infants were at least one week old and all received enteral feeding. Studies on each infant were repeated weekly. The mean gestational age was 33 wks (range 27-38 wks). In all, 72 studies were performed on 20 infants. Results were expressed as the mean ± SEM in μmoles $kg^{-1}hr^{-1}$ for BAO and MAO, and pg ml^{-1} for SG.

	POSTNATAL AGE 1-2 wks(n=17)	3-4 wks(n=20)	5-8 wks(n=20)	9-14 wks(n=15)
BAO	24±4	27±6	26±4	30±5
MAO	30±5(NS)	46±7(p<.05)	49±6(p<.02)	80±6(p<.001)
SG	60±10	76±8	61±12	85±11

In healthy preterm infants, BAO and SG were similar to previous studies in term infants and did not change with age. The efficacy of PG increased with postnatal age, but was unaffected by gestational age. Maturation of gastric acid secretory function may be due to growth of parietal cell mass or to an increased response of the parietal cells to PG, and appears to be the result of postnatal influences.

● **528** ENTERAL FEEDING STIMULATES THE DEVELOPMENT OF GASTRIC ACID SECRETION IN HUMAN INFANTS. Paul E. Hyman, Edward J. Feldman, Marvin E. Ament. UCLA School of Medicine, Center for the Health Sciences, Department of Pediatrics, Los Angeles.

Enteral feeding promotes the growth of gastrointestinal tissue in laboratory animals. The effects of enteral feeding on the development of the gastrointestinal tract in human infants are unknown. Basal gastric acid secretion (BAO) and pentagastrin stimulated maximal acid secretion (MAO) were significantly decreased (p.<01) in 12 infants with intestinal disorders requiring total parenteral nutrition (TPN) a mean of 10 mo. (range 1.5.-24 mo.) compared to 10 infants with similar illness but nourished with a combination of enteral and parenteral alimentation. Results were expressed as the mean ± SEM.

	TPN	TPN plus Enteral
BAO (μmoles H^+ $kg^{-1}hr^{-1}$)	15 ± 30	35 ± 29
MAO (μmoles H^+ $kg^{-1}hr^{-1}$)	39 ± 44	131 ± 75

In each of 6 infants fasted a mean of 5 mo. (range 1.5.-10 mo.) BAO and MAO increased after a 6 to 8 wk. trial of enteral feeding, a highly significant difference.

	TPN	TPN plus Enteral
BAO (μmoles H^+ $kg^{-1}hr^{-1}$)	4 ± 1	38 ± 5
MAO (μmoles H^+ $kg^{-1}hr^{-1}$)	34 ± 16	121 ± 30

In one infant, the ability to secrete normal amounts of acid in response to pentagastrin, achieved after an initial trial of enteral feeding, was lost after a 4 mo. enteral fast, but returned following a second period of enteral feeding. These results demonstrate that in human infants, enteral feeding is necessary for the development and maintenance of gastric acid secretory function.

529 LACK OF EFFECT OF HEPARIN ON TRIGLYCERIDE LEVELS IN PREMATURE INFANTS GIVEN INTRALIPID INFUSIONS. Evelyn Jeffrey, Celia Satterwhite, Judy Bonner, Joseph B. Philips, and George Cassady. University of Alabama in Birmingham, Department of Nutrition Sciences and Pediatrics, Birmingham.

To determine if heparin enhances triglyceride (TG) clearance during Intralipid infusion, we measured serum TG, using an enzymatic technique, in 10 preterm infants. Mean gestational age (± SD) was 28 ± 2 weeks, birthweight 1055 ± 215g and postnatal age 3.5 ± 2.1 days. Intralipid was infused at 2g/kg over 8 hours. A crossover design was used, with each subject serving as his own control. During the experimental period, 150 IU heparin/kg was infused over 12h; during the control period, no heparin was given. TG levels were determined preinfusion (0h), midpoint (4h), endpoint (8h), 2h postinfusion (10h), and 4h postinfusion (12h) of Intralipid.

Mean TG levels (mg/dl) were:

	Hours				
	0	4	8	10	12
Intralipid with Heparin	84	346	485	264	182
Intralipid without Heparin	108	374	468	360	167

At no sampling times were significant differences seen between control and experimental TG levels. Mean TG levels remained significantly elevated 4h postinfusion when compared with preinfusion concentrations, both during the control and experimental periods. These findings indicate that the concomitant infusion of 150 IU heparin/kg with 2g Intralipid/kg over 8h does not significantly affect triglyceride levels.

530 FUNCTIONAL SIGNIFICANCE OF SERUM VITAMIN E LEVELS L. Johnson, C. Dalin, R. Dworanczyk, B. Harrison, Univ. of Pa. Med. Sch. Penn. Hosp. Dept Peds, Phila,Pa.

Over the past decade there has been an increase in the serum E levels measured shortly after birth and during the next few weeks among well preterm infants admitted to our nurseries. However, susceptibility to oxidant stress as estimated by % hemolysis or production of malondialdehyde (nM/gmHgb) by red blood cells on exposure to H_2O_2 (2.4%) has not shown a similar pattern.

	Age 1 - 6 days			Age 15 - 21 days		
	Serum E mg/dl	RBC H_2O_2 %	RBC MDA nM/gm	Serum E mg/dl	RBC H_2O_2 %	RBC MDA nM/gm
1972	0.31	54%	-	0.29	59%	-
N=30	σ 0.12	σ 20%	-	σ 0.09	σ 17%	-
1978	0.76	80%	586	1.1	48%	463
N=38	σ 0.29	σ 16%	143	σ 0.36	σ 36%	σ 191

Adults (Phila) $\bar{x}E=1.1\pm0.2$, $\bar{x}RBC\text{-}H_2O_2=15\%\pm5\%$, $\bar{x}RBC\text{-}MDA=132\pm59$

The data suggest that an increased placental transfer of both polyunsaturated fats and alpha tocopherol occurred during the gestation of infants born during 1978 as compared to 1972. This is not unexpected, considering the continuing emphasis on the value of diets with a greater proportion of unsaturated (vegetable) as compared to saturated (animal) fats. While a relative increase in E intake and transfer probably did occur (most prenatal and other vitamins contained an E supplement in 1978 but not in 1972), its functional significance appears to be less than expected. Regardless, the increased E/PUFA ratio of 1978 nursery formulas did provide increased antioxidation protection by age 3 weeks.

531 α- AMYLASE IN PRETERM HUMAN MILK. Jay B. Jones, Nitin R. Mehta and Margit Hamosh. Georgetown University Medical Center. Washington,D.C. (Spon. by J.W. Scanlon.)

Pancreatic α amylase activity is low or absent in preterm infants, who depend on alternate sources of enzyme for polysaccharide digestion. We have measured α - amylase activity in the milk of 18 women who delivered prematurely or at term. α -amylase was measured by automated assay (HARLECO) in a microcentrifugal analyzer. The data are given in U/L.

PREGNANCY			LACTATION		
wks	n	0.2 wk	1 wk	3 wks	6 wks
25-30	7	8973	3494	2595	2007
31-35	5	4422	3288	2300	1462
36-40	6	3550	2660	1711	1373

α- amylase is highest in colostrum and decreases as a function of both length of pregnancy and lactation. The enzyme is relatively stable at pH 3.0 for 2 hrs at 37°C (22% loss of activity), and has a broad pH optimum of 5.0 to 7.0. Therefore, milk α amylase maintains most of its activity during passage through the stomach and has maximum catalytic activity at the pH range of the duodenum.

The high activity of α - amylase in preterm milk suggests that mixing of human milk with formula might facilitate digestion and absorption of formula polycose and furthermore, that starch containing supplements could be well tolerated by breast fed premature infants (Supported by a grant from Mead Johnson.)

532 PROTRACTED DIARRHEA OF INFANCY ASSOCIATED WITH RENAL TUBULAR ACIDOSIS TYPE IV (RTA IV). Robert E. Kane, Jay A. Perman, Harold A. Conrad, Anthony Portale, M. Michael Thaler. University of California, San Francisco, Department of Pediatrics.

RTA IV results from a defect in the distal convoluted tubule inducing hyperkalemic hyperchloremic metabolic acidosis. A subtype in infants attributed to transient partial end-organ unresponsiveness to aldosterone is associated with failure to thrive, vomiting, and requirement for bicarbonate (HCO_3) until 3-5 yr of age. Six infants developed watery diarrhea persisting 4-12 wks, with serum $K^+>5.0$ meq/L, $Cl^->109$ meq/L, and $HCO_3^-<19$ meq/L. Age at onset averaged 4 wks. All were <3rd percentile for weight at diagnosis. Vomiting was present in 5/6, and symptoms suggestive of viral illness in 3/6. Diarrhea remitted in all during parenteral therapy, but recurred repeatedly in 4/6 upon advancement to full-strength formulas. Oral HCO_3 sufficient to raise serum HCO_3^->23 meq/L reversed the diarrhea induced by enteral feedings. In the remaining 2 infants, institution of HCO_3 following NPO was associated with tolerance to enteral feeding. HCO_3 requirements sufficient to maintain normal acid-base status ranged from 2.5-15 meq/Kg/day. All patients demonstrated catch-up growth following institution of alkali, and 2 who no longer require alkali at age 12-18 m are >25th percentile for weight. Conclusion: Infants with growth retardation who develop protracted diarrhea may have RTA IV. Such infants may not tolerate the osmotic load of full-strength formulas until HCO_3 therapy is instituted. End-organ resistance to aldosterone, present in the distal renal tubule, may also cause inhibition of aldosterone-mediated water and electrolyte reabsorption in the small and large intestine.

● **533** LYMPHONODULAR HYPERPLASIA OF THE COLON (LNHC) AS A PATHOLOGIC FINDING IN CHILDREN WITH LOWER GI BLEEDING. Barbara Kaplan, Jane Benson, Fred Rothstein, Beverly Dahms and Thomas Halpin (Spons. by William Speck), CWRU, Depts. of Peds. and Path., Rainbow Babies & Childrens Hosp., Cleveland.

Published studies have reported LNHC as a normal radiographic finding in children with lower GI bleeding. Over 3 years, 95 children (2-48 mo) were referred for evaluation of hematochezia. Sixty were examined with fiberoptic proctosigmoidoscopy or colonoscopy. Examination revealed colitis (15), juvenile polyps (10), normal (15), LNHC (20) and rectal ulcer (1). All 20 patients with LNHC exhibited diffuse nodularity of the bowel, 13 had friable mucosa and 2 had discrete ulcerations. Thirteen patients in this group had rectal biopsies (11 suction and 2 grasp). All were abnormal on pathologic examination. Review of the biopsies revealed 1) a diffuse lymphoplasmocytic inflammation in 12 (9 mild, 2 moderate, 1 severe), 2) enlarged lymphoid follicles (#1-6 phf) extending from mucosa to submucosa, and 3) 8 of 11 had mucosal thinning overlying the follicles. All stool examinations for bacterial and parasitic pathogens were negative. In children biopsied, there was a good correlation between endoscopic findings and pathologic abnormalities. The finding of inflammation with diffuse LNHC in a group of children with lower GI bleeding suggests that LNHC is not always a normal finding. We speculate that this previously unreported finding may be related to an unidentified intestinal pathogen that stimulates gut-associated lymphoid immune systems. We feel that LNHC as an endoscopic and pathologic lesion represents a potential source of GI bleeding in children.

● **534** RELATIONSHIP OF MILK SODIUM (NA) TO URINARY NA EXCRETION DURING THE FIRST 6 MONTHS OF LIFE IN BREAST-FED INFANTS, Bruce S. Keenan, Susan W. Buzek, Cutberto Garza. Baylor College of Medicine, Dept. of Pediatrics Houston, Texas, 77030.

23 healthy breast-fed term infants and their mothers were admitted for 24 h. Mean milk Na concentration ($\bar{X}_{Na}$) was the average of 6 samples, 4 h apart. Blood and urine were obtained from the infants to determine indices of Na excretion: In the boys, U_{Na} in mEqNa/kg/24 h; in all infants, mEqNa/gm creatinine, fractional excretion (Fe_{Na}) and plasma renin activity (PRA). Milk $\bar{X}_{Na}$ decreased from 7.3 mEq/l ± .8 at 3-8 wk postpartum to 5.4 ± .3, s.e. at 8-20 wk then was constant to 32 wk. The decrease in $\bar{X}_{Na}$ was highly significant by t-test ($p<.005$). From 3 to 20 wk of age in exclusively breast-fed infants, U_{Na} decreased from 0.95 ± 0.19, to 0.28 ± 0.04 $p<0.01$, Na/gm creatinine from 97 ± 15 to 43 ± 10, $p<.01$ and Fe_{Na} from .23 ± .05 percent to .15 ± .05, $p<0.05$. PRA increased over this period from 17.0 ± 4.2 ng/ml/h to 39.4 ± 11.0, $p<0.01$. Data for infants were analyzed by nonparametric statistical methods. The decrease in $\bar{X}_{Na}$ plus previous estimates of milk volume suggest decreased total Na delivery to the infant. Decreasing indices of Na excretion plus increasing PRA from 3-20 wk suggest a response to decreasing availability of Na to the infant. Between 20 and 32 wk PRA decreased or remained constant. When PRA was 0-15 ng/ml/h, Fe_{Na} was .34 ± .14 in the younger infants (3-8 wk) and 0.11 ± .07 in the older subjects $p<0.05$. This suggested decreased efficiency of sodium conservation in younger infants. Supported by USDA #58-7B30-9-60 Children's Nutrition Res. Ctr.

● **535** TRANSEPITHELIAL TRANSPORT OF MACROMOLECULES IS INCREASED ACROSS INTESTINAL PEYER'S PATCHES. David J. Keljo and J. Richard Hamilton, University of Toronto, Department of Pediatrics, Research Institute, Hospital for Sick Children, Toronto, Ontario, Canada.

We measured horseradish peroxidase (HRP) (MW 40,000) transport rates across stripped piglet jejunum in vitro in Ussing chambers, comparing segments containing Peyer's patches (n=17) with segments containing no patch tissue (n=25). The appearance of HRP in the serosal chamber was determined enzymatically at intervals for 80 minutes after the addition of HRP to the mucosal compartment (final conc. 20 mg/ml). In patch and control (no patch) segments, HRP appeared in the serosal chamber after a lag of 30 min. and steady state conditions were observed from 40 to 80 min. Transport rates across segments with patches, 22.4 ± 4.4 ng/min/cm^2 (M$\pm$SE), were increased 3-fold ($p<0.0025$) compared with control tissue (7.5 ± 2.9). In both preparations, release of endogenous peroxidase activity was negligible and light microscopy showed the tissue well preserved at 90 minutes. HRP transport rates did not saturate with increasing concentrations of HRP in either preparation. 1mM NaF consistently inhibited transport across patch tissue (48 ± 6%, n=5, $p<0.0025$) but produced inconsistent results with control tissue. Reduction of temperature from 37° to 15°C resulted in 75-95% inhibition of transport in both tissues. We conclude that macromolecular uptake is increased across jejunal mucosa containing Peyer's patches; this phenomenon does not involve specific receptors and depends on metabolism. Our findings support the concept that Peyer's patches perform an antigen sampling function in the gut.

536 INCREASED PROTEIN TURNOVER IN CHILDREN WITH CANCER. Craig L. Kien and Bruce M. Camitta (Spon. by Jerome V. Murphy), The Medical College of Wisconsin, Milwaukee Children's Hospital, Department of Pediatrics and Biochemistry, Milwaukee, Wisconsin.

We are studying whether accelerated rates of protein turnover in normal and/or cancer cells might result in elevated energy requirements in cancer patients and thus promote cachexia. Using a single dose, [^{15}N]-glycine technique (Am J Physiol 235:E165, 1978), we assessed ^{15}N enrichment of urine ammonia and calculated rates of whole body protein synthesis (S) and breakdown (B) in children who are healthy (H) (N=6) (5-17 yr) or had newly diagnosed leukemia or lymphoma (L) (N=8) (4-15 yr). The cancer patients showed significant 51-112% elevations in rates of S ($p < 0.025$) and B ($p < 0.01$); however, the patients were not in a hyperalimentary state and actually had a lower protein intake ($p < 0.005$) than controls (Table) (two sample t test). The rates of S ($p < 0.05$) and B ($p=0.01$) were also significantly higher in the L group using the Wilcoxon test.

TABLE (Mean ± S.D.)

Group	Protein Intake (g/kg/d)	Energy Intake (kcal/kg/d)	Protein Turnover g prot/kg/d S	B
H	2.6 ± 0.9	62 ± 14	3.5 ± 0.9	2.5 ± 1.1
L	1.3 ± 0.5	52 ± 19	5.3 ± 1.5	5.3 ± 1.9

Thus, some cancer patients may require high energy intake to maintain both high rates of protein synthesis and normal body composition.

537 THE EFFECT OF KETONE BODIES AND FATTY ACID ON DEVELOPING INTESTINAL GLUCOSE METABOLISM. Robert E. Kimura, Gunilla Thulin, Joseph B. Warshaw. Yale Univ. Sch. of Medicine, Dept. of Pediatrics, New Haven, CT.

Serum concentrations of ketone bodies in suckling rat pups are six fold greater than in the adult. Serum fatty acids are two fold greater. Pyruvate dehydrogenase in adult rat intestine is inhibited by fatty acids and 3-β hydroxybutyrate (βHB). To determine if this increase in ketone bodies and fatty acids may influence neonatal intestinal glucose metabolism, we measured the effect of βHB and palmitate on glucose and pyruvate oxidation by suckling and adult rat intestinal slices. Glucose oxidation to CO_2 by developing rat intestine increased from suckling rates of 0.69 to 1.26 n mole/mg/hr in the adult. In the presence of βHB (2 mM), glucose oxidation by adult intestine decreased by 50%. However, βHB did not inhibit glucose oxidation in suckling rat intestine. Palmitate (1 mM) inhibited glucose oxidation by approximately 25% in both suckling and adult intestine. Pyruvate decarboxylation to CO_2 by developing intestine increased from 2.1 n mole/mg/hr in suckling rats to 2.88 in the adult. βHB inhibited pyruvate decarboxylation by 30% in adult intestine and only by 10% in suckling intestine. Exogenous βHB does not inhibit glucose or pyruvate oxidation in the suckling rat intestine but does inhibit oxidation in the adult intestine. Glucose oxidation in suckling rat intestine therefore appears to be inhibited by endogenous ketones. Exogenous palmitic acid inhibits glucose oxidation in both suckling and adult intestine. these data suggest that ketones are important for regulation of intestinal metabolism during development.

● **538** A NEW METHOD FOR DETERMINING LEAN BODY MASS IN INFANTS. W.J. Klish, W.J. Cochran, G.B. Forbes, A. Gordon. Dept of Pediatrics, Univ. of Rochester, Rochester, N.Y.

The determination of lean body mass in infants is difficult and unreliable. We describe an innovative, safe and rapid (1 sec) method for the determination of lean body mass which can be applied to infants. This machine, called an EMME(EMME Corp.Phoenix, AZ), operates on the principal that a biological specimen in an electromagnetic field perturbs the field proportional to its conductivity which is dependent upon the amount of electrolyte present. It operates at 10 megahertz and delivers 1mW/cm^2 for 1 sec. about 1000 times below the permissable standards set by OSHA. Phantoms containing Na, K, Ca, Mg and PO_4 in concentrations simulating lean body mass and in volumes of 2-6 liters were measured. Varying amounts of corn oil (5-40% by vol.) were added and the measurements repeated. 1-3 kg samples of ground beef (10-15% fat) were measured and the fat content chemically determined. The EMME reading increased in an exponential fashion with increases in the total "lean" volume. The regression line for the phantoms was: Ln EMME reading =.78+.41 x "lean" vol.(L). r=.99. The addition of oil to the phantoms showed the ability of the instrument to discriminate the "lean" volume from fat. The regression line for the ground beef was: Ln EMME reading =.44+1.5 x lean wt in kg. r=0.96. Live rabbits are currently being investigated. The initial studies reveal: Ln EMME reading =2.8+.42 x lean wt. in kg (chemical assay). r=.96. The EMME instrument appears to hold promise as a rapid non-invasive means of determining lean body mass which can be applied to infants.

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539 THE ROLE OF PICOLINIC ACID (PA) IN ZINC ABSORPTION. Ingeborg Krieger, Wayne State University, Department of Pediatrics, Detroit Mich.

Picolinic acid (PA) is a chelating agent that was recently shown to decrease the zinc requirements of patients with acrodermatitis enteropathica to 1/3 of minimum therapeutic dose. PA alone was ineffective. The role of PA in zinc absorption was therefore studied in groups of rats, 6 each. Group A received a tryptophan (tryp) deficient diet that contained half normal dietary zinc requirements, 6ppm, while pairfed controls received the same diet with normal tryp and 12 ppm zinc. Group A lost weight, developed CNS symptoms (6/6), alopecia (6/6) and diarrhea (2/6). Plasma zinc was 25 - 48 μg/dl; controls 91 - 118 μg/dl. Groups B and C received a tryp and B_3 deficient diet and either 6 ppm (B) or 9 ppm (C) dietary zinc. Pairfed controls were supplemented with PA, 0.2 μg/ml in drinking water. Plasma zinc was 15 - 59 μg/dl in group B and 38 - 88 μg/dl in group C. PA supplemented controls had significantly higher values (53 - 77 and 63 - 98 μg/dl, respectively) but only a slightly lower incidence of clinical symptoms. In a fourth experiment, tryp and B_3 deficient rats on normal dietary zinc (12 ppm) developed the same symptoms but had normal plasma zinc values. Pairfed controls received either PA or zinc supplements (24 ppm, total). Plasma zinc was normal in all three groups and there was no difference in bone zinc concentration. The data are consistent with the presence of two separate absorption mechanisms, one for low and one for high dietary zinc. PA did not raise body zinc uptake when dietary zinc was normal or increased, but did prevent hypozincemia in rats on a zinc deficient diet.

540 PORTAL VEIN MEASUREMENTS BY ULTRASONOGRAPHY IN PATIENTS WITH CYSTIC FIBROSIS (CF). Sheila Kumari, Jack D. Gorvoy, Peter Ross, Gail Phillips, (sponsored by Philip Lanzkowsky). Sch. of Med., Health Sciences Ctr., SUNY at Stony Brook, Long Island Jewish-Hillside Medical Center, Dept. of Pediatrics, New Hyde Park, N.Y.

With prolonged survival of CF patients, hepatic involvement has become an important complication. Conventional liver tests may not be helpful since portal hypertension may occur with little changes in liver function studies. Abdominal ultrasonography was performed on a group of 14 patients selected at random from our adult CF population numbering 35. The age span was 20-44 years. The real-time sector scanner was used, delineating longitudinal, transverse and oblique planes. Measurements of portal vein were obtained just proximal to the formation of the PV by the junction of the splenic and superior mesenteric veins. Of 108 non-CF patients without clinical or laboratory evidence to support cirrhosis, the PV diameters ranged between 8.5mm ± 2.7 SD under 20 years and 10mm±2.5 SD for those over 20 years of age. Of the 14 CF patients, 9 had PV diameters between 15 and 20mm. Those with PV diameters greater than 12mm had elevated serum alkaline phosphatase. Of those with the widest PVs 3 had splenomegaly and thrombocytopenia. The data suggests that PV diameter measurements by the real-time scanning may be a valuable diagnostic test for recognizing portal hypertension.

541 DIETARY CARBOHYDRATE AS A DETERMINANT OF DISACCHARIDASE SYNTHESIS IN RAT INTESTINE. Linda K. Kwong, Kenneth K. Tsuboi, Otokar Koldovsky, Kazuhiko Yamada, and Philip Sunshine. Dept. of Peds., Stanford Univ. Sch. of Med., Stanford, CA, and Univ. of Arizona, Tucson, AZ.

Rats maintained on a synthetic low starch diet (5 cal%) when placed on a high starch diet (70 cal%) show rapid increase in activity levels of the intestinal disaccharidases, sucrase-isomaltase, maltase and lactase as a group (Yamada et al, Biochim Biophys Acta 676:108, 1981). Examination of mechanism's leading to these activity increased revealed synthesis rates of the α-glucosidases S/I and maltase to be increased 10-11 times as an accompanying event. On the other hand, similar changes in synthesis of lactase were not evident. Relative disaccharidase synthesis rates were determined by comparing incorporation rates of [^{3}H]-leucine, following isolation of each in high radiochemical purity by selective immunoprecipitation technique. These studies demonstrate dietary carbohydrate to be a determinant of α-glucosidase synthesis. Since S/I and maltase contain about 30% and 20% structural carbohydrate, respectively, (Tsuboi et al, J Memb Biol 50:101, 1979) it is proposed that their synthesis rates may be limited by the amount of carbohydrate ingested. Failure to demonstrate changes in lactase synthesis rates under comparable dietary carbohydrate changes may reflect its lesser (9%) structural carbohydrate contents (Tsuboi et al, Biochim Biophys Acta 554:234, 1979). Mechanisms effecting lactase activity changes under variable dietary carbohydrate regimens remain to be assessed further.

542 NECROTIZING ENTEROCOLITIS (NEC) IN THE FIRST 24 HOURS OF LIFE. R.A. Lazarte, E.H. Thilo, and J.A. Hernandez. Department of Perinatology, The Children's Hospital, Denver, Colorado.

NEC usually occurs in preterm infants, particularly in those who weigh 1500 g or less. The mean postnatal age at onset of clinical manifestations has been reported between 5-10 days.

From January 1976 to December 1980, there were 79 infants admitted to our Neonatal ICU with the diagnosis of NEC. In 13 of these infants the onset of the disease occurred within the first 24 hours of life. These infants were found to have a clinical profile which differed from infants with later onset of disease:

Clinical Features	<24 hrs	>24 hrs	P Value
Number of Infants	13	66	-
Birth Wt (gms)	2624±586	1519±586	.001
Gestation (wks)	37.9±2.5	29.3±9.0	.001
Apgar 1 min	6.1±2.3	4.6±2.5	.057
5 min	8.2±1.1	6.8±1.8	.014
Age feeds begun (hrs)	7.0±3.9	72.3±42.7	.001
Interval between feeds & onset of NEC (hrs)	11.8±4.6	152.0±171.3	.001

In summary, infants with onset of NEC in the first 24 hours of life were larger, more mature and less asphyxiated than infants with later onset of disease. They were fed more vigorously at an earlier age, and the latency period between onset of feedings and onset of NEC was significantly shorter. We speculate that, in these infants, the feedings were more directly involved in the pathogenesis of NEC.

543 PRECOCIOUS OR DELAYED DEVELOPMENT OF RAT SMALL INTESTINE; DIETARY AND HORMONAL MEDIATION. Ping-C Lee, and Emanuel Lebenthal. Gastroenterology and Nutrition Division. Children's Hospital and SUNY at Buffalo, Buffalo, N.Y.

Small intestines of rats change rapidly at weaning, a period when characteristic changes in diet occurs. To evaluate the interactions of diet, genetic preprogramming and hormones in inducing these changes, small intestinal development was followed in rats from 17 to 28 days of age. Pups weaned at 17 days or nursed until 25 days were compared to control weaned rats of the same age. Pups weaned at 17 days showed an immediate increase in intestinal length but no change in segmental mucosal weight, DNA and protein contents. They showed an immediate decrease in lactase and a precocious increase in sucrase and maltase between days 19 to 22. At 19 days, early weaned pups had serum corticosteroid levels about 3x that of control or prolonged nursed pups. Pups nursed to 25 days had smaller body weight, shorter intestinal length, lighter mucosa, and lower mucosal protein content. They also showed a delayed increase in sucrase and maltase and a sustained higher level of lactase at day 25. Enterokinase and leucine aminopeptidase showed little changes. Significant increases in mucosal mass, DNA and protein content were seen in all animals at day 25 when compared to 17 day old pups. These results suggest an inherent biological program as a basic control of intestinal ontogeny with diet as a modifier acting directly or in concert with hormonal changes.

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544 SHORT-CHAIN BILE ACIDS IN MECONIUM. Roger Lester, Jan S. Pyrek, Roman Sterzycki, and Eugene W. Adcock. The University of Texas Medical School at Houston, Depts. of Internal Medicine and Pediatrics, Houston, Texas.

We have previously shown that acidic steroids with fewer carbon atoms than are found in conventional bile acids (24 carbons) exist in meconium. Thus, etianic acids (20 carbons) and bis-nor cholanoic acids (22 carbons) are demonstrable. We now show that large quantities of 21 carbon acidic steroids exist in normal human meconium. Methods: Extracts (containing sodium borohydride) from normal full-term infants were subjected to solvolysis and mild alkaline hydrolysis. An acidic fraction was obtained, and was separated into hydroxylated components by adsorption chromatography of the methyl esters. The preparative technics employed have been standardized and extensively tested to rule out artefact formation. Results: Two dihydroxylated C_{21} acidic steroids were obtained and characterized by MS, and by proton and carbon NMR spectroscopy. The major component was shown to be 3α, 20ξ-dihydroxy-5α-pregnan-21-oic acid, while the 5β-isomer was a second component. Additional minor components were identified. The concentrations of the major component were comparable to those of chenodeoxycholic and cholic acid in meconium. Conclusions: (1) This is the first demonstration of C_{21} acidic steroids in meconium; (2) In view of the quantity in meconium, it will be essential to study their effect on hepatic function; (3) Their origin is unknown, but it is probable that C_{21} acidic steroids are hormone degradation products.

545 PREDUODENAL FAT DIGESTION IN THE NEWBORN: QUANTITATIVE CONTRIBUTION OF LINGUAL AND GASTRIC LIPASE THROUGHOUT POSTNATAL DEVELOPMENT. Teresa H. Liao, Paul Hamosh and Margit Hamosh. (Spon. by J.W. Scanlon). Georgetown University Medical Center, Washington, D.C.

Preduodenal fat digestion is an important compensatory mechanism in newborns because of immature pancreatic (lipase) and hepatic (bile acid synthesis) function. Hydrolysis of fat in the stomach is catalyzed by enzymes of lingual (LL) and possibly gastric (GL) origin. The developmental pattern and quantitative contribution of these two enzymes to intragastric fat digestion was studied by measuring lipase activity in lingual glands and gastric mucosa of rats from birth until after weaning.

AGE (days)	2	7	11	17	30
LL*	140	202	241	257	125
GL*	2.8	5.6	6.1	12.0	2.0

*Hydrolysis of tri ^{3}H-olein at pH5.4, μmol FFA produced per h per 100 g body weight.

LL and GL activity was optimal at pH 5.4 and was 2.5-5.0 fold higher on medium (tri ^{14}C-octanoin) than long chain triglyceride. Low activity of GL (1-4% of LL level) and characteristics similar to LL, suggest that GL represents LL adsorbed onto gastric mucosa. High activity immediately after birth, suggests that LL is a major digestive enzyme in the newborn. (Support, NIH Grants HD 10823 and AM 26641.)

546 COLONIC METABOLISM OF MALABSORBED CARBOHYDRATE (CHO) IN INFANTS WITH DIARRHEA. Carlos H. Lifschitz, Charles S. Irving, Kim Evans, and Buford L. Nichols. USDA/ARS, Children's Nutrition Research Center, Department of Pediatrics, Baylor College of Medicine, Houston.

Fermentation and nutritional scavenging of malabsorbed CHO reaching the colon was studied semiweekly by measuring peak breath H_2 (PBH) production between feedings in 32 H_2-producing, hospitalized infants (<3 mo) recovering from diarrhea. PBH (alveolar ppm) was calculated using the methof of Niu et al. (J. Lab. Clin. Med. 94:755, 1979) from breath H_2 and CO_2 levels obtained by GC analysis of end expiratory gas samples collected with a modified oxygen therapy mask. Patients who required less than 1 wk hospitalization had lower PBH on admission than those who required longer stays (PBH: 21±18, n=12 vs 244±183, n=9, P<.01). Patients hospitalized for less than 1 wk had lower PBH at discharge (44±25, n=9, P<.012) than on admission. PBH decreased when glucose was substituted for glucose polymer in formulas (34±33 vs 150±82, n=7, P<.01). PBH decreased when milk drip was used in place of bolus feeding (219±185 vs 13±23, n=6, P<.025). Glucose-positive and acidic stools were encountered occasionally and were associated with decreased PBH. Changes in PBH levels and stool pH and glucose following changes in patient management and/or intestinal handling of CHO could be interpreted as the balance between proximal intestinal absorption and distal colonic fermentation. Malabsorbed CHO reaching a competent colon is utilized via microbial conversion as demonstrated by high PBH levels in the absence of glucose-positive and acidic stools. The presence of the latter two signifies colonic failure. (Supported by USDA/ARS).

547 PERINATAL CHANGES IN ACTIVITY OF ACID GLYCOSIDASES IN RAT COLON. B. Litin and O. Koldovský. Departments of Pediatrics and Physiology, University of Arizona College of Medicine, Tucson, Arizona.

Although a considerable amount of information is available about lysosomal enzymes in various mammalian organs, very little is known about lysosomal enzymes of the colon. We have therefore studied changes in lysosomal enzymes, β-N-acetyl-D-glucosaminidase (HEX), β-D-galactosidase (G), α-L-fucosidase (F) and β-D-glucuronidase (GL) in proximal and distal portions of the large intestine of fetal, newborn, suckling, weanling and adult rats. All these enzymes exhibit substantial changes in activity perinatally. The activity in the proximal colon peaks around the middle of the first week. In the distal colon either no substantial change (G,GL) or a transient peak around day 14 (F) or a steady increase from day -1 until day 80 (HEX) is observed. These changes lead to a shift of the locus of maximal activity from proximal to distal colon. Whereas 1 to 8-day-old suckling rats exhibited higher enzyme specific activities in the proximal than in the distal colon, the activities were always higher in adult rats in the distal than in the proximal colon. The gradient of enzyme activity along the colon varied more in sucklings (2.3 to 10 fold) than in adults (1.3 to 3.0 fold).

Demonstration of substantial changes in activity of these enzymes known to be involved in the turnover of carbohydrate-containing macromolecules both during development and along the length of the large intestine, clearly stresses the need for further studies of metabolism of glycoproteins and glycolipids in this organ during development.(Support: Cystic Fibrosis Found.).

● **548** LACTOSE ASSIMILATION BY FULL-TERM INFANTS. William C. MacLean, Jr., Dale A. Schoeller, William Wong & Peter D. Klein, Johns Hopkins Univ., Dept. of Pediatrics, Baltimore; U. of Chicago, Dept. of Med., and Baylor College of Med., Children's Nutrition Res. Center, USDA/ARS, Houston.

Lactose assimilation was studied in 19 full-term infants (age: 4.6±0.5 d, wt: 3.37±0.45 kg) after 30 mg/kg ^{13}C-1-lactose was added to the 8 am formula feeding (intake: 97±14 Kcal/kg/d, 14±3 Kcal/kg/feed). Breath was collected a.c. and 0.5, 1, 1.5, 2, 3, 4, etc. hrs to 8 hrs p.c. ^{13}C was recovered as early as 0.5 hr in 17 of 19. Peak respiratory excretion occurred at 2-4 hr. The 8 hr cumulative % dose (assuming CO_2 production rate of 9 mM/kg/hr) was 33±3%. The % dose/hr at each time and the 8 hr cumulative % dose recovery did not differ between 11 infants with peak breath H_2 <20 and 8 infants with peak H_2 >20 ppm (range 25-158). Breath tests with ^{13}C-1-glucose in a subset of 9 infants showed significantly greater % dose excretion at 0.5 hr, greater 8 hr cumulative % dose recovery than with lactose. Fecal excretion of ^{13}C after ^{13}C-lactose was >1% of dose (range 1.4-6.8%) in 10 of 17, and <1% in 8 of 17 infants with complete collections. All fecal ^{13}C was dialyzable, suggesting little or no incorporation into bacteria or macromolecules, as previously documented in adults. Fecal ^{13}C excretion was unrelated to H_2 production status. Both breath and stool data suggest that less lactose reaches the colon in term than in premature infants. Colonic salvage is variable in term infants at the ages studied and appears to be less quantitatively important than is suspected in premature infants.

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549 BEHAVIORAL MANAGEMENT OF ANOREXIA IN SEVERE BURN TRAUMA PATIENTS. Lana M. Mahon, Norma (Winn) Neufeld, Mani M. Mani, Edward R. Christophersen. University of Kansas College of Health Sciences and Hospital. Departments of Dietetics and Nutrition, Surgery, and Pediatrics. Kansas City, KS

Four patients with severe burns (average 48% TBS) requiring from at least one to five surgical eschar debridement and autografting procedures, and who failed to ingest at least 80% of their prescribed protein and/or kilocalories were studied using a multiple baseline (time series) analysis. After a varying number of baseline days, Informational Feedback was introduced consisting of (a) daily reminder of their prescribed levels of protein and kilocalories, (b) the protein and kilocalorie count of every item available, and (c) their actual intake of protein and kilocalories. Bar graphs on the wall next to the bed of the patient showed the prescribed levels of daily protein and kilocalories and the actual daily intakes of these nutrients. Menus listed protein and caloric values for each food available as well as the minimum number of protein and calorie values needed for each meal to assure the prescribed levels of protein and kilocalories for the day. Daily kilocalorie intake improved from 5104 per day to 6143 per day (a 20% improvement), with the intake of prescribed levels improved from 0% of baseline days to 35% of treatment days. The informational feedback techniques described herein suggest an effective and practical method for improving the eating behavior of burn patients.

550 CYSTEINE SUPPLEMENTATION DURING TOTAL PARENTERAL NUTRITION (TPN). Michael H. Malloy, David K. Rassin and C. Joan Richardson. University of Texas Medical Branch, Department of Pediatrics, Galveston, Texas.

In order to investigate further whether or not cyst(e)ine (sulfhydryl and dissulfide form) is an essential amino acid during infancy, plasma and urine amino acids were measured in two groups of low-birth weight infants (mean birth weight = 1497 gm). Five infants received cysteine-supplemented (S) TPN (72 mg/kg/day cysteine-HCl) and 5 infants received unsupplemented (US) TPN. For both groups the non-protein calorie intake was 63 cal/kg/day and the mean nitrogen intake was 0.243 g/kg/day.

Plasma methionine, cystathionine, and taurine were not significantly different between the 2 groups after 5.5 days of TPN. Plasma free cyst(e)ine, measured by a new colorimetric method, was significantly increased in the S group (11.3 ± 3.4 um/dl) compared with the US group (4.3 ± 1.1). Plasma free ½-cystine measured by an automatic amino acid analyzer was not significantly different between the 2 groups. In the urine, methionine excretion was significantly greater in the US group (5.3 ± 2.9 um/kg/day) than in the S group (0.058 ± .13). Urine cyst(e)ine excretion in the S group (41.3 ± 15) was significantly greater than in the US group (9.3 ± 4).

These data suggest the following: (1) cysteine supplementation during TPN increases plasma and urine cyst(e)ine conc, (2) cystine supplementation promotes more efficient utilization of methionine during TPN in infancy, and (3) measurement of both the sulfhydryl and dissulfide forms of cyst(e)ine is required to assess the effects of cysteine administration.

551 ENDOGENOUS GASTRIC PROSTAGLANDIN E_2 (PGE_2) PRODUCTION IN THE STRESSED NEONATE. Lucyndia Marino, Thomas Halpin, Jeffrey Blumer (Spons. by William Speck), Case Western Reserve University School of Medicine, Department of Pediatrics, Rainbow Babies & Childrens Hospital, Cleveland, Ohio.

PGE_2 is cytoprotective to gastric mucosa, and endogenous production may play an important role in prevention of serious gastrointestinal complications in neonates. Gastric secretions were obtained from 7 premature (P) and 8 full-term (FT) infants with pulmonary disease in the neonatal ICU. Gastric secretions from 16 children (6mo-12yr) admitted for elective surgery served as controls (C). Infants were studied in the first 10 days of life. All patients were NPO 24 hrs prior to collection. PGE_2 concentration was determined by single-phase antibody radioimmunoassay and compared to [H+] and volume in timed colelctions. There was a correlation between PGE_2 and gestational age ($r=.35$, $p<.05$). No correlation between PGE_2, [H+] or chronologic age was found. Comparison of PGE_2 concentration among the groups is shown below.

	$\bar{x}$ PGE_2 (pg/ml)	$\bar{x}$ [H+] mEq/l	Comparison	p
P	2370 (1320-4800)	15.2	P vs FT	<.05
FT	5660 (2040-14,400)	25.2	FT vs C	<.001
C	1440 (190-3360)	17.3	P vs C	<.1

Above data demonstrate that PGE_2 production in P infants is less than FT infants similarly stressed. FT infants responded to stress with gastric PGE_2 concentration greater than controls. PGE_2 production in P infants may represent deficiency in an important cytoprotective mechanism which could increase the risk of serious gastrointestinal complications to these severely ill infants.

552 HEPATITIS B VIRUS (HBV) INFECTION IN MENTALLY RETARTED INSTITUTIONALIZED CHILDREN AND THEIR FAMILIES. John McPhillips, Janna C. Collins and Ilya Spigland (Spon. by Michael I. Cohen) Albert Einstein College of Medicine, Department of Pediatrics, Bronx, N.Y.

HBV infection is endemic among the institutionalized retarded, who usually have mild, anicteric hepatitis after non-parenteral exposure. We studied long term effects of HBV exposure and risk to caretaker contacts during brief home exposure.

Six retarded patients, known HBSAg+ (m=4.6yrs) were institutionalized 4-12yrs (m=10) by ages 11-23 (m=16). All had abnormal transaminases; two had portal hypertension. Liver biopsies (5 pts) showed chronic active hepatitis with cirrhosis(2) chronic persistent hepatitis(2) and ground glass, aldehyde fuchsin positive cells(5). Viral DNA was integrated into hepatocyte genome in 3/3.

Caretakers shaved, bathed, and changed diapers for patients during home visits or foster home placement. 7/14 caretakers exposed 5-12 mos (m=6) developed antibody to HBSAg or HB_cAg. Only 1/9 play contacts and 0/7 other casual contacts had markers of past or present HBV infection.

Conclusions: (1) Retarded institutionalized HBSAg carriers can have progressive liver disease, with integration of HBV-DNA, and are at risk for future hepatocellular carcinoma. (2) 50% of caretakers had serologic evidence of silent HBV infection following brief non-parenteral exposures, whereas other contacts had a risk no greater than the general population. These data may help form guidelines for active immunization against HBV for communities providing non-institutional care for the retarded.

553 SUBCELLULAR METABOLIC PROPERTIES OF HUMAN PLACENTA AS INDICATORS OF THE FETAL NUTRITIONAL STATUS. Jerzy W. Meduski, Paul Y.K. Wu, Jerzy D. Meduski, Franklin C. Miller, Florence H.Y. Wong, Ann Pendo, and Nancy Tanaka. Univ.of So. CA. Sch. of Med., Depts. Peds., Neurol., Obstet & Gynecol.

Fetal malnutrition is associated with deviations of structure or function of the placenta. In an attempt to aid in assessing the nutritional status of a neonate at birth, the subcellular metabolic properties of human placenta were studied. Two preparations were used: mitochondria, obtained by classical techniques and a postmitochondrial supernatant containing microsomes and other cytosol components of placental parenchyma. Results: Human placental mitochondria obtained from full-term normally grown infants consume O_2 at specific rates (11.00 to 20.00 nmoles O_2/min/mg mitochondrial protein). Measurements of state 3 and 4 respiration rates led to respiratory control ratios from 1.00 to 1.74. Adding some essential nutrients (e.g. thiamine pyrophosphate) increased frequently the O_2 consumption (12%); this suggests a state of unsaturation with respect to the nutrient tested. Postmitochondrial supernatants were used for multi-test evaluation and demonstrated consistency of albumin, globulin, SGOT, lactic dehydrogenase, alkaline phosphatase, and creatinine content. Because placental parenchyma was found to contain high concentration of ascorbic acid (from 8.9 to 11.6 mg/100 g tissue) and this is associated with oxygen metabolism, the level of superoxide dismutase in the umbilical blood was assayed and found to be consistent from 9 to 24 units/g Hb). These studies indicate that the subcellular metabolic profile of the placenta may be used to characterise fetal nutritional status.

● **554** CHOLESTATIC EFFECT OF TRYPTOPHAN AND ITS METABOLITES IN SUCKLING RAT PUPS: Russell J. Merritt, Frank R. Sinatra and Donaby H. Henton Spon. by Robert M. McAllister University of Southern California, Childrens Hospital of Los Angeles, Dept.of Pediatrics,Los Angeles.

Recent *in vitro* perfusion studies of rat liver have demonstrated cholestatic effects of some amino acids and whole animal experiments have shown hepatotoxic effects of light-exposed tryptophan. Since TPN-associated cholestasis is a common problem in sick neonates, we studied the effect of amino acid injection in suckling Sprague-Dawley rat pups. One day old animals received daily IP injections of 4 mM/kg of a single amino acid for 7 days. They were sacrificed on day 8 and serum analyzed for cholyglycine (CG) by radioimmunoassay. Of the amino acids present in TPN solutions, only tryptophan significantly elevated serum CG. Tryptophan exposed to sunlight for 12 hrs caused higher elevations (one tailed t-test $p < .05$). Metabolic products of tryptophan were evaluated using the same procedures. Tryptamine (0.8mM/kg), quinolinic acid (0.8 mM/kg), kynurenic acid (4 mM/kg), 3-OH-anthranilic acid (0.8 mM/kg), and kynurenine sulfate (1.3 mM/kg) did not elevate CG. The following agents elevated CG compared to saline control (n 14, serum CG = 3.2 ± 0.2 μM/L):

	Dose (mM/kg)	N	Serum CG (μM/L)	p
Tryptophan	4.0	6	14.4 ± 1.7	<.005
Exposed tryptophan	4.0	12	21.5 ± 8.6	<.0005
Anthranilic acid	0.8	9	8.0 ± 0.9	<.0005
Kynurenine	1.3	12	5.6 ± 0.4	<.0005

None of these agents was cholestatic in 21-day old animals. Conclusion: Tryptophan and its metabolites are mildly cholestatic in suckling rat pups.

555 RELATIONSHIP OF PROTEIN INTAKE TO NUTRITIONAL STATUS DURING RECOVERY FROM INTRACTABLE DIARRHEA OF INFANCY Russell J. Merritt, Daniel W. Thomas, Pratul H. Shah, Shirley L. Hack, and Frank R. Sinatra Spon. by Robert M. McAllister, University of Southern California, Childrens Hospital of Los Angeles, Dept of Pediatrics, Los Angeles, California

Standard pediatric total parenteral nutrition (TPN) solutions contain 8-10% amino acid calories (AAC). We compared the efficacy of a TPN solution containing 16% AAC as Aminosyn with one containing 8% AAC in a randomized study of 10 infants with intractable diarrhea syndrome (IDS) aged 5 ± 1 months (mean ± SEM). Infants received 2 wks of TPN followed by 2-3 wks of transition to oral feedings at the same % AAC. Initial weight for height was <5th%-ile for 9/10 and serum albumin <3.5gm/dl in 8/10. Energy intake was 124 cal/kg on TPN and 109 during transition. Infants on 16% AAC achieved better Nitrogen (N) balance (N_{in}-N_{urine}) during TPN (399 ± 10 vs. 263 ± 12 mg N/kg/day, $p < .005$), earlier increase in serum albumin ($p = .05$), and higher values for serum prealbumin ($p < .05$). Weight gain during TPN was equivalent (10.4 vs. 11.6g/kg). 16% AAC was associated with higher peak concentrations of BUN (17 ± 1 vs. 7 ± 1 mg/dl, $p < .0005$)and alkaline phosphatase (344 ± 32 vs. 221 ± 9 IU/dl, $p < .025$). Two infants receiving 16%AAC demonstrated moderate cholestasis with peak serum concentrations of cholylglycine of 99 and 81 μM/L and bilirubin of 1.6 and 2.4 mg/dl. The frequency of abnormal plasma amino acid concentrations was equivalent in the 2 groups. Conclusion: 16% AAC in IDS improves N balance, but is associated with mild urea retention and increased risk of cholestatic liver damage.

556 CREATININE EXCRETION BY CRITICALLY ILL CHILDREN John J. Mickell, (Spon. by H. Maurer) Medical College of Virginia, Department of Pediatrics, Richmond, Va.

Urinary creatinine (UCR) excretion as an index of muscle catabolism was assayed in 37 children (2m to 15y, median 5y) during an ICU course of 1 to 10 days. A total of 122 daily urine collections was analyzed utilizing a Mallinckrodt Serometer photometer and premeasured blood chemistry reagent cuvettes. Mean daily UCR excretion was 10.3 ± 6.6 mg/kg. There was no significant inverse relationship between daily UCR excretion and simultaneous serum creatinine values ($r = -0.16$).

The mean daily creatinine height index (CHI) (measured UCR excretion / UCR excretion predicted from height) was 0.53 ± 0.33 (79% below 0.8). Daily CHI values averaged for each child were significantly higher in the surgical subgroup (mean 0.82 ± 0.31, N=14) when compared to the medical subgroup (mean 0.50 ± 0.27, N=23) ($p = 0.002$).

The influence of protein calorie malnutrition on UCR excretion was estimated through determination of the weight for height index (WHI) (actual weight / 50th percentile weight for height). The mean WHI was 0.99 ± 0.21 (13.5% below 0.8). There was no significant correlation between CHI and WHI in this study population ($r = 0.417$). Nor was there any significant difference in WHI between medical (mean 0.98 ± 0.23) and surgical (mean 0.99 ± 0.17) subgroups.

This study shows that 1) CHI does not accurately reflect the protein calorie nutritional status of critically ill children, and that 2) surgical injury may be associated with greater muscle catabolism than that encountered with most medical illnesses.

557 CORRECTION OF ESSENTIAL FATTY ACID DEFICIENCY IN CYSTIC FIBROSIS(CF). Elaine H. Mischler, Philip M. Farrell, Sara W. Parrell, and Richard J. Lemen, Univ. of Wisconsin, Department of Pediatrics, Madison, WI.

The significance and possible effects of previously described fatty acid abnormalities in CF are controversial, particularly the decrease in linoleate(18:2), an essential fatty acid. The 18:2 deficit, however, provides evidence of biochemical malnutrition which is commonly found in CF patients with steatorrhea and may contribute to growth retardation and membrane dysfunction. Therefore, we evaluated plasma and erythrocyte fatty acid composition, identified 43 CF patients with low 18:2 (67% of those surveyed), and have carried out a dietary supplementation protocol. The pathologic triene characteristic of essential fatty acid deficiency(5,8,11-eicosatrienoic acid) was found in 43 patients, and one had a triene/tetraene ratio above 0.4. Fifteen patients, aged 10 to 24 years, agreed to take Microlipid (a safflower oil emulsion containing 72% linoleate) for one year, and nine have completed a 6 month trial thus far. As shown below, % 18:2(mean ± SD) increased in plasma ($p<.01$) and erythrocytes ($p<.002$).

Time	Plasma	Erythrocyte 18:2
Pre-treatment	23.0 ± 2.24	10.3 ± 1.32
Six months	28.4 ± 5.58	12.5 ± 1.80

In all compliant patients, the pathologic triene disappeared. Biochemical correction is therefore possible by dietary supplements. Clinical and further biochemical parameters such as prostaglandin levels are being followed to assess the impact of 18:2 deficiency. (Supported by the CF Foundation and Organon.)

558 THE CONCENTRATION AND DAILY OUTPUT OF TRACE ELEMENTS, VITAMINS AND CARNITINE IN BREAST MILK FROM MOTHERS OF PREMATURE INFANTS FOR 7 POST NATAL WEEKS. Roberto Moran, Peggy Borum, Ross Vaughn, Sandra Bennett, and Harry Greene. Departments of Pediatrics, Vanderbilt University, Nashville, TN; UNC, Chapel Hill, NC.

Thirteen upper middle class mothers who delivered at or before 32 weeks gestation, pooled all expressed breast milk for 24 hours and had an aliquot analyzed. Samples were obtained weekly for 7 weeks. Representative measurements were:

wks post delivery	1	3	7
Zn (μg/dl)	507 ± 55	292 ± 34*	157 ± 20**
Cu (μg/dl)	58 ± 4	38 ± 2*	27 ± 4
Vit A (μg/dl)	20 ± 5	14 ± 4	18 ± 3
Vit E (μg/dl)	1253 ± 23	531 ± 40*	483 ± 34
Vit C (mg/dl)	7.8 ± 1.5	8.7 ± 1.1	8.1 ± 1.9
Carnitine (nmol/ml)	88 ± 5	71 ± 13	49 ± 6

means ± S.E. *$p<0.05$ for wk 1 vs wk 3; **$p<0.05$ for wk 3 vs wk 7

There were no significant differences in concentrations of nutrients between mothers ≤ 30 wks vs 32 weeks gestation except for Zn at 1st and 2nd week (lower in ≤30 wks gestation). Daily output of all nutrients did not change significantly with duration of lactation and it was not influenced by length of gestation. Our data illustrate 4 unreported findings: (1) daily output of Zn, Cu, Vits. A, E, C and Carnitine is constant during 7 wks lactation, (2) concentration of Zn, Cu, Vit E and Carnitine decreases during lactation, (3) Zn content is lower in the first 2 wks of lactation in mothers ≤30 wks, (4) individual variation in concentration is enough to suggest that some infants may need vitamin or zinc supplements in addition to their own mothers milk.

559 EPIDERMAL GROWTH FACTOR (EGF) CONCENTRATIONS AND DAILY PRODUCTION IN BREAST MILK DURING SIX WEEKS POST DELIVERY IN MOTHERS OF PREMATURE INFANTS. Roberto Moran, Ross Vaughn, David N. Orth, Charles D. Mount, Barbara J. Sherrell, Mary Courtney, and Harry Greene. Departments of Pediatrics and Medicine, Vanderbilt University, Nashville, TN, and Department of Pediatrics, UNC, Chapel Hill, NC.

EGF is a small polypeptide that stimulates proliferation and differentiation of a variety of cell types, including bowel epithelium. Since there is biologically active EGF in breast milk, it is possible that EGF may promote optimal growth and/or maturation of the bowel epithelium in premature infants. Immunoreactive (IR) EGF has previously been found at concentrations of 50 ng/ml in isolated samples of mature breast milk, but its levels have not been systematically analyzed. We studied the IR-EGF content in breast milk as a function of duration of lactation in 13 mothers delivering at or before 32 weeks gestation. Expressed breast milk was collected for 24 hours once a week for 6 weeks. Representative results are as follows:

wks post delivery	1	3	5	6
IR-EGF (ng/ml)*	83.1 ± 13.8†	91.2 ± 30.9†	121.0 ± 57.0†	97.0 ± 32.9†
IR-EGF (µg/day)*	25.3 ± 2.8§	24.7 ± 5.3§	33.9 ± 4.2§	28.4 ± 5.2§

*(means ± SE)
†§differences not significant ($p>0.05$)

These data indicate that: (1) IR-EGF production in milk is not a function of duration of lactation; (2) concentration of IR-EGF varies widely from the milk of one mother to another, but (3) total daily production is similar; and (4) IR-EGF concentrations in the breast milk of mothers delivering prematurely may exceed those of mothers delivering at term.

560 GROWTH FOLLOWUP IN PRETERM, LOW-BIRTH-WEIGHT INFANTS FED BREAST MILK OR STANDARD INFANT FORMULA. Laurie Moyer and Gary M. Chan (Spon. by Lowell Glasgow), Department of Pediatrics, University of Utah, Salt Lake City.

Studies have shown that low-birth-weight (LBW) infants experience a faster rate of weight gain when fed a more calorically dense formula with a higher protein content than those receiving pooled human milk. Recent data indicate that the composition of "preterm" human milk differs significantly (protein, Na, Cl) when compared with pooled term human milk and may be adequate to meet the preterm, LBW infant's needs. It has not been shown that the preterm LBW infant fed his own mother's milk "ad libitum" will simulate the growth of the formula-fed infant. To compare growth, 9 breast-fed (BF) and 9 standard 20 calories/oz formula-fed (FF) preterm LBW infants were matched for gestational age (GA) and birth weight (BW) (BF:GA = 31.4 ± 1.9 weeks, M ± SD, BW = 1.7 ± 0.4 kg; FF:GA = 31.8 ± 1.6 weeks, BW = 1.5 ± 0.3 kg). Measurements of weight (W), length (L), and head circumference (HC) were determined at 42, 48 and 56 weeks postconceptual ages (GA + postnatal age). Results showed no differences between the two groups in W, L or HC during study.

	Postconceptual Age (Weeks)					
	42		48		56	
	BF	FF	BF	FF	BF	FF
W (kg)	3.1±0.2	3.1±0.4	3.9±0.6	4.5±0.6	5.3±0.6	5.4±0.8
L (cm)	52±2	51±3	54±3	55±3	59±2	60±3
HC(cm)	35±1	36±1	37±3	38±1	41±2	40±1

Thus, it appears that preterm LBW infants, whether fed breast milk or infant formula "ad libitum", experienced similar growth.

561 PROSTAGLANDINS ALTER GROWTH AND SMALL INTESTINAL DEVELOPMENT IN THE RAT. Josef Neu. (Spon. by Jerome V. Murphy). Medical College of Wisconsin, Department of Pediatrics, Milwaukee.

To determine if exogenously administered prostaglandins affect growth or biochemical ontogeny, prostacyclin(PGI_2) and 16,16 dimethyl prostaglandin E_2 (16,16DPGE$_2$) were administered to infant and weanling rats. PGI_2 was injected at 0.0, 0.1, 0.2 and 0.3 mg/kg three times a day between 10-13 and 19-22 days of age with sacrifice at 14 and 23 days respectively. 16,16DPGE$_2$ (0.3 mg/kg/min) was infused continuously from days 10-16 using subcutaneous minipumps. The following decreased after PGI_2: body, kidney, intestine weights and intestinal protein content. Similar effects on growth were detected after 16,16DPGE$_2$. Representative data are tabulated below for sucrase(S) and maltase(M): (#=Difference among groups; *=Dose related linearity; Mean±t S.D.)

PGI_2 14 Day	S	M	S/mg.Protein	M/mg.Protein	(n)
0.0 mg/kg	0.015±.005	0.56±.08	.0014±.0009	.037±.006	(5)
0.3 mg/kg	0.138±.39	1.45±.25	.0126±.0030	.087±.009	(5)
	#p=.077	#p=.0033	#p=.05	#p=.001	
	*p=.017	*p=.0006	*p=.01	*p=.0002	
PGI_2 23 Day					
0.0 mg/kg	6.1±.65	2.47±.6	.33±.06	1.04±.50	(5)
0.3 mg/kg	4.65±.92	1.65±.3	.45±.11	1.56±.40	(5)
	#p= N.S.	#p=.01	#p=.052	#p=.05	
	*p=.03	*p=.002	*p= N.S.	*p= N.S.	

Similar to the PGI_2 administered rats, S and M were also elevated in the 16,16DPGE$_2$ administered animals. These alterations in growth and biochemical ontogeny induced by prostaglandins should be considered when administering prostaglandins.

● **562** EFFECTS OF CONCEPTUAL AGE AND DIET ON PROTEIN METABOLISM IN PREMATURE INFANTS. Itzhak Nissim, Marc Yudkoff, Gilberto Pereira, and Stanton Segal. Children's Hospital of Philadelphia, Department of Pediatrics, Philadelphia, PA.

Protein turnover was studied in 12 premature babies with a conceptual age of 26-37 weeks. A stochastic model based upon [^{15}N]urea excretion following an injection of [^{15}N]glycine was used. Muscle protein breakdown was estimated from 3-methylhistidine excretion. A significant inverse correlation obtained between nitrogen flux, protein synthesis and breakdown, and the degree of maturity. Muscle protein breakdown increased linearly with conceptual age and comprised from 7-38% of the total protein catabolism. Efficiency of protein synthesis with respect to protein and caloric intake were many times higher in the least mature infants. We conclude: (1) Mean rates of protein synthesis and breakdown are 2-5 times higher in premature infants than in young adults and are especially high in less mature babies; (2) Muscle protein breakdown increases with maturation and contributes a large fraction of total protein turnover; (3) The efficiency of protein synthesis (S), either S/calories or S/dietary protein, was greatest in the youngest infants and declined with maturation.

563 NUTRITIONAL STATUS OF HOSPITALIZED CHILDREN (EFFECT OF SOCIOECONOMIC STATUS). Pam Oatis, Robert Bobo, Deb Herman.(Spon. by Margaret Robinson)Medical College of Ohio,St.Vincent Hosp.(SVH),Dept.Ped.Gastroenterology,Toledo.

One hundred children had nutritional and socioeconomic status assessment performed on admission to SVH,a 667 bed general hosp. in the indigent area. Anthropometric(A)abnormalities included 14% height (<5th percentile),19% weight,23% weight for height,15%head circumference,8% triceps skinfold (<15th percentile),25%upper arm circumference,32% upper arm muscle area and 23% upper arm fat area. Lab(L) abnormalities included 29% hemoglobin,3% albumin,11% total lymphocyte count,15% transferrin and 21% serum iron.One anthropometric and/or lab abnormality was found in between 40 to 86% of the children and more than one in 29 to 71%.

Chi-square analysis comparing the frequency of abnormalities in the socioeconomic groups found significant differences (level of significance in parenthesis). Nearly 50% of the children were in the lower socioeconomic group.

Age	N	Welfare vs.Insurance	Clinic vs.Private	1 vs. 2 Parents
<2	63	-	A(5%),A&/or L(1%)	-
3-5	33	A(1%),A&/or L(1%)	A(1%),A&/or L(1%)	A(1%),A&/orL(1%)
6-12	14	L(1%)	-	-

Our results confirm our expectation that a significant number of children have nutritional deficits that may adversely affect the hosp. course and increase morbidity and mortality and that nutrition is affected adversely by poor socioeconomic conditions.

Supported by a grant from Douglas Research Foundation.

564 ELEMENTAL DIET INDUCED ESSENTIAL FATTY ACID(EFA) DEFICIENCY RESULTING IN CHANGES IN RED BLOOD CELL (RBC) MORPHOLOGY.HOWARD G. PARSONS, PAUL PENCHARZ, RICHARD HILL,JAMES PHILLIPS, ARNIS KUKSIS,UNIV. OF TORONTO,ONT. UNIV. OF CALGARY, ALBERTA.

Elemental diets deficient in EFAs(linoleic acid)are frequently used for nutritional support.Since linoleic acid deficiency has been shown to alter RBC shape we examined morphological and lipid characteristics of RBC in 3 cystic fibrosis adolescents receiving exclusively an elemental diet(Vivonex)low in EFAs.The diet was given continuously for 14 days at 1.5 times the recommended daily caloric requirements.At 0,7 and 14 days we studied RBC morphology by scanning electron microscopy to determine the percentage of discoid cells and ecanocytes.In addition the RBC concentrations of cholesterol, total phospholipids, individual phospholipids and the fatty acid moities of the individual phospholipids were measured.From 0 to 7 days there was a significant decrease in discoid shaped RBC from 57.7±3.3%(S.E) to 35±5.2($p<0.01$)with a significant increase in ecanocytes I from 31.7±1.5% to 49.7±5.3($p<0.5$). These findings persisted on day 14 and in addition there was a significant increase in ecanocytes II from 6.3±4.8% to 16.3±2.9 ($p<0.25$).The only significant change in the RBC lipid profiles was a decrease over the first week in the concentration of phos photidylcholine linoleic acid from 15.63±0.78%to 8.63±1.10($p<0.05$) which persisted on day 14(8.53±1.03).This would suggest that diets deficient in linoleic acid can alter RBC morphology and therefore should not be used continuously as the sole source of nutrients for periods even as short as one week.

565 THE EFFECT OF VARIOUS STIMULI ON THE SECRETION OF PROSTAGLANDIN E_2 AND LYSOZYME AND PHAGOCYTOSIS BY HUMAN BREAST MILK MACROPHAGES. Justen H. Passwell, Hannah Blau and Bracha Ramot (Spon. by Zvi Friedman). Sackler School of Medicine, Chaim Sheba Medical Centre, Dept. of Pediatrics, Tel Aviv.

Breast milk macrophages cultured in vitro, synthesized and secreted increasing amounts of protein, lysozyme and prostaglandin E_2 (PGE_2) into the extracellular medium. These cells were also shown to actively phagocytose labelled zymosan particles in culture.

Concanavalin A, endotoxin and zymosan particles, but not latex particles, all resulted in an increased PGE_2 secretion (3-10 fold) into the medium compared to basal secretion (1ng/ml/10^6 cells). A dose dependent increase of PGE_2 production was also observed when lactoferrin (optimal dose 50 µg/ml) was added to the macrophage cultures, while neither lactalbumin nor lactoglobulin had any stimulatory effect. Varied effects on the secretion of lysozyme and phagocytosis were found with the different stimuli.

These findings indicate that phagocytosis and the secretory products of milk macrophages may be altered depending on the nature of the stimulating agent.

● **568** D-LACTIC ACIDOSIS, A NEW METABOLIC COMPLICATION OF SMALL BOWEL RESECTION. D. Perlmutter, J.T. Boyle, J.M. Campos, J.M. Egler, & J.B. Watkins. Univ. of Penn. Sch. of Med., The Children's Hospital of Philadelphia, Dept. of Pediatrics & Divisions of Gastroenterology, Endocrinology & Microbiology, Philadelphia, PA

Acidosis due to D-lactate production by intestinal bacteria occurs in ruminants engorged with carbohydrate (Ann. N.Y. Acad. Sci. 119:1109, 1965). A similar event was identified in two children who developed metabolic acidosis and peculiar neurologic symptoms in response to increased dietary carbohydrate after major small bowel resections. Both children were found to have elevated plasma levels of D-lactic acid (4.0-9.87 mM/L, normal 0.05-0.07 mM/L). Acid-base and neurologic abnormalities responded immediately to neomycin therapy. Amongst a number of microorganisms isolated from stool cultures of these patients, one anaerobic Lactobacillus acidophilus species produced in vitro high levels of D-lactate (31.8 mM/L vs. 0.48-0.53 mM/L in three other anaerobes). Reduction in carbohydrate intake in one patient tested led to a fall in D-lactate generation. These data suggest that excessive D-lactate production by intestinal bacteria, from malabsorbed carbohydrate, may produce metabolic acidosis and neurologic symptoms in children with small bowel resection.

566 AMILORIDE EFFECT ON RECTAL TRANSMUCOSAL POTENTIAL IN CYSTIC FIBROSIS. Claude J. Patton, Margaret Q. Jenkins, and Samuel S. Spicer (Spon. by Milton Westphal), Depts. of Pediatrics and Pathology, Medical Univ. of S.C., Charleston, S.C.

The principal manifestations of Cystic Fibrosis (CF) include elevated sweat electrolytes and a generalized exocrinopathy. Subnormal net transport of Na^+ across affected epithelial cells could underlie both the sweat ion abnormality and the exocrinopathy in CF. This unifying concept was tested by assessing electrogenic Na^+ transport in colon where the epithelium is involved in the disease and generates a measurable transmucosal potential difference (PD) by Na^+ transport. The resting PD across the rectal mucosa was measured in 22 CF patients and 20 normal controls, together with the effect on this PD of the diuretic drug amiloride, which specifically blocks channels for passive Na^+ diffusion and inhibits electrogenic Na^+ transport. The resting PD was determined between an isotonic saline-filled, rectal catheter connected to the recording electrode and a silver chloride-silver plate applied to a site of intradermally injected normal saline as the reference electrode. The mean resting PD was -26.5 ± 6.0 mV (mean ± SEM) in controls and -14.5 ± 5.0 mV in CF patients, a difference not statistically significant ($P > 0.25$). Amiloride induced a dose-related decrease in the transmucosal PD in all subjects, confirming Na^+ transport as the basis for the PD. The decrease was 6.0 ± 2.5 mV at 10^{-6}M, 15.8 ± 3.0 mV at 10^{-5}M and 27.0 ± 4.4 mV at 10^{-4}M amiloride in controls as compared with 1.0 ± 1.3 mV, 7.4 ± 1.9 mV and 18.9 ± 3.4 mV in patients, respectively. The lesser amiloride effect in CF was significant at 10^{-5}M ($P<.01$) and 10^{-6}M ($P<.05$) amiloride and suggests alteration of Na channels in CF. (Supported by NIH Grant AM-10956).

567 THE MINERAL STATUS OF ADOLESCENTS ON A HIGH PROTEIN WEIGHT REDUCING DIET. P.Pencharz, E.Archibald. (Spon: T.Heim) Research Institute, Hospital for Sick Children Toronto, Canada.

The effect of a high protein (2.5g/kg/d) diet consisting of lean meat, fish and poultry on the mineral status of 10 obese adolescents was studied. The diet was continued for a total of 3 months and was supplemented with minerals and vitamins. K, Mg and Ca balances were measured during the baseline and after 2 weeks on the diet. Total body potassium (TBK) and red cell (RBC), K and Mg were measured during the baseline, at 2 weeks and 60-90 days. No change was seen in Ca balance; the data for Mg and K are given below.

	K Balance (mg/d)	TBK (g)	RBC K (mEq/L)	Mg Balance (mg/d)	RBC Mg (mEq/L)
Control	402±287	126±28**	86.9± 7.5	-24±90	6.5±2.2*
14 d	298±276	120±27	93.1±13.5	294±22	5.6±1.2
60-90 d	ND	105±27**	84.9± 5.5	ND	3.6±0.5*

p values: * <0.01; ** <0.001; ND - no data

Of particular note is the absence of any significant change in RBC K despite a significant fall in TBK. Over 95% of TBK is in cells. It follows since there were no changes in hemoglobin, hematocrit or red cell count, that in this model the red cell does not reflect the K changes in other cells. Although there was no worsening of Mg balance after 14 d on the diet there was a consistent fall in RBC and serum Mg (from 1.82±011 to 1.68±0.08 mEq/L). Both values are still within normal ranges but the falls are of particular note in light of the obese adults who died of ventricular fibrillation on liquid protein diets.

● **569** CLASSIFICATION OF ENTEROPATHY IN TRANSIENT HYPOGAMMAGLOBULINEMIA(THI) OF INFANCY. D.Perlmutter, A.Leichtner, H.Winter, and R.Grand. Harvard Med. School, Children's Hos. Med. Ctr., Div. of Gastroenterology, Boston, MA

THI is thought to be uncommon; gastrointestinal manifestations have only recently been recognized, and potential small bowel lesions have not been defined. From a group of 370 children evaluated for chronic diarrhea in a subspecialty clinic over a 5-year span, we identified 40 patients with THI (10.8%). Criteria for diagnosis were: reduction in one or more of the 3 major immunoglobulins (Ig) of 2 S.D. or more below the mean for age, absence of nonspecific gut protein loss, presence of specific antibody production, and subsequent rise in Ig levels with age. Investigation of diarrhea included small bowel biopsy in 26 patients; normal mucosa was present in 14, patchy enteropathy in 7, and partial or severe diffuse villous atrophy in 5. Duration of diarrhea was similar in those patients with and without histologic abnormalities (16±11 vs 14± 2 mos.). Ig deficiency was prolonged in patients with patchy enteropathy as compared with patients having normal bowel mucosa (36.8±9.0 vs 17.2±8.0 mos., $p<0.01$). Six patients had serial small bowel biopsies over a mean observation period of 39 months; in 4, repeat biopsies were normal. In 65% of patients with THI, diarrhea resolved before Ig began to rise. CONCLUSION: 1) These data describe for the first time the histologic spectrum of enteropathy associated with THI, 46% of patients having patchy or diffuse villous lesions; 2) chronic diarrhea may be the sole clinical manifestation of THI; 3) small bowel mucosal abnormalities in THI are associated with more prolonged Ig deficiency.

570 MODULATION OF HUMAN POLYMORPHONUCLEAR LEUKOCYTE (PMNL) FUNCTION BY HUMAN COLOSTRUM AND MATURE MILK. Larry K. Pickering, Thomas G. Cleary, Susan Getz. Univ. of Texas Medical School, Program in Infectious Diseases and Clinical Microbiology and Dept. of Pediatrics, Houston, Tx.

To compare the effect of human colostrum (1-3 days) and mature milk (314 ± 150 days) on PMNL function, Ficoll-Hypaque separated PMNL from blood of 78 healthy volunteers were incubated with whole colostrum, colostral lipid and colostral aqueous phase from 39 mothers or with mature whole milk, and its separated components from 39 mothers and tested for resting and zymosan stimulated oxidative metabolism, functional activity and the presence of Fc receptors. Stimulated oxygen consumption, quantitative NBT dye reduction, $1\text{-}^{14}C$ glucose utilization and Fc receptors were significantly ($p<0.05$ to $p<0.001$) less in PMNL exposed to whole human colostrum or colostral lipid than in non-lipid exposed cells or cells exposed to the aqueous phase of colostrum. In contrast PMNL exposed to whole mature milk or to its lipid or aqueous phase had no significant decrease in any of these parameters when compared to non exposed cells. In assays of phagocytosis, colostral PMNL or blood PMNL exposed to colostral lipid had a significant ($p<0.001$) decrease in their ability to ingest ^3H methyl thymidine labeled S. aureus when compared to non-lipid exposed PMNL. Blood PMNL exposed to lipid from mature milk had no decrease in ability to ingest S. aureus. Lipid or lipid soluble material present in human colostrum but not mature milk causes inhibition of phagocytosis and respiratory burst related activities in PMNL. Supported by NIH grant HD13021.

571 EFFECT OF FETAL GROWTH ON THE CELLULAR IMMUNE SYSTEM. W.B.Pittard, K.Miller, R.U.Sorensen, Dept. Ped., RB&C Hosp., CWRU, Cleveland, Ohio.

Cell mediated immunity(CMI)is impaired in malnourished children and adults. These same individuals are often infected presenting a dilemma as to cause and effect. To determine the influence of intrauterine growth retardation(IUGR)on CMI in the uninfected fetus we measured lymphocyte proliferation in response to a panel of 4 mitogens in 90 appropriately grown(AGA)and 20 growth retarded(SGA)neonates. Proliferation/10^5 cord blood mononuclear cells was measured with a whole blood assay using tritiated thymidine incorporation. Neonatal lymphocyte proliferation did not differ

	PRETERM		TERM		ADULT
	AGA	SGA	AGA	SGA	
n	31	6	59	14	
GA*	30±.4	28±.7	40±.1	40±.2	
B Wt.*	1.3±.1	.8±.1	3.2±.1	2.2±.1	
PWM*	26±2	20±7	25±2	27±10	24±3
Con A*	88±11	69±20	66±6	77±18	62±8
PHA*	60±5	63±11	45±4	74±25	122±14**
SpA*	40±5	40±14	33±3	32±8	37±7

*Values represent Mean±SEM X 10^3; **p<.001

with gestational age, was unrelated to intrauterine growth (nutritional) status, and differed from adult lymphocyte responses only in response to PHA. In contrast to other observations these data demonstrate no effect of IUGR on fetal CMI development. This difference may be related to the use of a whole blood lymphocyte culture technique, use of a noninfected patient population, and/or a broader spectrum of mitogens.

572 CHRONIC NONSPECIFIC DIARRHEA, OR THE "IRRITABLE BOWEL" IN CHILDHOOD: A NEW LOOK THROUGH THE SCANNING ELECTRON MICROSCOPE. J.R.Poley and D.Bullock. Depts. of Pediat. and Electron Microsc., East. Virginia Medical School, Norfolk, VA

Since we obtained preliminary evidence linking chronic nonspecific diarrhea (CND) to increased bacterial contamination of the upper small intestine, we studied the surface morphology of small bowel mucosa with the scanning electron microscope (SEM). Biopsied tissue was prepared from 70 children aged 10 months to 5 years with CND and from 5 controls for SEM, light (LM) and transmission electron (TEM) microscopy, and for disaccharidase (DD) assays. By SEM, the following changes in surface morphology were identified: 1. Partial villous atrophy (PVA); 2. Increased extrusion of cell cytoplasm (ECC); 3. Excessive mucus on the mucosal surface; 4. Alterations of the microvillar surface and the brushborder; 5. Presence of micro-organisms (MO). The most common finding was the presence of MO (bacteria, rods, cocci, filamentous MO, candida), considered most likely responsible for the pathologic changes, which were usually present in variable combinations. PVA, although infrequent, was always associated with decreased DD activities, but these were also found in histologically (LM) normal mucosa: by SEM, there was evidence of increased EEC, suggesting that immature enterocytes populated the villi. Clinical intolerance to carbohydrate in presence of normal DD activities was best explained by an excessive layer of mucus on the mucosal surface, inhibiting contact of the carbohydrate with DD. TEM supported findings by SEM. The diarrhea responded favorably in all children by measures, mainly dietary, implicated in decreasing populations in the small intestine.

573 EFFECT OF NUTRITIONAL DEPLETION ON PHYSIOLOGIC STABILITY, Murray M Pollack, Jeannette S Wiley, Timothy S Yeh, and Urs E Ruttiman (Spon. by G Rosenquist), George Wash. U., Children's Hosp Nat'l Med Ctr, Washington, D.C.

Acute and chronic protein-energy malnutrition (PEM) and depletion of body stores of fat and somatic protein are common in critically ill children. In order to better define the effects of these depletions, we related them to physiologic stability. The nutritional status of 60 critically ill medical patients with normal hydration status and without chronic organ failure was evaluated by anthropometric techniques within 48 hours of admission to the ICU. Daily assessments of physiologic stability were done using a new, validated, scoring system (Physiologic Stability Index, PSI) based on the degree of abnormality of 34 physiologic variables (e.g. BP, HR, CVP, PCWP, cardiac output, ABG's electrolytes, ICP, Glascow Coma Score). Overall, the incidence of nutritional depletion was acute PEM - 13%, chronic PEM - 10%, fat store depletion - 38%, and somatic protein store depletion - 8%. Pts. with acute PEM had PSI scores indicative of more physiologic instability (higher scores) compared to pts. without acute PEM. These scores included admission (15.3 vs. 8.1, P=.002), maximum (18.4 vs. 10.0,P=.001), and 4-day average (12.2 vs. 7.0, P=.002). Chronic PEM and depletion of fat or somatic protein stores were not significantly associated with high PSI scores. We conclude that critically ill children with acute PEM have a higher level of physiologic instability compared to children without acute PEM. Acute PEM seems to be a contributing factor to this instability. This information is important in evaluating the need for nutritional therapy.

574 PSYCHOLOGICAL CHARACTERISTICS OF CHILDREN WITH CHRONIC ABDOMINAL PAIN. Deborah Raymer, Richard Hamilton, Ronald J. Friedman, Donald F. Burrill, The Hosp. for Sick Children, Dept. of Pediatrics and the Ontario Inst. for Studies in Education, University of Toronto, Toronto, Canada.

We studied specific features of emotional adjustment in children age 8-16 with abdominal pain. In 4 study groups 1) Crohn's disease, n=24 2) ulcerative colitis (UC) n=20 3) non-organic, recurrent abdominal pain (RAP), n=16 4) healthy school children, n=30, we used a self report technique to measure self-esteem, helplessness, self-blame and depression as well as psychological stress occurring in the year preceding onset of symptoms. Controls were similar with respect to age, sex and socio-economic status. Compared with controls, children with Crohn's disease demonstrated depression ($p<0.025$) and low self-esteem ($p<0.005$); those with UC, depression ($p<0.05$); and those with RAP, very low self-esteem ($p<0.005$). Incidence of stressful events also differentiated the 4 groups ($p<0.025$), with the Crohn's children reporting the highest number. We conclude that significant psychological problems accompany chronic abdominal pain, and that knowledge of these difficulties in both organic and non-organic cases can be utilized to provide psychological support in the comprehensive care of children with these common disorders.

575 ROLE OF THYROXINE IN THE DEVELOPMENT OF FEEDING CONTROLS IN THE RAT. Tami J. Romano and Susan J. Henning, University of Houston, Department of Biology, Houston, TX 77004.

The effect of hyper- and hypothyroidism on the development of caloric control of feeding behavior was studied in suckling and weanling rats. The suckling behavior of fed and fasted rat pups aged 6-21 days was assessed by measuring 2 parameters: milk intake and nipple attachment latency. For euthyroid pups aged 7, 14 and 17 days the milk intake during a 2-hr suckling session was the same in pups fasted for 16 hr as in pups which were allowed to feed until the time of testing. Only on day 21 did the euthyroid pups display greater milk intake when in the fasted state than in the fed state. This maturation of fed/fasted differences of milk intake was advanced to day 17 in hyperthyroid pups. Conversely, propylthiouracil-induced hypothyroidism prevented the normal development of feeding controls, indicated by failure of these pups to display fed/fasted differences of milk intake even at 21 days of age. The results of the studies of nipple attachment latency indicated that thyroid status has only a modest effect on the tendency to initiate suckling. Thus the dramatic effects of hyper- and hypothyroidism on the developmental patterns of milk intake are probably mediated via modification of the tendency to terminate suckling. In other words, it seems that the maturation of satiety mechanisms may be cued by the ontogenic rise of serum thyroxine levels.

This work was supported by NIH grant number HC 14093.

576 ANORECTAL MANOMETRY: A NEW SIMPLIFIED TECHNIQUE FOR INFANTS AND CHILDREN. Allan J. Rosenberg and Adan R. Vela (Spon. by Richard L. Fowler), Louisiana State University School of Medicine, Department of Pediatrics, New Orleans

The purpose of this study was to develop a simple technique that is well-tolerated and rapid for assessing anal sphincter functions in pediatric patients with fecal incontinence and constipation. Other methods used in diagnosis include barium enema, biopsy, and histochemistry. Several non-invasive techniques using anal balloon or catheter perfusion associated with rectal balloon distention have been used in differentiating causes of constipation. We have developed a method using a micro-tip pressure transducer for recording anal sphincter responses to rectal balloon distention. The responses are recorded on a direct writing multichannel recorder. Results are obtained within 15 to 30 minutes. This test has been applied to 54 patients presenting with varying degrees of anorectal dysfunction; 3 patients were age under 1 month, 10 were from 1 month to 1 year, 22 were 1-5 yrs., 13 were 5-10 yrs. and 6 were 11-13 yrs. In 13 patients, the internal anal sphincter showed no response or positive spike to balloon distention, consistent with the manometric diagnosis of aganglionic megacolon. These findings were confirmed by absence of ganglion cells on rectal biopsy. Forty-one children had normal internal sphincter relaxation to rectal distention. Ganglion cells were present in 13 biopsy specimens. In the remaining 28 patients, no further workup of aganglionosis was necessary. There were no false-positive or false-negative results. This technique has proved to be a rapid, safe way to initially evaluate infants and children with constipation and encopresis.

577 POSTNATAL MALNUTRITION IN RATS: EFFECT OF FEEDING FREQUENCY ON THE REVERSIBILITY OF PANCREATIC (Pan) AND SMALL INTESTINAL (Int) ENZYMES. Thomas M. Rossi, Ping-C Lee, and Emanuel Lebenthal. Gastroenterology and Nutrition Division. Children's Hospital and SUNY at Buffalo, Buffalo, N.Y.

Changes in the frequency of feeding influence Int. functions. Restricted feeding has been shown to increase absorption and metabolism. To see if these acquired proficiencies are advantageous in speeding up recovery, postnatal malnourished pups, obtained by the expanded litter technique, were weaned onto an ad libitum (ad lib) (food available 24hr/day) or restricted feeding schedule (food available 2hr/day). Subsequent development was followed. At 21 days, malnourished pups showed a drop in body weight (BW), Pan. and Int. masses, amylase (A) and lipase (L), but lactase was higher. With subsequent ad lib feedings, Int. mass attained control level after 28 days. The BW and Pan. masses remained lower than control even after 49 days. Both A and L, however, rose to control levels after 14 days. Lactase declined in all groups after 7 days. With restricted feeding, both malnourished and control pups had higher disaccharidases. Pan. enzymes showed no distinct pattern. Differences in BW, Int. and Pan. masses were maintained throughout subsequent feedings. Both restricted fed groups were lower compared to the corresponding ad lib groups. (A) increased by 14 days, but (L) remained depressed. Thus, except for BW and Pan. mass, the effects of malnutrition on Pan. and Int. enzymes studied are reversible with ad lib feeding. Restricted feeding does not allow for catch up growth. It also delays recovery of A and prevents recovery of L. Supported in part by NIH Grant #12586.

578 TRANSFER OF VITAMIN D (D) VIA BREAST MILK. Alan D. Rothberg, John M. Pettifor and Desmond F. Cohen (Spon by M. Jeffrey Maisels). Witwatersrand University, Johannesburg Hospital, Dept. of Pediatrics, Johannesburg, South Africa.

To evaluate the transfer of D via breast milk, white nursing mothers of term infants were given placebo (P, n=10), 500 IU D/day (A, n=9), or 1000 IU D/day (B, n=9) for 6 weeks after delivery. These mothers received no additional D in other vitamin preparations or milk (South African milk is not D-fortified), and the infants were not given supplemental D. A control group (C, n=12) of mothers received no D, but their infants were given 400 IU D/day. Serum calcium (Ca), phosphorus (Pi), alkaline phosphatase (AP) and 25 hydroxy D (25HD) were measured in mothers and babies at 6 weeks. Maternal levels of 25HD were similar in the 4 groups (mean 10.0;13.8:12.9;11 ng/ml for groups P, A, B, C resp.). However, P infants had a mean 25HD of 1.1+0.5 ng/ml (±SEM), significantly below the means of the other groups (A 10.2±2.0, $p<.01$; B 7.1±1.7, $p<.01$; C 15.3+1.4, $p<.001$). C infants had higher 25HD levels than A and B infants (C 15.3±1.4 vs A + B 8.5±1.3 ng/ml, $p<.01$). Despite the 25HD findings in infants, no intergroup differences were observed for Ca, Pi, AP; all being within normal range. Similarly, maternal Ca, Pi, AP were normal. This study clearly shows that D or metabolites cross in breast milk, but in the absence of maternal or infant supplementation, the infant becomes D deficient in the first 6 weeks of life. Even in sunny climates, if milk supply is not D fortified, supplemental D to nursing infants seems prudent.

579 PREALBUMIN: A SENSITIVE INDEX OF DISEASE ACTIVITY IN INFLAMMATORY BOWEL DISEASE. Fred C. Rothstein, Michael D. Reed, Thomas C. Halpin (Spons. by William T. Speck), Case Western Reserve University School of Medicine, Department of Pediatrics, Rainbow Babies & Childrens Hospital, Cleveland, Ohio.

Serial serum prealbumin (PALB), albumin (ALB), transferrin (TF) and retinol-binding protein (RBP) concentrations were prospectively monitored to evaluate 1) relationship of serum protein concentrations to disease activity and 2) visceral protein response to therapy in 7 hospitalized children with Crohn's disease (5) and chronic ulcerative colitis (2). All children (9.5-15.5 yrs) presented with weight loss (range 4-13 kg) which reflected a 10-25% change in body weight and had clinical scores consistent with severe disease. Therapy consisted of bowel rest, intravenous prednisolone, 1.5 mg/kg/d (maximum 60 mg/d) and parenteral nutrition. Parenteral nutrition was administered for a $\bar{x}$ 34 days and provided a minimum of 55 Kcal/kg/d and 0.3 gm N/kg/d. Serum protein concentrations were determined in duplicate utilizing a radial immunodiffusion technique. Prior to therapy, PALB and RBP were abnormal in all children. Despite the severity of the disease, 5 of 7 children had normal ALB, and 7 of 7 children had normal TF concentration. PALB, ALB and RBP normalized with therapy. PALB was the most sensitive indicator of disease activity and response to therapy. During followup, a decrease in PALB preceded clinical signs of disease activity, suggesting that it may be useful as an objective parameter for prospective monitoring of children with inflammatory bowel disease.

● **580** TAURINE PREVENTS CHOLESTASIS INDUCED BY LITHOCHOLIC ACID SULFATE IN GUINEA PIG. C.C. Roy, N. Dorvil, B. Tuchweber, M. Audet and I. Yousef. Departments of Pediatrics and Nutrition, Hôpital Ste-Justine and University of Montreal, Montreal, Quebec.

There is a considerable interest in the biological importance of taurine particularly in species dependent on a dietary source. The observation that glycine conjugated sulfolithocholate (S-LCA) is cholestatic in the rat while taurine conjugates have no cholestatic properties suggest that the glycine/taurine (G/T) ratio of conjugated bile acids may be an important determinant of certain forms of cholestasis (Gastroenterology 80:233, 1981). Thus it was of interest to explore the role of taurine supplements in the guinea pig which conjugates over 90% of its bile acids with glycine. Body weight, liver morphology, bile flow and bile acids were monitored at 1,3,5,10 and 21 days in 4 groups of 20 animals each. Taurine at a concentration of 0.5% in the drinking water increased bile flow and bile acid secretion when compared to controls and led to an almost complete disappearance of glycine conjugated bile acids. Animals who were not pretreated with taurine prior to an I.V. injection of 180 μmoles/kg body weight of S-LCA showed numerous cytoplasmic vacuoles with normal bile canaliculi and a striking reduction of bile flow to less than 20% of values obtained in controls. In contrast, the group who had taken taurine for various periods before the S-LCA injection showed no histological changes and no decrease in bile flow. These data indicate that dietary taurine increases bile flow, bile acid secretion and exerts a protective effect against cholestasis induced by monohydroxy bile acids.

● **581** NORMAL CONCENTRATIONS OF SERUM AND INCREASED INTESTINAL APO-B WITH FAILURE OF CHYLOMICRON SECRETION:A NEW DISORDER OF LIPID TRANSPORT. C.C. Roy, A. Sniderman, R. Deckelbaum, J. Letarte, P. Brochu, A. Weber, C.L. Morin, J.-P. Buts and P. Green. Depts. of Pediatrics and Medicine,Hôpital Ste-Justine, Univ. of Montreal, Royal Victoria Hospital, McGill Univ. Montreal, Hadassah Univ. Hospital, Jerusalem and Columbia Univ. College of Physicians and Surgeons, New York.

Seven children aged $1\frac{1}{2}$ to 19 years who, during the first few months of life, developed a celiac-like syndrome were recently studied. Psychomotor retardation (1/7), absent reflexes (2/7), abnormal electrooculograms (3/7) and electroretinograms (1/7) were noted. All were hypocholesterolemic (70.1±5.8 mg/dl). Fasting triglyceride levels (74.9±38.5 mg/dl) did not change during the 5 hrs following a fat load of 50 g/1.73 m^2. Furthermore chylomicrons were not detected by agarose gel electrophoresis or by ultracentrifugation. HDL-cholesterol (14.3±3.9 mg/dl) and LDL-cholesterol (20.7±11.4 mg/dl) were both reduced as were fasting levels (mg/dl) of Apo A-I (90.1±12.1) and of Apo A-IV (8.9±3.0). However serum Apo B levels (mg/dl) were normal (61.4±8.6) when compared to those (80±15) of 65 controls. Total (8.2±4.6 μM FFA/ml/hr) and residual (6.5±2.6) lipoprotein lipase activities were somewhat reduced. Small bowel biopsies in all patients showed fat-laden enterocytes on light microscopy and E.M. demonstrated chylomicron-like structures. Immunoperoxidase staining of these cells revealed the presence of superabundant amounts of Apo B. Although the exact pathophysiologic defect remains to be determined,the data are consistent with a disorder in the final assembly or secretion of chylomicrons.

582 CAMPYLOBACTER ENTERITIS: EPIDEMIOLOGIC AND CLINICAL FEATURES. Venusto H. San Joaquin, David F. Welch, and Melvin I. Marks. University of Oklahoma Health Sciences Center, Department of Pediatrics, Oklahoma City, OK.

To improve understanding of the epidemiology and clinical features of campylobacter infection, we reviewed our 2 year experience with the disease. From January 1980 to November 1981, 77 cases were identified comprising 20% of 401 bacteriologically confirmed gastroenteritis in the same period. Shigella (182-45%) and Salmonella (142-35%) accounted for the others. The epidemiologic distribution of the campylobacter patients were as follows:

Season	# cases (%)	Age (yrs)	# cases(%)	Sex;Race	# cases(%)
Jan-Apr	9 (12%)	<1-14	63 (82%)	Males	43 (56%)
				Females	34 (44%)
May-Aug	40 (52%)	5-10	8 (10%)	White	55 (71%)
				Black	14 (18%)
Sept-Dec	28 (36%)	>10	6 (8%)	Am Ind	6 (8%)
				Others	2 (3%)

No cases occurred in February. Twenty-one (27%) were <1 yr of age; the youngest were twins who developed bloody stools at age 3 days; they were otherwise well. Diarrhea with or without blood and mucus, abdominal pain, & fever were prominent. Unusual presentations included: fever and abdominal pain without diarrhea in 2 cases; asymptomatic rectal bleeding, without diarrhea - 1 case; pseudoappendicitis, 1 case; dehydration followed by hemolytic uremic syndrome - 1 case. Most cases were outpatients. Thirteen presented with chronic diarrhea of several weeks duration. Campylobacter is a common pediatric pathogen with protean manifestations.

583 EFFECT OF ORAL LIPID ADMINISTRATION WITH 67% MEDIUM CHAIN TRIGLYCERIDES (MCT) ON GLUCOSE HOMEOSTASIS IN SMALL-FOR-DATE (SFD) INFANTS. L. SANN, P. DIVRY, Y. LASNE, A. RUITTON. (Spon. by Mark A. Sperling). Hopital Debrousse, Lyon, France.

The metabolic effect of oral feeding with 1.3 g/kg bw lipids (67% MCT) was studied in 14 term SFD infants. It was compared to a control group of term SFD infants, to a group of 7 term infants with an appropriate birth-weight (AGA) and to 7 AGA preterm neonates. Plasma glucose concentration rose from (m±sem) 65 ± 3,5 to 80 ± 5,5 mg/dl at 30 minutes and 86 ± 5 at 60 minutes. While no change was observed in the control group, this glycemic effect was found also in AGA term and preterm infants. In term SFD infants, the disappearance rate of glucose in plasma after the lipid load 1,24% per minute was similar to SFD control infants. The lipid load produced no change of insulin/glucagon molar ratio in SFD infants. Despite lower basal free fatty acid and ketone bodies (KB) concentrations in SFD infants than in AGA infants, this lipid load induced a larger increase in KB in SFD infants (+ 220%) than in AGA infants (+ 40%).

These data show that lipids with 67% MCT increase the blood levels of glucose and KB in SFD infants. They suggest that the rise of glucose is due to stimulation of gluconeogenesis.

584 MANAGEMENT OF IRRITABLE COLON WITH FIBER DIET. S.J. Schwarzenberg, D.D. Black and P.F. Whitington (Spon. by J.F. Griffith), Dept. of Peds., Univ. of Tn. Ctr. for the Health Sciences, LeBonheur Children's Med. Ctr., Memphis.

Forty-four children with irritable colon syndrome, diagnosed because of frequent, small stools without evidence of infection or malabsorption, seen over a three year period, had an average age of 23.9 months and duration of symptoms of 11.3 months. They were treated with a high fiber diet and counseling to assure the parents their child was not ill, the stooling pattern was not harmful, and enhanced dietary bulk would improve the symptom. They were instructed that this was not a "diet" but a pattern of healthy eating for both children and parents. The outcome, one to three years after the initiation of the diet, was evaluated by questionnaire, and 26 responded. Compliance with the diet was good; an 89% increase in fiber foods was observed. This increase did not reflect a general liberalization of the diet although many patients had been on elimination diets. For example, dietary fat, considered by some to be important in the pathogenesis of this syndrome, increased only 13%. These changes in diet resulted in marked improvement of the stool number and character, as noted in the table.

	Number	Watery	Pellet	Mixed	Formed	Mucus	Undig. Food
Before	6.1	69.2%	11.5%	15.4%	0	50.0%	61.5%
After	1.7	0	11.5%	0	88.3%	3.8%	15.4%

Overall, 96.2% achieved results satisfactory to their parents. We conclude irritable colon can be successfully treated with a combination of counseling and high fiber diet.

585 BREAST FEEDING BY TWO MOTHERS WITH CYSTIC FIBROSIS. Thomas W. Seale, Marinus Flux, Owen M. Rennert, Mitchell Shiffman* and Philip T. Swinder*. University of Oklahoma Health Sciences Center, Department of Pediatrics, Oklahoma City and *Department of Pediatrics, SUNY UpState Medical Center, Syracuse, New York.

Vigorous supportive therapy has led to the survival to reproductive age of an increasing number of cystic fibrosis (CF) patients. Because the breast is a modified sweat gland and the electrolyte composition of sweat is abnormal in CF, concern has been expressed that CF breast milk also might contain high levels of Na and Cl which could endanger the neonate. Protein content might also be abnormal. To examine this question we analyzed the chemical composition of 72 breast milk samples obtained within the first two postpartum months from two women with cystic fibrosis. Na, K, Cl, osmolality, total reducing sugar, total fat and total protein were determined. Na levels ranged from 22-2 mM in colostrum and decreased to 7-8 mM in mature milk. Cl ranged from 29-5 mM in colostrum and decreased to ≤15 mM in mature milk. K+ was rather constant (15 mM) in one patient but ranged from 2-16 mM in the other. Osmolality ranged widely (70-238 mOsm/kg) in colostrum but was about 220 mOsm/kg in mature milk. Total reducing sugar (80-85% lactose) was 6-8 g/100 cc in mature milk. Protein content was ≤1.1 g/100 cc in both colostrum and mature milk. These data show that the electrolyte and macronutrient composition of CF milk is in the normal range. Variations in clinical and nutritional status among CF patients warrant monitoring of milk quality and quantity in individual cases.

586 TOXIC BREAST MILK: NEONATAL HYPERNATREMIA ASSOCIATED WITH ELEVATED SODIUM IN BREAST MILK. Thomas W. Seale, Owen M. Rennert, Mitchell Shiffman* and Philip T. Swinder*. University of Oklahoma Health Sciences Center, Department of Pediatrics and *SUNY UpState Medical Center, Department of Pediatrics, Syracuse, New York.

Low Na levels and the low renal solute load of human milk protect breast fed neonates against the development of hypernatremia. We have identified a 33 year old gravida 3 para 2 Caucasian female who after each of two pregnancies produced mature breast milk with high Na levels (64mEq/L and 13-36mEq/L respectively) in the absence of abnormal salt intake or any significant clinical findings. Her 1st child, the product of a full term uncomplicated pregnancy, was a healthy 3.1 kg male who was solely breast fed every 3 hours. By day 6 the child became lethargic, had decreased urine output and fed poorly with no vomiting or diarrhea. Upon admission on day 10 the child weighed 2.2 kg, had serum Na of 183 mEq/L, K 4.7 mEq/L, Cl 143 mEq/L, HCO_3 of 6 mEq/L, BUN 183 mg/dl, creatinine 4 mg/dl, pH 7.17. The child died of a cerebral hemorrhage on day 11. Subsequently 3 samples of her breast milk were found to contain 61-64 mEq/L Na. Her 2nd child was fed formula but milk collected q.i.d. for 20 days contained elevated Na, normal K (12-20 mEq/L), slightly elevated Cl (14-22 mEq/L) and normal levels of total fat (3-4 g/dl), total protein (1.8-2.2 g/dl), reducing sugars (6-8 g/dl) and normal osmolality (200-285 mOsm/kg). Abnormally high breast milk Na levels of constitutional origin should be considered among the causes of neonatal hypernatremia. This, as in 3 other recently reported cases, is unrelated to maternal cystic fibrosis.

587 DUODENAL FLUID ANTIBODIES TO COW'S MILK PROTEINS: RELEASE ENHANCED BY PANCREOZYMIN (PZ-CCK) AND SECRETIN (S). Praful C. Shah, Serem Freier, Byung H. Park, Ping-C Lee, and Emanuel Lebenthal. Department of Pediatrics. Children's Hospital and SUNY at Buffalo, Buffalo, N.Y.

Complexing of food protein by IgA antibodies has been shown to improve the efficiency of proteolysis. The coordinated secretion of antibodies and proteolytic enzymes would therefore be advantageous. We investigated the possibility that PZ-CCK and S, which are known to release pancreatic enzymes, fluid and bicarbonate, also increase the amount of food specific antibody. Duodenal fluid was collected before and after administration of PZ-CCK and S. Protein content, proteolytic enzyme and antibody activities against 5 milk proteins were measured. ELISA were developed for the detection of IgA, M, and G antibodies against α-casein, α-lactalbumin, bovine serum albumin, β-lactoglobulin A and B. Both IgA and IgM antibodies showed significant response to PZ-CCK and S. After PZ-CCK, IgA and IgM antibody activities rose 6-fold and reached peak levels in 5-10 minutes. The increase in antibody activity against the milk proteins paralleled the increase in protein content and proteolytic enzyme activity. In spite of the known dilutional effect of S on duodenal fluid enzyme concentration, a parallel decrease in antibodies was not seen. Instead, S produced a 4-fold rise of IgA antibodies and a 16-fold rise of IgM antibodies. It is suggested that the secretion of PZ-CCK and S following food intake may increase the availability of antibodies to food proteins in the GI tract.
Supported in part by USPS grants DE-05505, AG-02417 and by a grant-in-aid from the National Dairy Council.

588 DELIVERY OF VITAMINS E AND C FROM TOTAL PARENTERAL ALIMENTATION (TPA) SOLUTION. Jayant P.Shenai, Peggy R. Borum. (spon. by M. Stahlman). Vanderbilt Medical Center, Departments of Pediatrics and Biochemistry, Nashville, Tennessee.

We have previously shown that substantial losses of fat-soluble (FS) vitamin A from TPA solution occur due to adsorption in the iv tubing and photodegradation in the bottle. This study assessed the delivery of FS vitamin E and water-soluble (WS) vitamin C from TPA solution.

A standard TPA solution containing 2.0 ml/L of an aqueous multivitamin infusion (USV Pharmaceutical) was infused at a constant rate of 10 ml/hr, using a standard iv administration set. Multiple aliquots of the solution from the bottle and the effluent were obtained at designated time intervals in a 24-hour period. From measurements of vitamins E and C in these aliquots, net delivery of each vitamin was estimated. Mean concentrations are shown in table:

Hours of use	Vitamin E (mg/dl)		Vitamin C (mg/dl)	
	Bottle	Effluent	Bottle	Effluent
0-6	0.40	0.25	26.9	26.8
6-12	0.42	0.39	27.3	28.8
12-18	0.42	0.41	25.1	25.3
18-24	0.43	0.44	25.2	24.3

Both vitamins remained relatively stable in the bottle. A significant amount of vitamin E was lost in the iv tubing. Its net delivery amounted to 88% of expected delivery. Conversely, no losses of vitamin C were incurred in the iv tubing. The data suggest that delivery of FS vitamins from TPA solutions is less than optimum because of adsorptive losses. Similar losses are not encountered with WS vitamins.

589 CARNITINE STATUS AT BIRTH OF NEWBORN INFANTS OF VARYING GESTATION. Jayant P. Shenai, Peggy R.Borum, Susan C. DonLevy. (spon. by M. Stahlman), anderbilt Medical Center, Departments of Pediatrics and Biochemistry, lashville, Tennessee.

Carnitine (C), β-OH-γ-trimethyl-aminobutyric acid plays an important ole in the mitochondrial oxidation of long chain fatty acids. Adequate lood and tissue concentrations of C may be important in promoting tilization of energy and growth. Various animal studies have emonstrated a transfer of C from the mother to the fetus during regnancy. Little is known of C levels during various stages of human estation. This study was designed to assess and compare the plasma (PL) nd red blood cell (RBC) concentrations of C at birth in a group of eterm (<36wk,n=41) and term (≥37wk,n=46) neonates. Results (mean ± E) are shown in the table.

roup	Gestation(wk)	Weight(gm)	PL(C)(nm/ml)	RBC(C)(nm/mgHb)
reterm	32.6 ± 0.4	1840 ± 89	28.2 ±1.9	0.22 ± 0.02
erm	40.0 ± 0.2	3380 ± 70	21.9 ±0.9	0.15 ±0.01
	<.001	<.001	<.01	<.01

Both PL(C) and RBC(C) correlated negatively with gestational age. revious studies have shown that neonates, including preterm infants may ave a decreased capacity for C synthesis. The higher concentrations of in blood in preterm neonates thus probably reflect enhanced ansplacental acquisition or decreased tissue utilization of C in the eterm period. Following birth, an abrupt cessation of C supply from the aterno-placental unit may predispose the immature neonates to C eficiency and its adverse effects, particularly in the absence of an dequate exogenous C intake in the postnatal period.

upported by a grant from The Nutrition Foundation.

590 VITAMIN A STATUS OF NEONATES WITH CHRONIC LUNG DISEASE (CLD). Jayant P. Shenai, Frank Chytil, Mildred T. Stahlman. Vanderbilt Medical Center, Departments of ediatrics and Biochemistry, Nashville, Tennessee.

Vitamin (vit) A influences the orderly growth and differentiation of ithelial cells. Vit A deficiency is associated with a generalized uamous metaplastic change in epithelial tissues. Such a change in the ing epithelium of the tracheobronchial tree may compromise mucosal nctions such as clearance of mucus and secretions, and protection ainst secondary infection. This change may be detrimental to neonates th CLD. We have therefore evaluated vit A status of infants with CLD.

Preterm infants (<1500gm,<31wk) requiring mechanical ventilation V) during the first week of life for a minimum of 72 hours were lected as infants at risk for CLD. 8/9 such infants in a 6 month period veloped clinically and radiologically confirmed CLD. Their clinical urse showed: MV: 43±19 days, O_2 therapy: 56±26 days, PDA requiring osure: 7/8, air leak: 3/8, NEC requiring surgery: 1/8, episodes of psis: 2.4/infant, mortality: 1/8. Their average vit A intake (IU/kg/d) and quential serum vit A (mcg/dl) determinations (mean±SE) are mmarized in the table.

eek	1	2	4	6	8
rum vit A	11.2±1.6	13.5±1.8	12.1±3.1	8.5±1.0	13.9±4.2
ake(iv+oral)	196±15	427±60	328±190	250±293	105±576

/40 serum vit A values were low (<20mcg/dl). We conclude that vit A atus of neonates with CLD is poor at birth and remains poor for tended periods of time despite increasing vit A intake. The cause and fect relationship between the vit A status and CLD remains to be vestigated. (Supported by NIH grants SCOR HL 14214, HL 15341, HD 195).

591 LIVER VITAMIN A RESERVES OF VERY-LOW-BIRTH-WEIGHT (VLBW) NEONATES. Jayant P. Shenai, Frank Chytil, Mildred T. Stahlman. Vanderbilt Medical Center, partments of Pediatrics and Biochemistry, Nashville, Tennessee.

The plasma concentrations of vitamin (vit) A and its carrier retinol-nding protein (RBP) at birth are lower in preterm neonates than in term ants. In adults, vit A content of the liver is believed to be a more curate indicator of the vit A status. This study assessed the liver vit A serves at necropsy of VLBW neonates (n=14) dying within 24 hours of th, prior to possible changes in vit A status induced by postnatal ervention. These infants (M=9,F=5) were < 28 wk in gestation,<1060gm birthweight, and without congenital anomalies or evidence of growth tardation. Death was secondary to complications of extreme ematurity. Autopsy was performed within 12 hours of death. Liver sue samples were obtained from the central portion of the right lobe. ood samples were obtained by cardiac puncture.

Measurement	Mean ± SE	Range	Reference values #
rum vit A (mcg/dl)	13.2 ± 2.2	6.7-19.7	25-90(20)*
rum RBP (mg/dl)	2.05 ± 0.22	1.5-3.2	2.5-6.4 (3.0)
ver vit A (mcg/gm)	30.5 ± 3.0	14.4-49.0	100-300(40)

Range in children and adults, (Critical levels of adequacy)*.

These data suggest that VLBW neonates are born with low blood levels vit A and RBP. Their liver reserves of vit A are also low, suggesting at their potential ability to offset an inadquate vit A intake may be or. A compromised nutritional intake resulting from problems sociated with extreme prematurity may predispose such neonates to vit deficiency in the postnatal period. (Supported by NIH grants SCOR HL 214, HL 15341, HD 09195).

592 THE INFLUENCE OF INTESTINAL BACTERIAL OVERGROWTH (BO) AND MALNUTRITION (M) ON MUCOSAL INJURY IN RATS. Philip Sherman, Gordon Forstner, Dept. of Ped., Univ. of Toronto, Hospital for Sick Children, Toronto, Canada.

The impact of M on disaccharidase deficiency (DD) associated with BO was studied in rats with self-filling (SFBL) and self-emptying (SEBL) blind loops. M was created with a paired, restricted-access diet in which the M BL rat received 50% of the daily intake of the normally fed (N) BL rat. Total viable anaerobic bacteria/ml of lumen content and BL mucosal disaccharidase activities/mg pr. were determined at weekly intervals postop.

In both SEBL and SFBL, M rats grew <20% as rapidly as N rats. BL bacterial counts were the same in M and N rats at all weeks. In the SEBL, disacch. levels in M were identical to N for 3 weeks postop. Maltase and sucrase were increased in M ($p < .05$) at 4 weeks. In the SFBL, disacch. activities fell between weeks 1 and 4 ($p < .01$) and were unchanged at 6 and 8 weeks. At 4 weeks disacch. activities were the same in M and N SFBL rats (table).

		Maltase		Sucrase		Lactase	
		(Units/mg protein, mean ± SEM)					
SFBL	(N=8)	.123 ± .021	NS	.026 ± .004	NS	.009 ± .001	NS
SFBL+M	(N=6)	.155 ± .022		.034 ± .006		.006 ± .001	

However, in the M SFBL, sucrase ($p < .01$) and maltase ($p < .05$) were significantly lower than in the N SFBL 1 week postop and fell more rapidly thereafter to 4 week levels.

Therefore, M does not affect the ultimate level of DD in BO, although it may hasten the rate of DD development. These results also support the view that the production of DD in malnourished states requires an additional factor such as BO.

● **593** DIRECT DEMONSTRATION OF STARCH UTILIZATION IN INFANTS. R.J. Shulman, W.L. Wong, C.S. Irving, B.L. Nichols and P.D. Klein. USDA/ARS,Children's Nutrition Research Center, Department of Pediatrics, Baylor College of Medicine,Houston.

The age at which infants can utilize dietary starch has only been inferred. One-month-old infants, with demonstrated hydrogen production after receiving 1 g/kg lactulose, were maintained on a low ^{13}C abundance formula. On days 4, 8, and 12, a single feed was given in which 1 g/kg of dextrose (D), Polycose® (P),or cornstarch (C) naturally enriched with ^{13}C replaced the formula sucrose. Breath samples for ^{13}C abundance, H_2, and CO_2 were obtained every 30 min for 6 h. All subjects had a rise in ^{13}C abundance ≥20x individual baseline variation on all 3 substrates. Average (±SD) area under the curve ($\Delta^{13}C \cdot min$) was D:562±62, P:553±187, C:492±110, (n=10). 5/15 infants produced a significant amount of H_2 on D,while 7/15 and 10/17 produced H_2 on P and C, respectively. Fecal stool carbon was analyzed for ^{13}C abundance in 3 infants prior to and following a 3-day period of starch feeding (0.5 g/kg/feed) added to the basal formula. The increase in ^{13}C abundance revealed that 21%, 21%, and 8% of fecal carbon arose from the starch. Conclusions: 1) These results directly demonstrate utilization of starch for energy production by one-month-old infants. 2) Incomplete absorption of starch in the small intestine is suggested by hydrogen production in more than 50% of the infants. 3) Although DeVizia et al. (J. Pediatr. 86:50, 1975) detected no glucose or starch in the stool after starch feeding, the recovery of excess ^{13}C in fecal carbon from starch documents partial malabsorption of starch. 4) It is probable that starch entering the colon is converted into other non-carbohydrate forms by colonic flora. (Work supported by NIH AM 28129 and USDA/ARS).

594 THE EFFECT OF PROTEIN ON ABSORPTION OF ORAL REHYDRATION SOLUTIONS (ORS). James R. Smalley, William J. Klish, Richard A. Lawrence, Marilyn R. Brown. University of Rochester School of Medicine, Strong Memorial Hospital, Department of Pediatrics, Rochester, New York.

Amino acids and dipeptides have been shown to increase jejunal absorption of sodium and water. However, glucose, which also enhances absorption has been traditionally added to ORS. For most of the world, malnutrition and diarrhea occur together and are the leading causes of death in children. The low nutritional quality of glucose-electrolyte ORS used to treat diarrhea can promote malnutrition. The addition of protein to ORS might not only improve their nutritional quality, but also increase jejunal absorption. This study compared the effect of Pedialyte® and Pedialyte® plus 1% whey protein on the jejunal flux of water, sodium, chloride, potassium, and glucose by intestinal perfusion using the method of Fordtran. Four young adults were perfused before and after oral inoculation with Norwalk virus. Results ($\bar{x}$ SEM) of the combined perfusions shown below expressed as units/min/30 cm jejunum:

	H_2O(ml)	Na(mEq)	Cl(mEq)	K(mEq)	Glucose(mg)
Pedialyte	1.63±.50	.127±.050	.035±.037	.029±.008	73.1±14.7
Ped + prot	2.17±.43	.199±.040	.078±.044	.042±.010	69.4±19.0
p value	<.005	<.005	<.005	<.005	N.S.

These results demonstrate the addition of protein to ORS enhances absorption of water and electrolytes, and does not interfere with glucose absorption. Consideration should be given to adding protein to oral rehydration solutions to increase their nutritional quality. Supported in part by Ross Laboratories.

595 VALUE OF DETAILED DIETARY ANALYSIS IN GASTROENTEROLOGY. Alice Smith and John D. Lloyd-Still. Northwestern University Children's Memorial Hospital, Dept. of Peds., Chicago.

A computerized dietary analysis program was used in a G.I. clinic to assess 1) adequacy of intake, 2) alterations in dietary constituents. A TRS-80 microcomputer was programmed using 1980 National Academy of Sciences recommended dietary allowances (RDA). Seventy two hour dietary analysis included data for average intake, nutrients/kg (including minerals and vitamins), %RDA and %total calories for fat, protein and carbohydrate. Dietary records from 29 patients were analyzed in a 4 month period including 6 FTT without diarrhea, 6 chronic diarrhea without malabsorption, and 17 chronic diarrhea with malabsorption. Results showed 50% of failure to thrive (all less than 3% for weight) had inadequate caloric intakes; 5/6 with decreased calcium. Only 1/6 of the chronic diarrhea had inadequate intake, but 30-50% had abnormal dietary distribution (2 excessive fluid intake; 1 toxic dose of vitamin A). Patients with chronic diarrhea and malabsorption ranged from inadequate (57%) to increased (209%) %RDA intake. Conclusions: 1) The program is an easy, practical method to analyze dietary intake. 2) Gross abnormalities in dietary analysis were demonstrated. 3) These results can be used to screen patients with failure to thrive and malabsorption.

596 REYE'S SYNDROME: PRIMARY CAUSE OF VOMITING AND HEPATIC DYSFUNCTION FOLLOWING VARICELLA OR URI. Ronald J. Sokol, James E. Heubi, Michael K. Farrell, Cynthia C. Daugherty, Philip K. Lichtenstein, George Hug, Frederick J. Suchy, William F. Balistreri. Children's Hosp. Res. Fdn., Cincinnati, O.

We conducted a prospective study from 11/80-11/81 (a non-influenza epidemic year) to determine the incidence of liver biopsy confirmed Reye's Syndrome (RS) in anicteric children with acute onset of vomiting and elevated serum transaminases (3x normal) following a prodromal viral illness. 24 of 31 consecutive patients meeting these criteria underwent percutaneous liver biopsies. Cerebrospinal fluid analysis, toxin screens and serologies for hepatitis A, B, CMV and EBV were negative. Group A (A) patients (10 URI, 4 varicella prodromes) were defined by liver biopsies diagnostic of RS based on microscopic, histochemical and ultrastructural criteria. RS clinical staging (Cincinnati System) in A was 9 Stage I, 2 Stage II, 3 Stage III. Group B (B) patients (3 URI, 5 varicella prodromes) were defined as liver biopsies consistent with but not diagnostic of RS. RS clinical staging in B was 7 Stage I and 1 Stage II. 2 additional patients (1 URI, 1 varicella) had non-specific changes on liver biopsy. No other diagnosis (specifically hepatitis) was made except for unsuspected Congenital Hepatic Fibrosis in 1 RS patient. Ornithine transcarbamylase activity of the 10 A (81.7 $\pm$ 37.9 nmoles citrulline/mg protein/minute, $\bar{x} \pm$ SD) and the 2 B (41.7, 93.1) liver biopsies analyzed was significantly decreased ($p < .05$) compared to controls (209.3 $\pm$ 52.1), whereas arginase activity was normal. Our study suggests that most children with varicella or URI followed by vomiting and elevated transaminases have RS and not hepatitis. Clinical Stage I RS is a more common illness than previously suspected.

● **597** UPPER ESOPHAGEAL SPHINCTER (UES) AND PHARYNGOESOPHAGEAL (PE) FUNCTION IN GASTROESOPHAGEAL REFLUX (GER) Judith M. Sondheimer (Spon. by Frank Oski). SUNY Upstate Medical Center, Department of Pediatrics, Syracuse, N.Y.

It has been suggested that low UES pressure(UESP), blunted UES response to refluxed acid or abnormal UES relaxation with deglutition is common in GER of adults and augments symptoms. To evaluate these suggestions and establish infant norms we assessed PE and UES manometry in 16 infants with GER and 8 controls (all < 18 mos) using a low compliance perfused 3-lumen assembly with posterior directed perfusion holes. UESP response to esophageal pH was monitored while infusing 3cc distilled H_2O or .1NHCl (random order, investigator blinded) 5cm below the UES for 1 min. Mean (+SEM)UESP was equal in control and GER infants(26.4$\pm$3.5 vs 26.6$\pm$2.7cm H_2O) and independent of age and lower esophageal sphincter pressure. Distance of UES from nares(y) was a linear function of body length (x)($y=1.18+.132x, r=.80$). Duration, speed and amplitude of pharyngeal peristalsis were equal in both groups. Spontaneous pharyngeal contractions coupled with full UES relaxation occurred in all patients at rates up to 60/min. Relaxation coincided exactly with peak pharyngeal pressure in 6/8 control and 14/16 GER infants. Percent pharyngeal contractions transmitted to upper esophagus(y) decreased with increasing pharyngeal contraction rate(x) $y=1/(.009+.002x)$; $r=.74$. Mean UESP was unaffected by esophageal H_2O perfusion but increased similarly and significantly($p<.01$) with acid perfusion in controls(+14.0+5.0) and GER infants (+10.6+1.7 cm H_2O).

This study establishes norms for UES and PE function in infants, suggests that factors other than UES relaxation initiate esophageal peristalsis and indicates that UES function is normal in GER.

● **598** MEASUREMENT OF TOTAL BODY POTASSIUM IN PREMATURE INFANTS. Donald W. Spady and Larry J. Filipow. Sponsored by E.E. McCoy. University of Alberta, Faculty of Medicine, Department of Pediatrics and Biomedical Engineering, Edmonton, Alberta, Canada.

We present data describing total body potassium (TBK) measurements of healthy, premature infants. Prior to this time, only data from stillborn infants, fetuses, and live infants over 1500 gm have been available. These new data are possible due to the availability of a whole body counter (WBC) designed for small infants. The WBC is of a shadow-shield design, comprising a single 10 cm x 10 cm x 45 cm NaI (Tl) 'log' crystal, positioned lengthwise underneath the infant and surrounded by 10 cm of lead. The maximum error for any measurement is ±15%. Fifty-three measurements of TBK have been made on 10 healthy premature infants with an average weight of 1.69 kg (0.9-2.55) and a mean age of 31.9 days (2-65). Statistical analysis showed that the best predictor of TBK was weight; TBK (mEq) = 30.73 + 25.76 (wt in kg), $r^2=0.673$, $r=0.82$. Using this equation, an infant of 1.0 kg has a TBK of 56.5 mEq. This may be compared to the value of 44 mEq for a 1 kg stillborn infant as calculated by Widdowson and Spray, however, for an infant weighing 2.7 kg, and using the above equation, the calculated TBK of 100 mEq compares favorably with estimates of TBK of 97 mEq for healthy newborns of similar weight derived from data reported by Christian et al. The results of this study illustrate the feasability of measuring TBK in the premature and provide the researcher with a new method of investigating the growth of the premature infant.

599 HLA PHENOTYPES IN REYE SYNDROME PATIENTS. Janet E. Squires, James P. Keating, Kathleen B. Schwarz, Robert H. Squires, Morey W. Haymond, Darryl C. DeVivo Glenn E. Rodey. Washington University School of Medicine and St. Louis Children's Hospital and St. Louis University School of Medicine(KBS) and Cardinal Glennon Memorial Hospital for Children.

A study of HLA A,B, and DR phenotypes was carried out between 1979 and 1981. The Subjects were 35 surviving Reye syndrome (RS) patients, including 3 sibling pairs. All patients met the CDC criteria (MMWR,1979) for RS. Typing of 113 healthy controls(C) of similar ethnic and geographic background was done concurrently.

HLA BW38 was detected in each individual member (6) of the 3 affected sibling pairs; none of the unrelated patients possessed BW38. If a child with RS possesses the antigen BW38, siblings positive for BW38 may be at increased risk for developing RS.

Differences between 32 RS survivors (one of each sibling pair excluded) and C include the following: B8 3.1%(RS) vs 23.9%(C) ($p<.02$) (X^2,Yates); B40 28.1% vs 10.6%($p<.03$); A10 25% vs 8.9% ($p<.03$); AW32 15.6% vs 3.5%($p<.04$); DR3 9.8% vs 24.6%($p<.12$); A1 18.8% vs 35.4%($p<.12$). Further statistical analysis, taking into account the number of the antigen specificities tested for, reduced the level of statistical significance.

HLA B8 and to a lesser extent DR3 and A1 were found in a lower frequency in RS patients than C. No patient had both B8 and DR3, the most common Caucasian haplotype. A factor linked to this haplotype may confer protection from RS.

The risk of developing RS may be influenced by HLA associated genetic factors.

600 BETHANECHOL TREATMENT OF GASTROESOPHAGEAL REFLUX. Alan D. Strickland and Jack H.T.Chang. (Sponsored by Chester W. Fink). University of Texas Health Science Center, Departments of Pediatrics and Surgery, Dallas.

Bethanechol has been recommended for the treatment of gastroesophageal (G-E) reflux. In order to quantitate the response of patients to bethanechol, we determined "reflux scores" on children thought to have reflux by performing 6 hour pH probe studies run and graded by the method of Jolley,et al (Surgery 84:16-24, 1978). Sixteen children were found with reflux scores above the 128 upper limit of normal. These sixteen children had a mean score of 571.5 with a standard deviation of 294.3. Their age was 4.8±8.9 months. All 16 children were placed on bethanechol 3 mg/m^2/dose q8h. After 2 to 4 weeks of this therapy, the pH probe studies were repeated. Fourteen of the children had marked improvement in clinical status and reflux scores. Two children had no improvement. The 16 children had a mean score of 148.0±170.5 after bethanechol. This difference is significant ($t=4.98$, $p=0.000025$). If only the 14 patients who improved on bethanechol are analyzed, the scores improved from 597.8±304.6 to 93.5±88.8 with $t=5.95$ and $p=0.0000028$. The average weight gain for all 16 children was 33.6±21.9 g/day. We conclude the G-E reflux can be treated successfully with bethanechol in about 90% of children with reflux. Such treatment can provide time for the child without reflux to allow the child to develop better control of the lower esophageal sphincter and resolve the reflux. Further studies are in progress to determine the length of time bethanecol is needed before the reflux is resolved.

601 STUDIES ON THE ETIOLOGY OF EXTRAHEPATIC BILIARY ATRESIA. Alan D. Strickland and Kevin M. Shannon, (Sponsored by Chester W. Fink). University of Texas Health Science Center, Department of Pediatrics, Dallas.

Since extrahepatic biliary atresia (EHBA) is commonly presumed to be the result of an unknown intrauterine viral infection, we decided to investigate this possibility when we observed two sets of twins discordant for EHBA. One set of twins were dizygotic since they were discordant for sex. The other set of twins had two males, so erythrocyte typing and mixed lymphocyte cultures (MLC) were performed to determine the zygosity. On the basis of these studies, the twins were monozygotic ($p<0.0026$). Viral infections acquired in utero are predominantly concordant when twins are affected while toxic substances usually cause discordant injuries to twins. We then decided to examine the cases to find evidence for what this toxic substance might be. The thirty cases of EHBA seen at our institution during 1972 to 1980 were clustered significantly with more cases coming from farming areas of northeast Texas ($p<5X10^{-7}$) and more cases being born during the months of August through October ($p<0.015$) than would be expected based on a random distribution among the number of live births in our referral area. Spitz has reported that all the morphologic changes of EHBA can be produced in fetal sheep by surgical ligation of the extrahepatic bile duct during the 80th day of the 155 day gestation of sheep. If a similar timing of the insult in humans is assumed, the mothers would have been exposed to the toxic substance during early spring in the farming areas of northeast Texas. Since this is a time of plowing, toxins from the soil may be causative in EHBA.

602 DIAGNOSIS OF BIOTIN DEFICIENCY PRIOR TO THE APPEARANCE OF CUTANEOUS SYMPTOMS. Sharon F. Suchy, Susanne B. Brown, Stephen I. Goodman and Barry Wolf (Spon. by H.M. Maurer). Univ. of N.M., Albuquerque; Univ. of Colo., Denver; Med. Coll. of Va., Richmond; Depts. of Human Genetics and Peds.

Biotin deficiency is characterized by an erythematous skin rash and alopecia which accompanies the biochemical abnormalities. We now report an 18 mo. old white male with developmental delay since 4 mos. who was identified as having biotin deficiency prior to the development of these typical cutaneous symptoms. At 14 mos. his mother placed him on a diet consisting of whole milk and 2 raw eggs/d. The child developed ataxia at 17 mos. but had no skin lesions or alopecia. At 18 mos. he had a mild acidosis and excreted β-hydroxyisovalerate (1.3 mg/mg Cr) and β-hydroxypropionate (0.02 mg/mg Cr). The activities of propionyl CoA carboxylase, β-methylcrotonyl CoA carboxylase and pyruvate carboxylase in his peripheral blood leukocytes were 12%, 6% and 8% of normal, respectively. His serum biotin concentration was <0.1 ng/ml (nl 0.5-0.8 ng/ml). One wk after changing his diet to formula supplemented with biotin (10 mg b.i.d.), his serum biotin concentration became > 25ng/ml, his urine cleared of abnormal organic acids and his leukocyte enzyme activities returned to normal. Enzyme activities and urinary organic acids remained normal after 6 wks of biotin at 300 µg/d (U.S. RDA). Although developmental delay and ataxia continued, a CT scan of his brain and an EEG were normal. The present case is the second report of biotin deficiency in a child caused by dietary indiscretion and indicates that the biochemical abnormalities may precede the cutaneous symptoms. Furthermore, it reemphasizes biotin's important nutritional role.

603 INDOMETHACIN AND NECROTIZING ENTEROCOLITIS (NEC) Shyan Sun, Zaneida Aranda, Kamtorn Vangvanichyakorn. (Spon. R. Levine) New Jersey Medical School, Dept. Neonatology, Newark, New Jersey

Cronen et al (1981) reported that Indomethacin reduced mucosal blood flow of stomach and terminal ileum by 50% in dogs and the area of ischemia in this animal model corresponded to clinical pathology noted in NEC. Prompted by this observation, we reviewed the outcome of our neonates (BW 500-1500 gm) who received Indomethacin during the past 5 years (1976-1981). There were 402 infants with BW <1500 gm, 125 (31%) developed PDA of which 74 (60%) received Indomethacin treatment.

	No	NEC	%NEC	Death	%Mortality
PDA	125	21	16.8	11	8.8
Control	277	16	5.8	8	2.9
P		<0.001		<0.02	

	No	NEC	%NEC	Death	%Mortality
Indocin	74	11	14.8	5	6.8
Control	51	10	19.6	6	11.8
P		NS		NS	

Our result implies that PDA might have significantly increased the incidence of NEC and contributed to its mortality, but there was no evidence that Indomethacin treatment further worsen the situation. Further stepwise discriminant analysis of 8 NEC associated factors disclosed that the use of umbilical catheters and low gestational age were the 2 most important contributory factors.

● **604** JUVENILE MULTIPLE CARBOXYLASE DEFICIENCY: EVIDENCE FOR IMPAIRED BIOTIN ABSORPTION. Jess G. Thoene, Rosemary M. Lemons, Katherine Z. Borysko, Herman Baker[1]. University of Michigan School of Medicine, Dept. of Pediatrics, Ann Arbor and College of Medicine and Dentistry of New Jersey, East Orange[1].

Juvenile multiple carboxylase deficiency (MCD) produces characteristic clinical findings of altered biotin metabolism (ataxia, alopecia, lactic acidosis, dermatitis, keratitis) associated with subnormal plasma and urinary biotin. A 5 yr old WF developed this syndrome in spite of a normal dietary biotin intake and required biotin supplementation to remain symptom-free. To investigate the source of her biotin abnormality, biotin (10 mg/day) was discontinued and her biotin absorption and excretion kinetics were measured. After 30 days she showed increasing signs of irritability; at 35 days an erythematous periocular rash appeared, at 42 days she complained of muscle pains. Acidosis, ketonuria and ataxia did not occur. A friable hypopigmented longitudinal band 10 mm long appeared at the growing end of her hair following this period. Plasma biotin declined from 29,639 pg/ml (while on 10 mg biotin/day) to 143 pg/ml (on day 42). (Nl 200-500 pg/ml) Urinary biotin declined from 30 µg/mg creatinine to 25.9 ng/mg creatinine in a biphasic manner (Ta 1/2=2d; Tb 1/2=8d). Plasma biotin concentration measured 1 hr and 24 hrs after orally adminstered biotin was:290 and 155 pg/ml (after 0.1 mg biotin); 2970 and 254 pg/ml (after 0.25 mg biotin); 6187 and 343 pg/ml (after 0.5 mg biotin). Thus this patient requires 0.25 mg exogenous biotin per day to maintain normal plasma biotin. This is 2.5 times the average daily adult requirement. 24° urinary biotin excretion equalled 10% of each ingested dose. These findings support defective intestinal biotin absorption in juvenile MCD.

605 ^{99m}Tc-PIPIDA SCANS (PS) IN NEONATAL CHOLESTASIS (NC). Vasundhara Tolia, Amir Kagalwalla, Veena Dua, Thomas L. Slovis, Reuben S. Dubois, Wayne State University, Children's Hospital of Michigan, Department of Pediatrics, Harper Hospital, Department of Nuclear Medicine, Detroit.

Various tests have been advocated to distinguish between neonatal intra and extra-hepatic cholestasis. Of these, liver biopsy (LB) has been the most valuable. The purpose of this study was to confirm earlier reports that PS can replace LB to exclude extra-hepatic biliary obstruction (EHBO). Ten infants with NC were studied with routine tests besides PS and LB. Non-visualisation of the isotope in the bowel at 24 hours was taken as evidence of total obstruction (TO) consistent with EHBO. Eight patients had PS before and after at least 10 days of medical treatment with phenobarbital and cholestyramine. In the remaining 2 patients, only one PS was done following at least 3 days of medical therapy. Percutaneous liver biopsy was done in all. Comparison of results of these two procedures in correctly identifying EHBO are shown below.

	EHBO	IHC	Correct	Incorrect
Liver Biopsy	4	6	4	-
^{99m}Tc-PIPIDA	8	2	4	4

Our results indicate that PS give false positive results of EHBO if severe intra-hepatic cholestasis (IHC) is present even after a course of medical therapy. If LB was not done to confirm the diagnosis, 4 patients would have been subjected to unnecessary exploratory laparotomy. So LB is still the most reliable test available to differentiate between IHC and EHBO.

606 GROWTH AND BODY COMPOSITION OF PREMATURES IN RELATION TO PROTEIN INTAKE. Frederick L. Trowbridge & George G. Graham, Johns Hopkins Univ., Dept. of Pediatrics, Baltimore.

Premature infants (1250-1750 g) were randomly assigned to receive standard formula (9% prot. Kcal., 82:18 casein-whey) or one identical in energy and mineral content but with protein level similar to breast milk (6% prot. Kcal.). The assigned formula was begun at 8 days and infants were followed to discharge with daily weights, 2 x wk anthropometric measurement of linear and circumferential growth & 4 skinfolds. Plasma proteins, amino acids, and total body water by $H_2{}^{18}O$ isotope dilution were determined at start and q. 2 wks. If wt gain was judged, double-blind, to be clinically unsatisfactory, all measurements were repeated and 9% formula was given. Five infants on the 6% diet had less wt gain and higher energy cost of gain during the first 8-10 days. Thereafter, 2 infants continued on 6% diet and 3 others changed to 9% formula attained a wt gain and energy cost of gain similar to 5 infants continuously on the 9% diet. The rate of wt gain increased and energy cost decreased with age for all infants, but over 25 days the 2 infants continued on 6% formula had consistently lower linear growth despite a similar skinfold thickness increase suggesting greater fat accumulation in relation to smaller body size increment. No consistent differences among diet groups were observed in TBW as % body wt, total amino acids, ratios of essentials to totals or plasma proteins. Feeding healthy prematures this 6% prot. Kcal. formula is associated initially with inferior wt gain and greater energy cost of growth and, if continued, with inferior linear growth. Support: USDA/SEA #78-50-2243-0-1-129-1.

● **607** BODY WATER MEASUREMENTS USING $H_2{}^{18}O$ ISOTOPE: NEW TECHNIQUES APPLIED TO STUDIES IN INFANTS. Frederick L. Trowbridge, George G. Graham, William W. Wong, Charles S. Irving and Peter D. Klein, Johns Hopkins Univ., Dept. of Pediatrics, Baltimore and Baylor College of Medicine, Children's Nutrition Res. Ctr., USDA/ARS, Houston.

Total body water (TBW) measurement in infants requires isotope safety, accuracy from small samples, least invasive procedures and adjustment for any intra-study feeding. $H_2{}^{18}O$ isotope is stable and has minimal isotopic effect compared to deuterium. Automated mass spectrometric analysis for $^{18}O/^{16}O$ ratio of sample volumes from 1 ml down to 0.05 ml showed similar variability (average S.D. of TBW estimates <±1.0%). Oral $H_2{}^{18}O$ administration and micro blood samples minimize invasiveness. In 29 studies in prematures and 42 studies in infants (6-36 months) TBW from 5-7 h urine samples averaged 99.5±3.7% and 99.6±2.1% of plasma-based TBW values respectively, indicating excellent potential for non-invasively obtained urine samples. In 18 studies in older infants plasma TBW values were 98.0±4.4% & 99.8+3.0% of 6 h values at 2 & 4 h respectively, showing complete equilibration by 4 h. Urine TBW estimates (excluding first voidings) were 107.5±23.0%, 96.6±2.5% & 99.5±2.6% of 6 h plasma TBW values at 1-3, 3-5 & 5-7 h respectively indicating urine equilibration by 5-7 h. Intra-study feeding of 19 prematures produced 5-7 h urine-based TBW estimates averaging 99.7±4.4% of pre-feeding plasma-based values, after adjusting urine estimates by subtracting feeding volume. TBW measurement in infants by $H_2{}^{18}O$ isotope dilution is safe, accurate and minimally invasive. Support: NIH AM-28129, NIH 5R22 HD10111-05 & USDA/SEA 78-50-2243-0-1-129-1.

● **608** AIRWAY RESPONSE TO ESOPHAGEAL AND TRACHEAL ACIDIFICATION: A POSSIBLE MECHANISM FOR THE ASSOCIATION OF GASTROESOPHAGEAL REFLUX (GER) AND BRONCHOSPASM. David N. Tuchman, John T. Boyle, Allan I.Pack, Jacob Schwartz, Mary Kokonos, Alan R.Spitzer, Sidney Cohen. (Spon.by John B.Watkins) U.of Penn.Sch. of Med.,Child.Hosp.and Hosp. U.of Penn.,Dept.Peds.and Med., Div. GI, Neonatol., CVP Div. Phila., PA.

Although the clinical association of GER and obstructive pulmonary disease is well established, the physiologic mechanism that results in airway obstruction is unclear. This study was designed to evaluate the effects of intraesophageal and intratracheal acid on airway resistance in the cat. Anesthetized cats breathed spontaneously a hyperoxic gas mixture(50%O_2) through an endotracheal tube. Upper and lower esophageal sphincters were located by manometry. Intrathoracic pressure(P) was measured by intrapleural catheter, air flow($\dot{V}$) by pneumotachograph and lung volume(V) by flow integration. Total pulmonary resistance(R) was calculated from the simultaneous measurement of P,$\dot{V}$ and V. Results show: 1) Esophageal instillation of up to 10cc of 0.2N HCl at various levels produced no significant change in R from control. 2) As little as 0.05cc of intratracheal 0.2N HCl produced an instantaneous increase of 455%±70%(mean±SE,p<.001) from baseline resistance,an effect which was reversible by 1 minute postinfusion. In contrast, up to 0.5cc of intratracheal saline had no effect on R. 3) Bilateral cervical vagotomy abolished the response to intratracheal acid. **Conclusion:** These studies demonstrate a dramatic vagally mediated reflex bronchoconstriction following minute quantities of intratracheal acid,but no effect on airway resistance of esophageal acid alone. The results suggest that acid-induced bronchospasm may occur in GER without clinical evidence of aspiration.

609 CERULOPLASMIN AND COPPER OXIDASE IN THE PREMATURE INFANT. E.E. Tyrala, J.I. Manser, N. Tran, Temple University School of Medicine, St. Christopher's Hospital for Children, Albert Einstein Medical Center, (North), Philadelphia, Pennsylvania. (Sponsored by V.H. Auerbach)

The relationship between serum ceruloplasmin, the major copper containing protein in serum, as measured by radial immunodiffusion, and copper oxidase (J. Lab. Clin. Med. 58:161, 1961), which is a measurement of the oxidizing capacity of ceruloplasmin, was serially determined in 31 relatively well, growing premature infants over the first 16.5 weeks of life. Mean birth weight of infants was 1230gms. (range 820-1560gms) and mean gestational age was 30.1 weeks (range 26 to 33 weeks). A total of 134 ceruloplasmin and copper oxidase measurements were compared using linear regression by the method of least squares. Correlation coefficient between the two tests was r=.712, $p<10^{-6}$.

	Cerulo. mg/dl	Cu oxidase (O.D.) units
0-48 hrs.	6.7	.070
Week 1	10.0	.099
Week 6	13.5	.139
Weeks 9-12	16	.196
Weeks 13-16	22	.216

Cu oxidase maintains a constant relationship to ceruloplasmin over the first weeks of life in the premature infant. Ceruloplasmin concentration can be determined using the formula: Cerulo. = .023 + .0077 (Cu oxidase). The measurement of copper oxidase, a relatively simple laboratory assay may be used as an alternative to the more complex ceruloplasmin assay in this age group.

610 A PEDIATRIC NUTRITIONAL ASSESSMENT SCORING SYSTEM. E.E. Tyrala, S.J. Widzer, R.M. Kravitz, S. Herman, N. Kelley, J. Stover, Temple University School of Medicine and St. Christopher's Hospital for Children, Philadelphia, Pennsylvania. (Sponsored by V.H. Auerbach)

A nutritional assessment scoring sheet for determining nutritional deprivation has been developed for the pediatric patient. A score of 0 (no significant deviation from norm for age) to 3 (significant deviation from norm for age) was given in each of 10 categories: % ideal body weight, % weight change, percentile for weight/height, right triceps and subscapular skin fold thickness, arm muscle circumference, skin tests (dT, Candida, and SK/SD), albumin, transferrin, and absolute lymphocyte count. Absolute lymphocyte count was not found to be a helpful indicator of nutritional deficiency in any age group nor was percent weight change in the child under two years of age.

A minimul of 5 tests or 15 possible points had to be scored for the assessment to be considered reliable. Actual points scored was divided by total possible points and a percentage score was derived. Scores of <20% were considered indicative of normal nutritional status, 21-35% mild, >35-50% moderate, and >50% severe malnutrition. Serial assessments were used to quantitatively document the nutritional progress of patients hospitalized for longer than two weeks.

Using this assessment, children hospitalized for deprivational failure to thrive, for example, generally displayed preservation of visceral proteins, but depletion of body fat, decreased arm muscle circumference and ultimately poor growth depending on the duration and degree of the deprivation.

● **611** PANCREATIC FUNCTION IN NEWBORNS AND INTESTINAL PERMEABILITY TO ANTIGENS: A PROBABLE ASSOCIATION. John Udall, Kurt Bloch, Paula Feldman and W. Allan Walker, Harvard Medical School, Massachusetts General Hospital, Department of Pediatrics and Medicine, Boston, MA. 02114

Neonatal animals absorb increased amounts of intestinal antigens. To study the effect of pancreatic function on intestinal uptake of antigen, we inhibited and augmented intestinal proteolysis in developing rabbits. Weight-matched newborn animals at birth were gavaged with the trypsin inhibitor aprotinin and 200 mg bovine serum albumin (BSA)/100 gm body weight, trypsin and BSA or saline and BSA. Plasma immunoreactive BSA (iBSA), small intestinal rinse (SIR) tryptic activity and SIR iBSA were measured after four hours. Plasma from the trypsin-BSA treated group had significantly less ($p<0.005$) iBSA (0 ug/ml) than the saline-BSA (4.7±0.8 ug/ml) and aprotinin-BSA treated group (7.4±1.2 ug/ml). SIR tryptic activity was significantly increased ($p<0.05$) and SIR iBSA significantly decreased ($p<0.005$) in the trypsin-treated animals compared to controls and aprotinin-treated animals. In additional studies, newborn (n=29), two (n=11) and four (n=8) week old rabbits were given aprotinin or saline followed by gavage with 200 mg BSA/100 gm body weight. The newborn and two week old animals treated with aprotinin had significantly increased plasma iBSA compared to saline-treated controls ($p<0.001$). However, no plasma iBSA was detected in any four week old rabbit. These studies suggest that pancreatic function may influence the uptake of intestinal antigens early in life, but later in development it does not appear to be as important in protecting the animal from antigen absorption.

612 ENHANCEMENT OF LEAD ABSORPTION BY DIETARY LACTOSE. Jon A. Vanderhoof, Dean L. Antonson, and Carol R. Angle. University of Nebraska College of Medicine, Department of Pediatrics, Omaha, NE

Lactose has recently been shown to enhance lead absorption. Because lead intoxication is most common in infants and young children at an age when dietary lactose is great, this study was conducted to determine if the presence of intraluminal lactose or its constituent monosaccharides enhance lead absorption directly, or whether this effect occurs indirectly through chronic stimulatory affect of dietary lactose on the mucosa. Fourteen 150 gm Sprague-Dawley rats were given 10% lactose in their drinking water for four weeks, 14 control rats were given sucrose. Ten cm of proximal and 10 cm of distal small intestine in each animal were perfused by recirculation for two hours at 1 ml/minute with a 125 mM NaCl solution containing 1 mcg/ml of lead as lead acetate, 5 g/l polyethylene glycol 4000 as a water marker and, in 1/2 of each group 20 mM lactose and 20 mM mannitol and in the other 1/2 of each group, 20 mM glucose and 20 mM galactose. In the proximal small bowel, chronic lactose feeding enhanced lead absorption by 68% in the presence of intraluminal lactose and by 24% in the presence of glucose and galactose. The presence of intraluminal lactose did not enhance lead absorption when compared to its constituent monosaccharides regardless of dietary carbohydrate. Nearly comparable results were observed in the ileum. Dietary lactose appears to enhance lead absorption indirectly by increasing the bowel's capacity to absorb lead. This effect is not dependent upon the presence of intraluminal lactose at the time the lead is being absorbed.

613 MATURATIONAL EFFECT OF TRI-IODOTHYRONINE AND ITS ANALOGUE ON SUCRASE ACTIVITY IN THE SMALL INTESTINE OF THE DEVELOPING RAT. Yvonne Vaucher, Judy Anna, Robert Lindberg, Sergio Bustamante, Eugene Jorgensen, Ladislav Krulich and Otakar Koldovský. Departments of Pediatrics and Physiology, Univer. Arizona, College of Medicine, Tucson, AZ.

DIMIT (3,5-dimethyl-3'-isopropyl-L-thyronine), an analogue of tri-iodothyronine (T_3), crosses the placenta readily and exerts thyromimetic effects upon the maturation of fetal liver and lung. DIMIT (5μg/100g BW) was injected into pregnant Sprague-Dawley rats on days 17-20 of gestation; DIMIT or T_3 (10,50μg/100g BW) were given to sucklings on days 4-7 (I) and 11-14 (II). All were killed 24 hours after the last injection.

Sucrase activity (SA) was increased in all small intestinal segments[proximal (P), middle (M), distal (D)] in the fetuses and older sucklings (Group II). In Group I the effect was seen only in the M and D segments. In Group II the response was greater, and the effect of DIMIT equaled that of T_3.

Sucrase Activity (μM/60'/mg protein) in 8-day-old Rats (Group I)

	DIMIT(10)	DIMIT(50)	T_3(10)	T_3(50)	Control
P	.07 ±.005	.16 ±.05	.07 ±.003	.07 ±.00	.07 ±.005
M	.28 ±.08	.67 ±.26†	.06 ±.004	.25 ±.06†	.08 ±.008
D	.34 +.05††	.54 ±.12††	.01 ±.01	.17 ±.05††	.03 ±.015

X ±SEM (n=6/group) †p < .05,††p < .002 from control.

Conclusion. DIMIT and T_3 have a maturational effect upon sucrase activity in the SI. The lack of sucrase reactivity in proximal segment of the 8-day-old sucklings is noteworthy but unexplained.

614 "HUMANIZED" COW'S MILK FORMULA RELATED TETANY: SECONDARY HYPERPARATHYROIDISM, NORMOCALCITONINEMIA, NORMAL VITAMIN D WITH PARADOXIC HYPERCALCEMIA AND HYPERMAGNESEMIA. P.S. Venkataraman, F.R. Greer, A. Noguchi, J. Moore, J.J. Steichen, D.D. Buckley, R.C. Tsang, Cincinnati, O.

Five term infants with appropriate birth wts fed Similac 20, a "humanized" cow's milk formula (P 39 mg/dl, Ca:P ratio 1.2:1) had hypocalcemic tetany at 5-9 d. Initial serum Ca (mean±S.E.) was 6.8±0.12, P 9.5±0.2, and Mg 1.6±0.1 mg/dl, and parathyroid hormone (PTH) was elevated 78±14 µlEq/ml (RIA 1-84 PTH, N≤57). On restoration of normocalcemia with Ca supplements, feeding was resumed with "humanized" formula. Controls were 18 term exclusively breast fed (breast milk P 10-14 mg/dl Ca:P ratio 2.3:1) infants 3 wks. to 6 mos of age. In tetanic infants, relative hypercalcemia 10.4±0.05 mg/dl occured at 6 wks (vs. 9.2±0.3 in breast fed, p<.025) till 12 wks; relative hypermagnesemia 2.26± 0.01 mg/dl occured at 4 wks (vs. 1.92±0.07 in breast p<0.05) till 8 wks. Mean serum P declined steadily to 6.2 mg/dl at 16 wks (n.s. vs. breast). Mean serum PTH progressively rose to 74, 73, 143, 103, 96 and 75 µl/Eq/ml at 2,4,6,8, 12 and 16 wks (vs. mean 28 to 35 in breast p< 0.005). Serum calcitonin ranged <10-118 pg/ml (N < 107), 25OH vit D were 25-63 ng/ml (N 11 to 63), and $1,25(OH)_2$ vit D 12-60 pg/ml (N 11-85 pg/ml). We speculate that acute hypocalcemic tetany was induced by the relatively high P load even in "humanized" cow milk formulas (vs. breast milk); with continued P loading, serum PTH rises as secondary hyperparathyroidism develops, maintaining normophosphatemia and eventually resulting in relative hypercalcemia and hypermagnesemia.

● **615** HUMAN MILK CHANGES BILE ACID KINETICS. John B. Watkins, A.L.Jarvenpää, N.Räihä, P.Szczepanik Van-Leeuwen,P.D.Klein,D.K.Rassin and G.Gaull.CHMC,Boston, MA, CHOP, Phila., PA, Helsinki Univ. Central Hosp., Helsinki, Finland, Argonne Nat.Labs.,Argonne,IL & Inst.for Basic Res.in Ment.Ret., S.I., NY.

In preterm infants, the bile acid(BA) pool increases nearly two-fold from 11-35 days independent of dietary regimen(ie, human milk(HM), formula(F_1),F_1 supplemented with taurine(30 umoles%)(F_2),or F_1+ Taurine + Cholesterol 12.7mg/dl(F_3) whereas,maintenance of BA conjugation with taurine requires HM or taurine supplementation (Pediatr.Res.14:512, 1980). In these previously studied infants and 41 additional preterm infants fed the same dietary regimens from 3 days of age, intraluminal BA concentrations were higher by 11 days of age in the HM fed vs. F_1,F_2 or F_3, 8.1±1.3 vs. 4.0±1.0, 2.5±0.5 vs. 4.3±0.5 mM (p<0.01)(Avg.±SD), a difference which was maintained at 21 and 35±9 days when infants reached 2400 grams. The difference is due to greater amounts of chenodeoxycholic acid(CDCA) irrespective of conjugate status. BA kinetic studies demonstrate that by 11 days,CDCA pool is greater in HM vs. formula infants 4.3±1 vs. 2.0±1mg/kg(p<.001) which was maintained at 2400 grams 11.6±4 vs. 4.1±2 mg/kg (p<.001) and the fractional turnover rates were lower 0.32±0.04 vs. 0.69±0.2 and 0.17±0.1 vs. 0.43±0.2 (p<.001). Total CDCA synthesis however remained similar in both groups at both time points 1.5±0.2 vs. 1.5±0.2 and 1.6±0.4 vs. 1.3±0.6 mg/kg/day. Conclusion: 1)BA pool and intraluminal BA and fat absorption increase with age in all infants independent of taurine and/or cholesterol supplementation. 2)HM alters BA kinetics as early as 11 days with increased CDCA conservation and reduced turnover. This suggests that HM feeding per se uniquely influences intestinal and possibly hepatic function independent of developmental factors.

616 FAT DIGESTION IN CF: INTRALUMINAL EVENTS FOLLOWING A SOLID MEAL. A.M. Weber, A. Fontaine, L. Chartrand, M. Roulet and C.C. Roy. Department of Pediatrics, Hôpital Ste-Justine and University of Montreal, Montreal, Quebec, and C.H.U.V., Lausanne, Suisse.

The extent of lipid digestion in humans has been questionable because of the use of either a liquid meal or of heat for lipase (L) inactivation. Boronic acid (B) has been shown to inhibit L activity. It was therefore of interest to use B for the study of intraduodenal digestion of fat in 2 CF patients and 2 controls following a solid meal. Inhibition of L activity was obtained by adding B to each aspirate collected at 5 min intervals over a 3 hr period. Micellar incorporation of lipids was measured after overnight ultracentrifugation. Total L and phospholipase (PL) activity was determined with and without a concomitant duodenal perfusion of pancreatic enzymes (PE). Low pH and low values of L and PL were found in CF. A good correlation was present between pH and activity of both enzymes. Only 36.7% and 39.4% of perfused L and PL were recovered during their perfusion. The extent of lipolysis in controls (18%) and in CF (7.8%) was surprisingly low and the degree of phospholipid hydrolysis was 55.8% in controls and 34.1% in CF. Bile acid concentrations were still within the range sufficient to form micelles in CF. Micellar solubilization of lipolytic products (42.2%) was higher than previously reported but comparable to controls and uninfluenced by the intraduodenal perfusion of enzymes. The extent of lipid and phospholipid hydrolysis rather than micellar solubilization limits fat digestion in CF. Correction of duodenal pH is necessary for improved efficacy of PE supplements.

617 MICROSOMAL MEMBRANE FLUIDITY OF THE CONGENITALLY JAUNDICED (GUNN) RAT. P.F. Whitington, D.D. Black, W. Struve and M.E. Dockter (Spon. by J.F. Griffith). Depts. of Peds. & Biochem., Univ. Tenn. CHS, Memphis, TN.

The failure of the Gunn rat to conjugate bilirubin is possibly related to the microsomal membrane matrix of bilirubin UDP-glucuronyl transferase (Odell,GB et al:Hepatology 1:307, 1981). To examine this, hepatic microsomes were isolated from Gunn (jj), outbred normal Wistar (JJ), and heterozygote (Jj) rats and were subjected to the following studies: Lipid analysis (gas chromatography and phosphorus determination following solvent extraction) of 5 preparations in each group demonstrated no differences in the ratio of cholesterol to phospholipid nor the percent contribution of these lipid components and individual fatty acids to the total lipid. Steady state anisotropy values of 1,6-diphenyl-1,3,5 hexatriene, determined at 37°C and 10°C in microsomal membranes from 5 rats in each group, did not differ among the groups. Electron paramagnetic resonance spectra of 7-doxylstearic acid incorporated into microsomes from one rat in each group, done at 6,10, 20,25,30 and 38°C, were superimposable at each temperature. Arrhenius plots of glucose-6-phosphatase activity from 15 to 38° (jj, n=6; JJ, n=9; Jj, n=8) demonstrated identical slopes, energies of activation, (12.8 kcal/mol) and changes in slope at 35°C. We conclude that several factors related to membrane fluidity and lipid bilayer organization do not differ among microsomes from jj, JJ and Jj rats, indicating that an anomalous microsomal matrix does not explain the observed defect in conjugation of bilirubin in jj rats.

618 INFANT COLITIS RESULTING FROM HUMAN BREAST MILK FEEDING. P.F. Whitington, A.M. Lake, and S.R. Hamilton (Spon. by J.F. Griffith), Depts. of Peds. and Path., University of Tennessee CHS, Memphis, and the Johns Hopkins Hospital, Baltimore.

Six infants presented from 3 wks to 3 mo of age with the symptom of bloody diarrhea, which had its onset at 1-4 wks. Dietary history revealed that all had been exclusively breast fed. Colitis was diagnosed by the presence of mucosal friability and focal ulceration of the rectosigmoid, limited to the distal 10 cm in 3. No infectious cause was identified. Biopsies obtained at proctosigmoidoscopy showed a range of findings from normal to low-grade, patchy active chronic inflammatory bowel disease. No evidence of graft-vs-host disease or vasculitis was found. Breast milk, as the etiology of colitis, was investigated by substituting hydrolyzed casein or soy formula for at least 3 days; all had cessation of bleeding within 36 hours of halting breast feedings. Rechallenge with breast milk was done in 5 cases, the 6th mother refusing, and all had recurrence of bleeding within 36 hours. The possibility of dietary antigens being passed into breast milk and resulting in colitis in the infant was investigated by systematic elimination of certain antigens from the mothers' diets. Elimination of cow's milk prevented colitis in 2 while elimination of cow's milk, soy and egg did not prevent it in 3, the ubiquity of these latter antigens perhaps precluding complete elimination. Thus, we conclude breast feeding is occasionally the cause of colitis in infants. Although the possibility was not proved conclusively, it may be related to the presence of dietary antigens in the milk.

619 CORRECTABLE PLASMA LIPOPROTEIN ABNORMALITIES IN INFANTS WITH CHOLEDOCHAL CYST. P.F. Whitington, G.J. Williams, and S.W. Weidman, (Spon. by J.F. Griffith). Department of Peds., Univ. Tenn. Ctr. Health Sci., Memphis, TN.

Plasma lipoproteins from two female infants-Patient A, 19 months and Patient B, 4 weeks-were examined prior to and at one and four weeks after surgical repair of choledochal cyst, and the findings were correlated with hepatic morphology and standard indices of hepatic function. Prior to surgery, plasma cholesterol, phospholipid and triglyceride were elevated; cholesterol esters (CE) were low, 25 and 33% of total; HDL cholesterol and apo A-I, the major protein constituent of HDL, were subnormal; most of plasma lipids were contained in the LDL density region; LP-X was found in 1.049<d<1.064. Patient A had had a relatively brief obstruction and suffered little secondary hepatic injury: one week after surgery, lipid concentrations returned to normal; apo A-I increased in HDL and a concomitant rise of CE to near normal, 65%, was observed; lipids were contained predominantly in HDL; hepatic function improved markedly. Patient B had had intrauterine obstruction and suffered cirrhosis: one week after surgery, lipid concentrations, CE, LDL lipid predominance and hepatic function remained essentially unchanged; in contrast, a many fold increase in HDL apo A-I was observed: one month after surgery, lipoproteins and hepatic function were near normal. In conclusion, children with biliary obstruction have lipoprotein abnormalities similar to those seen in adult patients and rapidly reversible with surgical relief. Recovery of HDL apo A-I precedes recovery of hepatic function and other lipoprotein abnormalities in children with secondary biliary cirrhosis.

620 EVALUATION OF SEVERELY RETARDED CHILDREN WITH SYMPTOMS SUGGESTIVE OF GASTROESOPHAGEAL REFLUX. Steven J. Widzer, (spon. by Maarten S. Sibinga) Temple University School of Medicine, St. Christopher's Hospital for Children, Department of Pediatrics, Philadelphia, Pennsylvania.

Nineteen severely retarded, institutionalized children aged 14 (5-21) years with anemia and gastrointestinal blood loss (11), recurrent pneumonias (2), or both (6) of 6.8 (1-24) months duration were evaluated for the presence of gastroesophageal reflux (GER). A history of vomiting was present in 8.

GER was documented in all 19 patients; barium swallow was positive in 18/19, 99m-TC sulphur colloid scan was positive in 19/19, manometry was positive with lower esophageal sphincter pressure less than 15 in 9/15 and endoscopy (with or without biopsy) was positive for esophagitis in 14/16. Three patients had 2, 10 had 3, and 6 had4positive tests.

All patients were treated with alginic acid-antacid combination and routine medical management and 14 were seen 6 weeks later. Seven of 10 previously anemic had normal hemoglobins and 3/5 with previous pneumonias had not had subsequent pneumonias. One child died and one child required fundoplication.

Conclusions: 1. Severely retarded children with these symptoms even in the absence of vomiting have a very high incidence of GER. 2. The simplest tests, barium swallow and nuclear medicine scan, may be adequate in this group. 3. These children have a very high incidence of esophagitis. 4. Medical treatment is difficult.

621 CALCIUM METABOLIC KINETICS OF CHILDREN WITH DYSTROPHIC CALCIFICATION, OSTEOGENISIS IMPERFECTA AND OF NORMAL CHILDREN. A.L.Yergey, N.E.Vieira and J.W.Hansen (Spon. by J.B.Sidbury) NICHD, NIH, Bethesda, MD 20205.

Stable isotopic tracers and thermal ionization mass spectrometry (Anal.Chem.,52,1181(1980)) are used to study kinetics of Ca. Two different isotopes are used simultaneously in each study to measure Ca kinetics by determining time dependent changes in Ca isotope ratios for each tracer relative to a third isotope at natural levels. Measurements are made on aliquots of diet, plasma, urine and feces. Physiological rates of absorption, urinary and fecal excretion, as well as bone deposition and resorption are calculated from the kinetic data. Results of studies with a subject with dystrophic calcification (A), a patient with osteogenisis imperfecta (B) and a normal neonate (C) are reported here as fractions of total Ca turnover (g/kg.day). There were no observable differences between the rates of dietary absorption and bone resorption as functions of turnover for subjects A,B, and C. The values for urinary (v_u) and endogenous fecal (v_f) excretion and bone deposition (v_o+) showed marked differences as functions of turnover:

	A	B	C
v_u/v_t	.026	.013	.006
v_f/v_t	.005	.47	.16
v_o/v_t	.965	.52	.82

The data for subjects A and B confirm theoretical calcium dynamics for such disorders. The data for subject C are consistent with other data for newborns.

622 POSTNATAL ADAPTATION OF SMALL INTESTINAL (SI) BLOOD FLOW (BF) IN LAMBS. M.K. Younoszai, R. Nathan, D. Weismann and J. Robillard. The Univ. of Iowa Hospitals and Clinics, Dept. of Pediatrics, Iowa City.

In contrast to the relative inactivity in utero, after birth the SI becomes highly active in absorbing dietary nutrients. The adaptation of BF during this period has not been studied. We evaluated growth and BF of SI in the perinatal period from difference in weight and BF of fetal (120-140 gestation) and (5-32 day old) lambs proximal jejunum (J) and distal ileum (Il). BF was determined from amount of radioactive labelled microspheres (12-15 μM), injected into the left ventricle, trapped in the microcirculation of SI. Portions of J and Il 18 cm long, were flushed with 150 mM NaCl solution and air and weighed. In alternating 3 cm long segments weight and radioactivity were determined in full thickness wall (W) or in mucosal scrapings (M) and underlying tissues. Weight and BF are tabulated below:

	Weight, mg/cm				BF, ml/hr/g			
Animal	fetus		lamb		fetus		lamb	
Tissue	W	M	W	M	W	M	W	M
J	203	139	394	215	1.35	1.48	2.61	4.54
Il	285	159	712	406	0.90	0.61	1.11	1.45

As expected, both weight and BF of SI increased in the neonatal period. However, while in J weight of M increased 1.5 fold, BF increased 3.5 fold, in Il both weight of M and BF increased 2.5 fold. The true significance of the discrepancy in increased weight and BF between J and Il in the neonatal period is unknown, but could be related to differences in functional properties of J and Il.

623 MASSIVE SMALL BOWEL RESECTION (SBR): GROWTH OF STOMACH (St), CECUM (Ce) AND COLON (Co) IN RATS. M.K. Younoszai and Adel S. Al-Jurf. The Univ. of Iowa Hospitals & Clinicis, Dept. of Peds., & Surgery, Iowa City.

In SBR growth of the remnant intestine is enhanced. We evaluated the effect of route and type of nutrition on growth of the St, Ce and Co in rats with >85% SBR. After surgery rats (140-170 g) were nourished orally ad libitum with a regular laboratory rat chow (Ch), or Flexical (Fl) or by vein with Travenol (T) along or in combination with oral Ch or Fl. A group of sham operated (C) rats were treated identically as the SBR rats. Growth was assessed as difference in weight and weight/body weight ratio of the organs between C and SBR rats, 8 days after operation. At the time of study organs were weighed free of contents. The change in body weight (Δ, g) and organ weight (g) are tabulated below:

Nutrient	Ch		Fl		T		T+Ch		T+Fl	
Rats	C	SBR	C	SBR	C	SBR	C	SBR	C	SBR
Δ	45	-13	13	-33	-9	-29	5	-22	5	-8
St	1.49	0.93	0.93	0.97	0.97	0.82	0.99	0.87	0.85	0.71
Ce	1.26	1.55	0.52	1.16	0.42	0.73	0.62	1.28	0.61	0.92
Co	1.47	1.27	0.85	1.40	0.68	0.89	1.07	1.26	0.82	1.08

SBR had no effect on growth of St. Becuase weight of Ce and Co was greater in TSBR than in TC rats, SBR had enhanced growth by humoral (hormonal) factor(s). The growth promoting effect of SBR was further enhanced by oral feedings. In rats nourished by vein the unrefined Ch diet had a greater growth promoting effect than the refined Fl diet. Further studies are needed to identify the growth promoting factor(s) in diet.

624 ESTIMATION OF WHOLE BODY PROTEIN SYNTHESIS AND BREAKDOWN IN PREMATURE INFANTS: COMPARISON OF RESULTS BASED UPON USE OF $^{15}NH_3$ OR [^{15}N]UREA AS END-PRODUCT. Marc Yudkoff, Itzhak Nissim, Gilberto Pereira and Stanton Segal. Children's Hospital of Philadelphia, Department of Pediatrics, Phila., PA.

Disagreement exists in the literature regarding rates of protein synthesis in premature infants. To determine whether these discrepancies might be referable to the use of urinary [^{15}N]urea or [^{15}N]ammonia as the basis for calculation of protein turnover, we measured this parameter in premature infants with a stochastic model predicated upon excretion of [^{15}N]urea or [^{15}N]ammonia over a 24 hour period following a single intravenous pulse of [^{15}N]glycine (5 mg/kg). Results for nitrogen flux, protein synthesis and protein catabolism were 36.4 ± 14.1 vs. 56.5 ± 16.4 mgN/kg/hr, 32.8 ± 14.5 vs. 52.5 vs. 17.5 g/kg/d and 21.3 ± 19 vs. 39.3 ± 20.3 g/kg/d for the ammonia-based and urea-based models, respectively. The urea-based results agree closely with studies involving a continuous 72 hour [^{15}N]glycine infusion. The lower values for protein synthesis with the $^{15}NH_3$ model suggest that premature infants preferentially utilize glycine nitrogen for renal ammoniagenesis, as has been suggested for the human adult.

625 LOCUST BEAN GUM IN FOOD PRODUCTS FED TO FAMILIAL HYPERCHOLESTEROLEMIC CHILDREN AND ADULTS. James H. Zavoral, Donna Fields, Madge Hansen, Peter Hannon, Kanta Kuba, Ivan Frantz, and David Jacobs (sponsored by Rolf Engel), University of Minnesta, Hennepin County Medical Center, Department of Pediatrics, Minneapolis.

Familial hypercholesterolemia (FHC) is associated with severe premature coronary artery disease, death, and is resistant to conventional dietary treatment. Locust Bean Gum (LBG) in food products was fed to children and adults with familial hypercholesterolemia. Twenty-eight children and adults (20 FHC, 8 N) were divided into two groups, using a cross-over design, and fed identical food products with and without LBG (8-30 gm/d) as outpatients in four-week periods. Diet records, food consumption, lipids, and lipoproteins were analyzed every two weeks. Total cholesterol was lowered 11% ($\bar{m}$ 275 to $\bar{m}$ 246) in Group A at four weeks and 16% ($\bar{m}$ 255 to $\bar{m}$ 215) in Group B at six weeks ($p < .01$). The difference in cholesterol between the LBG and control diet was 19% at four weeks ($p < .01$). Low-density lipoprotein (LDL) fell 10% at four weeks in Group A and 20% at six weeks in Group B. HDL/LDL ratios increased. LBG food acceptance was good. There were no significant side effects of the diet. LBG was more effective than several pharmacological agents in lowering serum lipids, and, in outpatients, appears to be one of the most effective dietary treatments of FHC. LBG in food products appears to be a safe, effective means of lowering serum lipids in normal and hypercholesterolemic children and adults in FHC-type families.

626 PARENTERAL NUTRITION IN SEVERE ANOREXIA NERVOSA. P. Zucker, S. Kleinhaus, S.J. Boley, and S. Levenkron. Spon. by M.I. Cohen, Depts. of Ped. and Ped. Surgery, Montefiore Hosp. & Med. Ctr., Albert Einstein Coll. Med., Bx.,NY

Although both behavior modification techniques and forced tube feeding may be used for the treatment of self-starvation in anorexia nervosa (AN) each is associated with potentially severe psychological sequelae and presents daily management problems. A prospective study was undertaken to determine if parenteral nutrition (PN) was a safe and efficacious alternative treatment. 15 courses of PN were employed in the treatment of 12 hospitalized patients with AN. All patients were more than 40% below ideal body weight and were unable to maintain their weight with intensive inpatient psychological and nutritional counseling. The average length of PN was 20 days (5-45). 3 patients required more than one course. Improvement in lethargy and affect occurred in all within 48 hours, and prompt improvement in psychotherapeutic progress was noted in 7. The most frequently encountered problems were catheter associated (6), failure to maintain ordered infusion rates (5), pneumothorax (2), rash (2), congestive heart failure (2) and liver toxicity (2). There were no episodes of infection. PN was decreased and subsequently discontinued as food intake improved. The parenteral caloric intake provided a reliable guide to educate the patient as to oral caloric needs. Follow-up revealed no recurrence of weight loss and continued outpatient progress in 8 of the 11 teenagers who have been discharged. Although not without problems, PN is a relatively safe, effective method of treating severe weight loss in AN and may aid psychotherapy.

GENERAL PEDIATRICS, EDUCATION AND TRAINING

627 HPYERPYREXIA IN CHILDREN: FACTORS INFLUENCING HOSPITALIZATION FROM THE EMERGENCY ROOM. Vincent I.Ahonkhai and Radharkrishna K.Reddy (Spon.by Senih M. Fikrig) SUNY.Downstate Med.Ctr.Kings Co.Hosp.Ctr., Dept.Ped. Brooklyn, N.Y.

Hyperpyrexia(HP) in children is alarming to parents because of the fear of convulsion, and to physicians because of the likelihood of a serious infection. Whether such children should be hospitalized(H) or not hospitalized(NH) becomes an important decision, especially in the absence of central nervous system infection. At the Kings Co.Hosp.Ctr. children's emergency room 65 children presenting with HP (temperature (T) of 40.5°C or above) were prospectively evaluated with history physical examination and laboratory studies by staff pediatricians or residents under supervision. Their ages and T ranged from two months to 14 yrs. and 40.5 to 41.5°C respectively. Seventeen (26%) were H and 48 were NH. Otitis media(OM) upper respiratory tract infection(U) fever without an apparent cause(F) and pneumonia(Pn) were frequent diagnoses (85%). When H and NH groups were compared, (1) there was no significant difference between the numbers of children with U (5.8%vs.12.5%), or F(17%vs.31%); (2) there was positive correlation between P and H (35%vs.8%,p=.02) and (3) negative correlation between OM and H(11%vs.37%,p =.02). Age,T and white blood cell counts were compar-

● **628** PSYCHOPHYSIOLOGIC AND BEHAVIORAL EFFECTS OF PATIENT DEATH ON PEDIATRIC HOUSEOFFICERS. Marylou Behnke, Greg J. Neimeyer, John Reiss, Emmalee S. Setzer (Spon. by Samuel Gross), Univ. Fla. Coll. Med., Department of Pediatrics, Gainesville.

Physicians confront death repeatedly. We surveyed 22 Pediatric houseofficers (11M; 11F) to assess their behavioral and psychophysiologic responses to patient death. The Death Threat Index (DTI) and two vignettes about a child's death were included. DTI measures the ability to view death personally based on George Kelly's personal construct theory (Death Education, 1979, 3:245). A higher score indicates death is a lower personal reality. The vignettes were followed by a 5-point scale of 14 behavioral and 21 psychophysiologic responses relative to the physician personally and to the perceived ideal physician. DTI was related to religion (Christian=16.3, non-Christian=30.8; $p<.005$) and to training level (PL1=14.6, PL2=28.2; $p<.05$) but not to sex, marital status, or personal death experience. Although male/female DTI scores were not significantly different, women grieved more intensely ($p<.005$) and tended to grieve longer with a greater sense of emptiness. Compared to the perceived ideal physician, houseofficers were more likely to feel guilty ($p<.02$), be anxious ($p<.05$), and have nightmares ($p<.05$); and less likely to search the patient records after death ($p<.02$) and seek professional help. This survey shows that education of the pediatric houseofficer should emphasize a personalized approach to death education as well as emphasize effective coping mechanisms to help deal with expected behavioral and psychophysiologic responses.

629 EYELASH MEASUREMENTS IN INFANTS Tim Bricker, M.D., Rebecca Kirkland, M.D., Ronald Harrist, Ph.D., Department of Pediatrics, Baylor College of Medicine and Texas Children's Hospital, Houston, Texas.

Eyelash length measurement in eighty-eight well infants and thirty-six ill infants between six and twelve months of age were analyzed with respect to diagnosis, age, race, sex, family history, and medications. Black infants had shorter eyelashes ($.63 \pm .14$ cm.) than white children ($.80 \pm .22$ cm.) or Hispanic surnamed children ($.90 \pm .25$ cm.). Other differences were not found. A reported feature of a number of illnesses in children is long eyelashes. Statistically signficant differences may be seen in children with other illnesses or at other ages than those included in the present study.

630 DEVELOPMENT OF A PROGRAM FOR RECERTIFICATION IN PEDIATRICS. Robert C. Brownlee, Fredric C. Burg, Diane W. Butzin, C. William Daeschner, Laurence Finberg, Robert O. Guerin, Charles F. Schumacher and Victor C. Vaughan, III. (From the American Board of Pediatrics (ABP), Chapel Hill, and National Board of Medical Examiners, Philadelphia).

In 1973 the ABP initiated research which led to a process for recertification of certified pediatricians. Problems examined were: (1) general purposes; (2) goal-setting; (3) content-specification; (4) standard-setting; and (5) program evaluation. Problems (1), (2) and (5) have received tentative solutions, open to further evaluation. Content-specification was made through a formal consensus-forming process, employing the examination of recent medical literature by panels of pediatric practitioners and educators, with explicit designation of educational and evaluative objectives for each content item. Standard-setting employed a unique modification of the Nedelsky technique, supported by an adaptation of the Rasch model for latent trait analysis. An absolute standard was arrived at through a process which set consensus as to relevance of each question against the difficulty of the question. The results suggest that the program has had a substantial impact upon the motivation of candidates for continuing medical education.

631 HOUSESTAFF STRESS IN NEONATAL INTENSIVE CARE UNIT: ANALYSIS OF FACTORS INVOLVED. T.A. Clarke, W.M. Manis calco, C. Hannon-Johnson, D.L. Shapiro, Univ. of Roch School of Medicine, Dept. of Pediatrics, Rochester, N.Y.

For housestaff, working in an intensive care setting can be stressful. To identify the factors in the NICU that housestaff perceive as stressful we constructed a questionnaire consisting of 114 statements distributed among 5 potentially stressful areas. Each ietm was ranked on a 5-point stress scale. 41 of 44 (93%) house officers surveyed replied. In general, working in a NICU was rated moderately to extremely stressful (score 3.96 out of 5). 12 house officers (28%) rated it extremely stressful, while only 2 rated it mildly stressful. Of the 5 major areas, the most stress ful was the working hours (score 4.02); the most stressful items in this area were working the day after being on night call (4.56) and working long hours on call (4.49). The second most stressful area was interaction with families (3.52), especially talking with parents of dead or dying infants (4.34) and dealing with parent's anger (4.04). Items related to staff interactions generally were not stressful (2.54) though interacting with uncooperative nurses was among the most stressful items (4.38). House officers off work hours were also affected; the most common effect was inability to sleep normally on nights off-call (83%) and effects on mood (74%). Sex, residency level or marital status did not influence the stress level but medical school experience in neonatology and relevance to career plans were associated with a lower stress level. These data indicate that working in a NICU is extremely stressful for a significant proportion of house officers and that certain areas can be isolated as highly stressful.

632 HEALTH HAZARDS OF PETTING ZOOS. David A. Clark and Jeffrey E. Thompson. (Spon. F. A. Oski). Dept. of Pediatrics, Upstate Medical Ctr., Syracuse, N.Y.

As western society has evolved from rural communities to urban centers, fewer children have been exposed to animals commonly found on farms. Petting zoos have appeared in an attempt to capitalize on this situation. They are frequently found in shopping centers and state fairs.

We observed children in five petting zoos in three states and were able to classify the types of adverse interaction into three groups: physical trauma, emotional trauma and potential infections. Physical trauma commonly observed included bites (during attempted feedings) and bruises, primarily of the hands and feet of small children who were knocked down and stepped on. Many instances of psychologic trauma were noted when young frightened children were repeatedly forced by the parents to feed or pet the animals. A frequently observed potentially infectious interaction was the repetitive close cuddling of the animals which exposed the children to secretions of animals and previous children.

Several instances of coprophagia were noted when a young child would spill a cup of animal feed pellets and while picking them up mix in feces which he would then eat while sharing with the animals. The petting zoo animals were frequently handled by many children simultaneously with no place to retreat. Petting zoos are crowded, artificial and with the usual poor adult supervision unsafe for both child and beast.

633 NUTRITION IN PRIMARY CARE PEDIATRICS. Jean Craig and Dianne Murphy. (Sponsored by P.A. Brunell). Univ. of Tx. Hlth. Sc. Ctr., Dept. of Pediatrics, San Antonio, Tx

It has been demonstrated that traditional pediatric training programs provide inadequate nutrition information concerning normal childhood requirements and infant feeding practices. A nutrition curriculum and evaluation process were developed to improve the nutritional knowledge base of pediatric housestaff (PH). Initial assessment of PH at all levels revealed knowledge deficits in well child nutrition. A "core" curriculum of six one hour small group or individual teaching sessions was developed and implemented by a nutritionist as part of a multidisciplinary teaching team in a continuity care clinic.

Nine of the 40 items on a comprehensive pediatric test are used to evaluate the nutrition knowledge of the PH. The entry scores of PL-1's, PL-2's, and PL-3's in 1979 demonstrated no significant difference in the nutritional knowledge base of the three groups, with both PL-2 and PL-3 scores being below 70%. With no intervention, the 1980 PL-3's had an exit score of 64%, which was below the entry level score of 68%. After one year of partial implementation of the program the 1981 PL-3's had an exit score of 82% which is significantly higher ($p<0.05$) than that of the 1980 PL-3's exit score of 64%, yet both groups had equivalent entry scores of 68%.

This program demonstrates that PH did not acquire competency in well child nutrition needs and practices in a traditional residency training program. With implementation of a "core" curriculum planned and delivered by a nutritionist the PH's nutrition knowledge significantly improved.

● **634** THE EFFECTS OF FREQUENCY ON BREASTFEEDINGS ON NIPPLE SORENESS AND BREAST ENGORGEMENT. M.DeCarvalho, M.Klaus, A. Friedman and R. Merkatz, Rainbow Babies & Childrens Hospital, Mt. Sinai Med Ctr., CWRU, Cleveland, Ohio.

To prevent breast complications in the first days after delivery, many maternity units advise mothers to limit the frequency and duration of nursings. To investigate the effects of the frequency and duration of feedings on nipple soreness and breast engorgement we studied 2 groups of mother-infant pairs in the first 10 post-partum days. Allocation to the groups was determined by the day of delivery. All mothers recorded daily the frequency and duration of each feeding, nipple soreness and breast engorgement. We measured milk output and infant weight gain on the 15th day. Infant and maternal characteristics were not significantly different between the groups. Mothers in the low frequency group (n=12) nursed on a routine 3-4 hours schedule while those in the high frequency group (n=15) were encouraged to feed frequently. Although mothers in the high frequency group nursed significantly more frequently they did not experience either more soreness or engorgement. However, mothers in the high frequency group produced significantly more milk (724 vs 502 ml, $p<.001$) and their babies gained significantly more weight (560 vs 347 gm, $p<.02$). High frequency of feeding improves milk output and infant weight gain and does not increase breast complications.

	FEEDING FREQUENCY/24h	DURATION OF FEEDINGS(min/24h)	NIPPLE SORENESS	BREAST ENGORGEMENT
LOW	7 ± 1.3	127 ± 37	0.75±0.5	0.75 ± 0.6
HIGH	10 ± 1.7*	134 ± 40†	0.63±0.4†	0.75 ± 0.8†

mean ± SD *p <.0001 †not significant

635 COMMUNICATION TRAINING IN A PEDIATRIC RESIDENCY, Lee Dickinson, Michelle Huels, Dianne Murphy. (Sponsored by P.A. Brunell). University of Texas Health Science Center, Dept. of Pediatrics, San Antonio, Texas.

A competency-based didactic program in interviewing was developed to improve communication skills of pediatric housestaff. The program, implemented in a continuity clinic, began with a videotape of PL1's and 3's in a first visit, well-baby exam. PL1's were then given a series of didactic presentations on communication skills and feedback on their videotape performance and then videotaped for follow-up measure. PL3's were used as a measure of the skills acquired in the "pediatric system." Comparisons were made between PL1 pre's and PL3 controls (C), 1-pre's and 1-post's, and 1-post's and C's. Comparisons were made on the basis of a 17-item interview scale developed in the clinic. It appears there is an acquisition during residency of interviewing skills that are deficient on entry. However, though C's outperformed 1-pre's on 12 of 17 items, the difference being significant on 4 items (p's ranging from .001-.003), they were deficit in 6 areas. 1-pre's equaled or outperformed C's on 5 items, significantly on 1 ($p=.01$). Implementation of the teaching/feedback (T/F) had 2 major effects. PL1's improved their skills in 13 areas, significantly in 3 (p's from .005-.02), being deficit on follow-up in only 4 areas. However, skills in 2 areas which had been relatively low on entry deteriorated almost to the even lower C level, despite teaching. Comparison of 1-post's and C's indicated that T/F resulted in substantial equivalence between the 2 groups, with no significant differences. These findings indicate that although residency training improves communication skills over entry, sig. deficits remain and that 1's can exceed the 3 level with intervention.

636 MULTIDISCIPLINARY RESIDENCY TRAINING IN AMBULATORY PEDIATRICS. Lee Dickinson, Dianne Murphy and Philip Brunell. Univ. of Tx. Health Sc. Ctr., Dept. of Pediatrics, San Antonio, Texas.

A multidisciplinary teaching program in comprehensive pediatric care (CPC) for housestaff was developed and implemented in a continuity clinic. Staff are a nutritionist, pediatric nurse practitioner, social worker, psychologist, and lab technician. The curriculum includes nutrition (Nu), health promotion, communication skills (CS), psychological aspects of health care and lab skills. Teaching residents in this setting offers 2 advantages: 1) the continuous patient contact necessary for CPC, e.g., nutrition and behavior counseling, parent education; and 2) feedback over time regarding interventions. Evaluation centers on 3 modalities: 1) pre and post minitests of each content area; 2) a comprehensive test covering all content areas and 3) assessment of videotaped patient/resident interviews. Preliminary pretest data show major deficits in many areas for both PL1's and 3's. PL3's scored below 70% on 75% of the psychosocial/growth and development (P/GD) items and on 35% of the communication/interviewing (C/S) items. PL1's scored below 70% on 100% of P/GD items, on 75% of lab skills, and on 65% of C/S items. All levels scored at or below 70% in Nu. Follow-up data showed significant improvement in Nu, CS and Lab (p's $<.05$). This program has: 1) identified specific deficits in knowledge of and skills in CPC at all levels and 2) shown that professionals from allied areas can significantly impact pediatric training.

637 RELIABLE INTERPRETATION OF THROAT CULTURES BY RESIDENTS., Paul M. Douthitt, John W. Greene, Michael Werner (Spon. by Peter F. Wright), Vanderbilt Univ. Med. Ctr., Department of Pediatrics, Nashville. Recent studies have questioned the ability of physicians in training to interpret throat cultures reliably. To investigate this and to evaluate our educational process, residents' interpretations of cultures performed in a pediatric clinic and student health service were compared to independent readings by laboratory technicians. Residents are educated in office bacteriology by reading throat cultures with faculty supervision during general pediatric rotations at a community hospital where they spend 2-3 months per year. Residents at the PGY-3 level of training on an adolescent rotation independently read throat cultures in a student health center. Eight residents at the community hospital and four residents at the Student Health Center read 474 cultures with no resident interpreting less than 10. Throat swabs were plated directly onto blood agar plates and incubated at 37° C. A bacitracin disc was placed in the original inoculum. After 18-24 hours plates were examined for colonies of group A beta hemolytic streptococci. 29% of the primary plates were considered unreadable and were subcultured because beta hemolytic colonies were present but not near the disc or if there was an overgrowth of other hemolytic organisms. Subcultures were examined in 24 hours. Only one culture at each location was read as positive by the lab technicians which had been read as negative by the residents. No cultures were falsely reported as positive by the residents. We conclude that residents can reliably interpret throat cultures and maintain this reliability when unsupervised.

638 CHLORAMPHENICOL USE AND ABUSE IN A PEDIATRIC HOSPITAL. Howard S. Faden, Lois Neidermeyer, Stanley J. Szefler. State University of New York at Buffalo, Children's Hospital of Buffalo, Department of Pediatrics, Buffalo, N.Y.

Emergence of ampicillin-resistant H. influenzae type b as a cause of serious infection in children has resulted in a resurgent use of chloramphenicol. Concern over the frequency of chloramphenicol use prompted a review of its use. Fifty-five of 1000 children admitted to the hospital received chloramphenicol for 1-17 days (median 2 days). They ranged in age from 1 month to 15 years (median 5 months). Chloramphenicol was administered by the intravenous route in doses from 50-100 mg/kg/d. Chloramphenicol was begun in combination with a penicillin as empiric therapy in children being evaluated for sepsis, meningitis, cellulitis, pneumonia, septic arthritis, osteomyelitis, and abscess. The initial diagnoses were substantiated in 31; H. influenzae type b was the etiology in only 4. A large number of children had documented viral diseases. Chloramphenicol toxicity was most often monitored with serial CBCs, rarely with reticulocyte counts or serum concentrations of chloramphenicol. These data demonstrate that chloramphenicol was used excessively as empiric therapy, although it was administered by the correct route, in appropriate doses, and for appropriate periods. Monitoring of toxicity appeared inadequate. These findings were presented to the medical staff in order to improve the pattern of chloramphenicol use.

● **639** SICKLE CELL SCREENING OF NEWBORNS. Ranjeet Grover, Doris L. Wethers, Genetic Screening Program, New York City Health Department, New York

Legislation in New York State mandates that all newborn babies be tested for sickle cell along with seven other conditions. Of 213,296 newborns tested in New York City over the period of two years (Jan. 1, 1979 - Dec. 31, 1980), 280 infants were diagnosed to have sickle cell disease (SS, SC and S Thal), 14 CC disease and 4 C Thalassemia on repeat testing. All those diagnosed to have sickle cell disease were given a specific appointment to a sickle cell clinic or other health agency for comprehensive medical care. Follow-up data is currently being collected re. the morbidity and mortality among these patients. In addition 7,039 infants were identified with sickle cell trait (AS), 1,921 AC and 12 AC^{Harlem}. Of 6,830 families who were notified of the trait (AS and AC) diagnosis in their infants and were invited for testing and counseling, 2,875 (42%) were tested and counseled during the study period. These figures have improved remarkably during the year 1981 because of the active participation of the hospitals. Testing of the families also identified 26 parents with the diagnosis of sickle cell disease (6 SS, 20 SC) and one with S/HPFH. Of these only 9 parents were aware of their diagnoses prior to testing.

640 THE EFFECT OF A COMPUTER GENERATED BLOOD GAS DISPLAY ON THE OUTCOME OF RDS. Marcus Hermansen, Harry Atherton, Neil Edwards, David Phillips, Paul Perlstein, Univ. Cincinnati Coll. Med., Dept. of Peds.

To improve outcome of neonatal RDS, an online computer system has been used to sort blood gas data, displaying the gases on TV screens if a markedly abnormal pH or a worsening pH trend is detected. The outcome of infants cared for with and without the display, the physicians' responsiveness to an abnormal pH, and the outcome of pH trends were studied. 32 newborns with RDS spending their first week with the display (DSPLY) and 22 spending it without the display (CONTROLS) generated study data. Groups were comparable for sex, race, APGAR's, gestation, B.W. and admission age. At one week, ventilator and O_2 requirements, and mortality were all less in DSPLY infants ($p>.05$). Of the infants <1501g and requiring ventilation, 5/15 DSPLY and 0/12 CONTROLS were living, extubated, and in room air at age 1 wk ($p<.05$). The elapsed times from abnormal pH to the next gas, to an improved pH, and to a normal pH were:

	Next Gas*	Improved pH**	Normal pH***
CONTROLS	96±10min	243±31min	421±45min
DSPLY	88±6 min	173±15min	321±32min
t-test	*p>0.3	**p<0.05	***p<.10

Fewer trends worsened in DSPLY (38/222 trends) than in CONTROLS (36/136) but more trends were overcorrected in DSPLY (12/222) than CONTROLS (1/136) (p=.03). The computer generated display was thus associated with improved outcomes in very low birth weight, ventilated infants, due to more rapid and improved physician responses to abnormal pH values.

641 STAFF ATTITUDES REGARDING A PEDIATRIC CARE-WITH-PARENT PROGRAM. Pamela C. High, Steven G. Weiss, Peter A. Gorski, Ronald I. Clyman. Mt. Zion Hospital and Medical Center, Department of Pediatrics, San Francisco, CA.

We have developed a program on our pediatric ward in which parents are encouraged to "room in" and participate in the care of a hospitalized child. The parent of any child may participate in the program, regardless of the child's diagnosis or acuity. Staffing of the unit is based on acuity and is not modified by parent involvement in the program. A 5-item Likert-type questionnaire was developed to survey the effects of the program as perceived by medical and nursing staff. Although the nursing staff constantly interfaces with parents in the program and might be expected to have sharper criticisms of it, we found no significant differences between their responses and those of the medical staff. Eighty-seven percent of the staff felt that the program made their jobs easier; 7% felt that it made their jobs more difficult; 63% felt that the program improved their efficiency, while 13% felt it decreased efficiency; 33% thought the program decreased patient care errors while 11% thought it increased errors. Ninety-two percent felt that the time they spent with parents was satisfying while 8% found it frustrating. One-hundred percent of the staff surveyed would choose a ward with a care with parent program should their child require hospitalization. These findings suggest that active parent participation on a busy pediatric ward serving children with a wide range of problems does not perceptibly increase staff's work or errors or decrease staff's efficiency.

642 TEETH IN PSEUDOHYPOPARATHYROIDISM: RESPONSE TO TREATMENT WITH 1,25-DIHYDROXYVITAMIN D OR VITAMIN D. George Hug, William A. Mueller, Clifford J. Steinle, Don P. Wilson and Sean J. Fennell. Department of Pediatrics, University of Cincinnati, Cincinnati, Ohio and The Children's Medical Center, Tulsa, Oklahoma.

A black girl age 12 y and an unrelated black boy age 11 y had hyperactive reflexes, positive Chvostek, hypocalcemia, hyperphosphatemia, mental retardation, cerebral calcification. Serum parathyroid hormone (PTH) was increased and $1,25(OH)_2D$ was low normal. Diagnosis of pseudohypoparathyroidism (PHPT) type I was consistent with lack of increased urinary excretion of phosphate and 3'5'-AMP after i.v. PTH. Both children had dental abnormalities typical of PHPT: enamel hypoplasia of permanent premolars and second molars; no eruption of permanent teeth (except lower central incisors in the girl) resulting in dentition as in a 6 y old child. In the boy abnormalities of teeth and serum were unchanged after 8 mo. of Vitamin D, 200,000-900,000 units p.o. every 2-5 weeks. The girl was treated for 8 mo. with $1,25(OH)_2D_3$ ($ROCALTROL^R$), 1 mcg p.o. daily. Her well being improved. Phosphate and calcium in serum became normal. Her primary canines exfoliated. Root resorption of remaining primary teeth increased. Eruption of permanent teeth resumed at a normal rate (retaining a 6 y delay). We conclude that teeth formed between ages 3-7 y (but not those earlier) suffered enamel hypoplasia. Hence PHPT seemed to reach clinical significance (with respect to teeth) when the patients were 3-4 y old. Enamel hypoplasia once it occurred could not be reversed. It might have been preventable if the patients had received $1,25(OH)_2D_3$ before the age of three years.

643 EARLY SEX MISEDUCATION. Betsy Lozoff, Abraham Wolf (Spon. by M. Klaus), Case Western Reserve University School of Medicine, Depts. of Pediatrics and Psychiatry, Cleveland, Ohio.

To describe some aspects of early sex education in U.S. families, 91 randomly-selected mothers of 1 to 4 year-old children were intereviewed at the time of well-child care in representative pediatric facilities. This age range was chosen because issues of sex differences and sexual identity are prominant during toilet training and the preschool years. The group was similar in racial and educational background to census data for the Cleveland area. 84% of the children were regularly exposed to adult nudity during bathing and dressing (not including those who observe parental toileting only). However, only half the mothers noted their children to be interested in the sex differences between boys and girls or between adults and children. Terms for male genitalia were used by 78% of mothers of boys, but words for female genitalia were significantly less commonly used with girls (58%), (p=0.04). For both girls and boys, slang or ethnic words were generally used, regardless of race or education. In contrast to a previous sample of highly educated mothers who regretted not learning words for female genitalia until adolescence or adulthood, mothers in this representative sample were embarassed and seemed at a loss to explain whether their terms referred to the vagina or external organs. Pediatricians could easily use specific labels during the genital examination of the young child, thus educating both parents and child and communicating that sex is not a taboo subject.

644 SLEEP PROBLEMS IN PEDIATRIC PRACTICE, B. Lozoff, A. Wolf (Spon. by M. Klaus), Case Western Reserve U. School of Med., Depts. of Pediatrics and Psychiatry, Cleveland, Ohio.

To determine if common sleep problems, readily ascertainable by pediatric professionals, are associated with other disturbances in young children and their families, a sample of 50 healthy children under 4 years of age was enrolled in an interview study on the basis of well-child care appointments in representative facilities. A sleep problem in a child 6 months of age or older was defined as bedtime struggles or night waking which involved the parents three or more nights each week for the month preceding the interview. By this definition, 31% had a sleep problem, of concern to the mother in each case. Of these, only one had a bedtime problem without night waking and the majority had both. Sleep problem children did not differ in demographic characteristics from non-sleep disturbed children, but were more likely to have parents who responded to night waking by bringing the child into the parental bed (p=0.03) or with other forms of body contact (p=0.02). Mothers of sleep-problem children were significantly less accepting (p=0.02) and reported more severe stresses (p=0.002), especially associated with family illness or accidents, sibling births, overnight and unaccustomed daytime separation from the mother, and depressed maternal mood. However, few pediatricians discussed sleep after a child's early months of life. Thus, night waking seemed to be an easily quantifiable behavior which should alert professionals to the existence of more pervasive disturbances in child and family.

645 INFANT FRACTURES: WHEN TO SUSPECT ABUSE. Michael G. Martin, David A. Clark, Dept. of Pediatrics, SUNY, Upstate Med. Ctr., Syracuse, NY (Spon. M. Williams)

The charts of 83 children admitted to two major hospitals serving metropolitan Syracuse with fractures (114) in the first year of life were reviewed for site of fracture and etiology.

The fracture site and etiology are summarized in the table.

	Abuse	Accidents	Birth Trauma	Unclear
Skull	7	54	2	2
Leg	11	5	1	3
Arm	8	4	--	1
Ribs	12	--	--	--
Clavicles	3	--		--
Scapula		1	--	

Thirteen of 17 old fractures were caused by abuse; 3 followed birth trauma. Eight of 18 (44%) abused children had multiple fractures versus four of 65 (6%) non-abused children. Expressed differently eight of 12 children with multiple fractures (66%) were abused children. Two of three fractured clavicles in abused children were old and probably due to birth trauma. Lab chemistries (Ca++, Phos., Alk P'tase) were normal when tested. No metabolic bone disease was diagnosed

In conclusion most fractures in infants occur in otherwise normal bones. Abuse should be suspected if the fractures are healing (old) or multiple (especially ribs, 100% in our series). Careful history and physical examination remain vital for diagnosing child abuse.

● **646** OBSERVATION SCALES TO IDENTIFY SERIOUS ILLNESS IN FEBRILE CHILDREN. Paul L. McCarthy, Michael R. Sharpe, Thomas G. DeWitt, Thomas F. Dolan, Brian W. Forsyth, Domenic V. Cicchetti. Yale University School of Medicine, Yale-New Haven Hosp. Dept. of Pediatrics. New Haven, Connecticut.

The pediatrician makes a judgment of degree of illness(Toxicity)of a febrile child based on observation prior to history(Hx) and physical exam(PE). In order to define valid and reliable observation data for that judgment, data from 2 previous studies were used to construct 3 point scales of 14 observation items correlated with serious illness(SI) in those reports. Between 11/1/80 and 3/1/81, these 14 scaled items were scored simultaneously by attendings, residents and nurses prior to Hx and PE on 312 febrile children ≤24 months seen consecutively in our Primary Care Center and one private practice; 37 had SI. Multiple regression analysis based on patients seen by at least 1 attending revealed 7 items(Quality of Cry, Reaction to Parents, Color, State Variation, Hydration, Eye Appearance, Respiratory Pattern) were significant and independent predictors of SI(Multiple R= 0.64). Interobserver agreement levels for scoring these 7 items between 1 attending pair who saw 1/3 of the patients were, with one exception, clinically significant(Kw=0.47-0.73). By discriminate function analysis, these 7 items had, when used together, a specificity of 86% and a sensitivity of 74% for SI. Only 2.1% of patients with a score of <0.10 from discriminate function analysis had SI; 91% with a score of ≥0.50 had SI. The sensitivity of these 7 items for SI when combined with Hx and PE was 89%.

This 7 item model, when used prior to Hx and PE, is reliable, predictive, specific and sensitive for SI in febrile children. For maximum sensitivity, it should be combined with Hx and PE.

● **647** CLINICAL LABORATORY PROGRAM FOR PEDIATRIC RESIDENTS. D Murphy G Macias and D Gessner.(Sponsored by P.A. Brunell). University of Texas Health Science Center, Dept. of Pediatrics, San Antonio, Texas.

The clinical laboratory plays an important role in health care today. Our preliminary data indicate that most residents (R) know suprisingly little about common office lab tests (COLT). Inadequate knowledge (below 70%) was demonstrated in 6 of 8 basic lab tests; the average score in the 2 tests involving cultures was 22% The results are consistent at all levels tested (PL1-3). A lab curriculum (LC) covering COLT and emphasizing one-to-one teaching and practical testing was implemented by a technologist/teacher in a small OPD lab. Baseline performances for each R were established Follow-up (FU) evaluations showed improvement in all 8 areas. The program demonstrates that without a LC, R's are markedly deficient in basic lab skills, beginning their residency with adequate knowledge and skills in only 2 areas. Knowledge of all other routine lab procedures is inadequate and remains so despite minimal improvement during training. A limited LC can overcome these deficits, bringing PL1's to the FU PL3 level within a year.

	Urine Cult		Throat Cul		WBC		Differen		sed rate		Hct*		Gram St*		UA		'N' values
LEVEL	pre-	post	pre-	post	pre-	post	pre-	post	pre-	post	pre-	post	pre-	post	pre-	post	average
PL-3 '79	42	85	28	82	60	95	55	83	65	82	88	99	78	99	70	92	11
PL-2 '79	25	74	22	78	55	88	35	85	66	99	88	99	62	95	62	92	13
PL-1 '79	26	-	10	-	45	-	42	-	58	-	85	-	58	-	58	-	11
PL-1 '80	18	-	20	-	37	-	50	-	44	-	72	-	52	-	59	-	10
PL-1 '81	12	-	11	-	30	-	42	-	35	-	83	-	63	-	61	-	10

648 SIMPLIFICATION OF CALCULATIONS IN THE NEONATAL AND PEDIATRIC ICU USING A PROGRAMMABLE HAND HELD CALCULATOR. Josef Neu, K. J. Sheth, Carl Eisenberg, Tom B. Rice, C. Larry Kien, Allen D. Wilson, Larrie D. Sarff. (Spon. by Jerome V. Murphy). The Medical College of Wisconsin, Department of Pediatrics, Milwaukee.

In order to improve accuracy, save time and focus ICU personnel on physiologic monitoring of the critically ill patient, we have developed several programs for a relatively inexpensive programmable, commercially available calculator. These include programs for calculations of: (1) Dilutions for constant infusion of frequently used medications such as dopamine, isuproterenol, nitroprusside, prostaglandins, etc. In order to avoid errors in data entry, safety flags have been incorporated. (2) Nutritional, fluid and electrolyte monitoring of patients receiving oral intake and/or up to three infusions of fluid or hyperalimentation; (3) Cardiopulmonary and echocardiographic monitoring; (4) Renal function calculations that aid in the differentiation of renal and pre-renal failure; (5) Aminoglycoside dosing.

Use of this calculator and the programs which we have developed are simple, relatively inexpensive, should improve accuracy and save considerable time in doing tedious repetitive calculations.

649 THE PREDICTIVE VALUE OF THE "IN-TRAINING EXAMINATION." Frank A. Oski and Ernest M. Post. Dept. of Pediatrics, SUNY, Upstate Med. Ctr., Syracuse, N.Y.

It is now customary for pediatric residents to take the In-Training Examination (ITE) of the American Board of Pediatrics. We reviewed our 10 yr. experience with the ITE in an attempt to determine if the performance on the exam during the PL-1 and PL-3 yrs. correlated with the performance on the written portion of the certification exam of the Board (ABP). We found that the percentile rank during the PL-1 and PL-3 yrs. was significantly correlated with the eventual score on the ABP exam (PL-1, r=0.64; PL-3, r=0.44) with the PL-1 performance having a better predictive value. When the relationship between PL-3 scores and Board scores was examined it was found that 42% of the group scored at least 10 points lower in the ABP; only 11% scored more than 10 points higher; 47% stayed within 10 points in the 2 exams. The performance of these 3 groups in terms of mean %tile scores was:

Group with:	PL-1 Score	PL-3 Score	Board Score
No change	74 %tile	79 %tile	82 %tile
Decline in score	70 %tile	85 %tile	61 %tile
Improved score	74 %tile	62 %tile	90 %tile

There was no way of predicting with certainty, from initial scores or PL-3 scores, the precise performance in the ABP. Even among residents in whom PL-1 and PL-3 scores were within 10 points of each other, 38% showed a deviation from this established pattern on the Board exam. Percentile ranks are subject to change as a result of effort and emotional factors. In our program the decrease in night call during the third yr. did not result in an increase in relative knowledge.

650 ASSESSING RESIDENCY TRAINING IN BEHAVIORAL PEDIATRICS S Phillips, SB Friedman, J Parrish, & B Zebal
Depts Ped and Psychiat, Univ Md Sch Med, Baltimore

Three groups of residency programs were compared: 11 funded (F) to provide mandatory behavioral training, 7 not funded (NF) but providing nandatory training, and 6 controls (C) not requiring training. At the beginning and end of academic year 80-81, 569 residents (70%) completed questionnaires assessing attitudes regarding behavioral disorders (e.g., chool phobia), physical disorders (e.g., pharyngitis), and "mixed" disorders e.g., failure to thrive). Behavioral knowledge was tested by 60 multiple-choice questions. ANOVAs evaluated amount of change, revealing that virtually all significant effects related to program type occurred in the PL-2 year. Regarding attitudes, similar results were found for 3 measures: competence in management", "ability to advise parents", and "prediction of future relevance". Only Group F demonstrated significantly higher change scores for both behavioral and "mixed" disorders, relative to physical disorders; F and NF were significantly superior to C regarding behavioral disorders. A different pattern was found for 2 other measures: knowlege of resources", and "perceived faculty interest". NF change was significantly superior to F, which was marginally superior to C. Since F ratings were higher initially, NF ratings became nearly as high as F by the end of the year. Regarding knowledge, there was a trend in all 3 residency years for Groups F and NF to show greater improvement than C. This was significant in the PL-2 year and marginal in the PL-3 year. These data demonstrate that changes in attitudes and knowledge are related to the presence of required training. Funded programs appear to generate the most positive attitudinal effects regarding both behavioral and "mixed" disorders, though change was not dramatic. These data also suggest that the impact of behavioral training is most evident in the PL-2 year.

651 DEVELOPMENT OF THE PHYSIOLOGIC STABILITY INDEX (PSI) FOR USE IN CRITICALLY ILL INFANTS AND CHILDREN. Murray M. Pollack, Timothy S. Yeh, Urs E. Ruttiman, Peter R. Holbrook, Alan I. Fields, (Spon by G. Rosenquist), George Washington U., Children's Hosp Nat'l Med Ctr, Washington, D.C.

The PSI was developed to aid in the evaluation of severity of illness, efficacy of therapy and care requirements for critically ill infants and children. Previously we confirmed the utility of the Therapeutic Intervention Scoring System (TISS) and Clinical Classification System (CCS) in pediatric ICU patients. The PSI is based on the degree of abnormality 34 physiologic variables e.g. BP, HR, CVP, PCWP, cardiac output, ICP, Glascow Coma Score, BG's, electrolytes). From Dec. 1980 to June 1981 all patients admitted to our 16 bed multidisciplinary ICU were classified by CS on admission and daily PSI and TISS scores were determined; 23 pts. (mean age 5.2 yrs) were classified by the CCS as class Cl) II 30%, Cl III 33% and Cl IV 37%. Overall mortality at 1 month was 9% (Cl IV- 23%, Cl III- 1%, Cl II- 0%). We found excellent correlation between CCS, TISS and PSI admission scores (Cl I- TISS 11.4, PSI 3.2; Cl III- TISS 20.3, PSI 5.2; Cl IV-TISS 4.8, PSI 12.1) and a significant difference between Cl IV survivors (S) and nonsurvivors (NS) for admission scores (TISS: S=34, S=39, $p<.02$; PSI: S=10, NS=18, $p<0.0001$), maximum scores (TISS: =37, NS=47, $p<0.0001$; PSI: S=13, NS=26 $p<0.0001$) and slopes of regression (TISS: S= -2.0, NS=0.7, $p<0.0001$; PSI: S= -0.65, NS= .1, $p<0.0005$). We conclude that the pediatric PSI correlated well with other methods of patient assessment (CCS and TISS). PSI scores reflect mortality as well as degree of change of physiologic abnormalities.

652 SCREENING FOR COLONIZATION WITH GROUP B STREPTOCOCCI (GBS): IMPACT ON THERAPEUTIC DECISION MAKING. Joan A. Regan, Jane O'Neill and L. Stanley James. Columbia Univ., College of P & S, Div. Perin. Med., Dept.Ped.,NY.

It has been alleged that screening programs result in unnecessary diagnostic and therapeutic intervention. In order to test this hypothesis during a 3 year period we advocated rapid screening of mothers for colonization with GBS at the time of admission for delivery. Screening was performed at the discretion of the obstetrician caring for the mother, generating a screened (N = 6,324) and unscreened group (N = 2,422). Among the screened group 12.4% of mothers were GBS ⊕.

Knowledge of culture status of each patient was made available to the pediatricians who would ultimately care for the newborn within hours of the mother's admission for labor and delivery. Prophylactic treatment was not advocated; rather, treatment upon recognition of symptoms was recommended.

Under these guidelines 5.6% of infants born to mothers in the screened group vs 11% in the unscreened group were evaluated and treated for sepsis. Ratio of infants evaluated to those with proven sepsis was 9.1:1 in the screened group vs 11.3:1 in the unscreened group but 4.1:1 in the GBS ⊕ screened group.

We conclude, that contrary to prevailing opinion, a screening program for GBS colonization did not increase the number of infants subjected to workup and treatment for sepsis, but significantly increased the sensitivity of the therapeutic decision making when culture status of the mother was known to the pediatrician.

653 ACUTE OTITIS MEDIA (AOM) SECONDARY TO AMPICILLIN RESISTANT HEMOPHILUS INFLUENZAE (Amp^R H.flu): EXPERIENCE WITH 71 CASES. Richard H. Schwartz, Wm. J. Rodriguez, Ronald Barsanti and Waheed N. Khan. Research Foundation of Children's Hospital and the George Washington University School of Medicine and Health Sciences, Washington, D.C.

In the past 3½ years, we treated 71 children with AOM secondary to Amp^R H.flu confirmed by myringotomy and culture of middle ear exudate. They ranged in age from 4 to 72 months (mean age 21.7 months); 9 were ≤ 6 months of age. At the time of myringotomy, 58 children (82%) had been receiving, or had recently completed therapy (≤ 3 days), with either ampicillin or amoxicillin. Cultures from all 71 children were plated on chocolate agar with bacitracin. A 10 μg ampicillin disc was placed on the streaked primary plate to select presumptive Amp^R Hemophilus which grew near the disc. β-lactamase determination was done on all isolates. Amp^R H.flu was recovered from all 71 children. Seven children (7/71) had myringotomy performed both before ampicillin therapy and on persistence of AOM. All 7 initially had H. influenzae sensitive to ampicillin recovered from the middle ear. After ampicillin treatment, when persistent AOM was diagnosed, Amp^R H.flu was recovered from the middle ears of all 7. Antimicrobial therapy for persistent AOM included erythro/sulfa (38), TMP-SMZ (17), ceclor (13), and other (3). There was no apparent therapeutic superiority of one modality over the others as determined by the persistence of AOM.

654 SURVEILLANCE OF AMPICILLIN RESISTANT HEMOPHILUS (Amp^R Hem) IN SICK AND WELL INFANTS. Richard H. Schwartz, Wm. J. Rodriguez and Tahir Sait. Research Foundation of Children's Hospital and the George Washington University School of Medicine and Health Sciences, Washington, D.C.

Simultaneous semi-quantitative throat cultures (TC) and nasopharyngeal cultures (NP) were obtained from 152 children. Sixty-five were well with no recent exposure to antibiotic; 51 had purulent nasopharyngitis; 36 were seen at 10-day follow-up after ampicillin treatment of acute otitis media. All cultures were plated immediately on chocolate agar with bacitracin. A 10 μg ampicillin disc was placed on the streaked primary plate to select presumptive Amp^R Hem which grew near the disc. β-lactamase determination was done on all isolates. H. parainfluenzae was recovered more often than H. influenzae, 55% vs 45%. Hemophilus species (H.flu) was recovered by TC from 92/152 children (60%); 27/92 (29%) were Amp^R Hem. NP recovered H.flu from 68/152 (45%); 19/68 (28%) were Amp^R Hem. TC was more sensitive than NP for recovering H.flu (92 vs 68); see table. Previous treatment with ampicillin did not increase the prevalence of Amp^R Hem.

RECOVERY OF HEMOPHILUS SPECIES FROM THROAT & NASOPHARYNX

SITE	Well children (65) H.flu (% resistant)	Nasopharyngitis (51) H.flu (% resistant)	Ampicillin Rx (36) H.flu (% resistant)	TOTAL (152) H.flu (% resistant)
Throat	36 (33)	35 (26)	21 (29)	92 (29)
NP	27 (4)	25 (56)	16 (31)	68 (28)

655 BENIGN TRANSIENT GASTROINTESTINAL DYSFUNCTION (TGD) IN TERM NEWBORNS (NB) IN THE FIRST 3 DAYS OF LIFE. L.D. Lilien, G. Srinivasan, J. Singh, S. Yoora, R.S. Pildes. Cook County Hosp. Dept. of Ped. Univ of Ill, Chicago, Ill.

Over 18 months all inborn term NB who presented with bilious vomiting were transferred to the NICU. Seventeen NB presented within 72 hours (incidence 0.2%); work-up led to surgical intervention in 3 (2 malrotation, 1 jejunal atresia). The remaining 14 NB were presumed to have TGD. TGD presented with bilious vomiting at <12 hours in 1 NB. between 12-24 hours in 9, between 24-48 hours in 2, and between 48-72 hours in 2. All 14 NB with TGD passed meconium within 24 hours of birth; 3 had a meconium plug. Abdominal x-rays showed generalized distended bowel loops in 10 and normal gas pattern in 4. Eleven NB with TGD had normal contrast studies; the remaining 3 improved before contrast studies could be done. Eleven NB with TGD had negative septic work-ups; the other 3 were not clinically septic and were not treated with antibiotics. Metabolic studies were normal except for 1 NB with hypocalcemia and 1 with hyponatremia. None of the mothers were given $MgSO_4$; 2 had demerol. One NB had fetal distress, 1 had a 1 min Apgar <3, and none were meconium stained. NB with TGD tolerated nipple feeding at a mean±S.D. of 4.3±1.5 days (range 2-6 days) and on clinical follow up had no subsequent GI disturbances. Although bile-stained vomitus is thought to be uniformly an ominous sign, it is not invariably associated with surgical problems in the NB. Our data indicates that 82% of NB with bilious vomiting in the first 3 days of life had TGD; however, appropriate work-up is still necessary to insure early diagnosis of potential surgical lesions.

656 A BEDSIDE TECHNIQUE OF MEASURING ARTERIAL PCO_2 USING A $tcPCO_2$ MONITOR. Arvind Shukla, Azra Nisar, Rama Phat, Dharmapuri Vidyasagar. Department of Pediatrics, University of Illinois Hospital, Chicago.

Transcutaneous blood gas monitoring has become a routine procedure in the neonatal intensive care unit. We describe yet another use of transcutaneous pCO_2 monitoring. Since a $tcPCO_2$ can be used on a single neonate at any given time. Application of this electrode for blood pCO_2 will increase the usefulness of the electrode. In order to establish the relationship of $PaCO_2$ to bedside pCO_2, we simultaneously measured $PaCO_2$ and pCO_2 by blood drop placed on $tcPCO_2$ electrode. The electrode was calibrated at 44°C. 44 paired samples in 11 infants were measured. For bedside $tcPCO_2$ measurements, 0.1 ml of arterial blood was placed on the electrode and immediately covered with a glass cover slip. The $tcPCO_2$ was recorded until a plateau was obtained. The time taken to plateau and time taken to reach 90% of the final value was also calculated. $PaCO_2$ was measured by Radiometer blood gas analyzer. A regression analysis of the data showed a significant correlation ($n=44$, $r=0.97$ $p<.005$). $PaCO_2=10.3+0.76$ ($tcPO_2$). A paired t test showed mean Δ of 0.20. The $\bar{X}$ time to reach 90% of the value using $tcPCO_2$ electrode was 59 seconds. Mean time to reach a plateau was 90 secs. These data suggest that the $tcPCO_2$ electrode can be used to measure arterial pCO_2 at bedside reliably. Further, the amount required to measure pCO_2 is only 0.1 ml, the time required is extremely short (<90 secs.). Multiple measurements can be done in the NICU using a single electrode. This technique can be of significant value in emergencies and critically ill patients to measure pCO_2 reliably and rapidly.

● **657** WHAT DIAGNOSIS DOES NOT TELL: THE CASE FOR A NON-CATEGORICAL APPROACH TO CHRONIC PHYSICAL ILLNESS. Ruth E. Stein and Dorothy J. Jessop (Spon. by Michael I. Cohen). Albert Einstein College of Medicine, Department of Pediatrics, Bronx, NY

The assumption that clinical diagnoses provide substantial information regarding the sequelae and treatment of chronic physical illness is based on the belief that great similarity exists among children with a particular diagnostic label. This hypothesis was tested using data collected at enrollment in a study of 209 children with diverse chronic physical illness. Data were analyzed on the child's functional status, impact of chronic illness on the family, child's and mother's psychological adjustment, utilization of services, satisfaction with care, unmet health needs of the child and other family members, a health care professional's assessment of the burden of illness, and an inventory of psychological and social resources for coping with the illness. These variables were remarkably similar for children with asthma, myelodysplastic disease, hemoglobinopathies, hydrocephalus, and seizure disorders. Differences exist on only 6 of 42 scales. Analysis of the data by body systems associated with traditional subspecialty designations revealed similar findings. In general the variability was far greater within than between disease categories. This suggests that children and families faced with a given condition do not as a group have a characteristic profile. These data underscore the need for individual assessment of variables relevant to the management of chronic childhood illness and support the legitimacy of a non-categorical approach for children with ongoing physical problems.

658 FEEDING AND STOOLING PATTERNS OF BREAST-FED AND FORMULA-FED INFANTS DURING THE FIRST MONTH OF LIFE. W. Daniel Williamson, Geraldine S. Wilson, D. LaRue. Baylor College of Medicine, Dept. of Pediatrics, Houston.

Data comparing feeding and stooling patterns of breast-fed and formula-fed infants are not readily available in the literature. To provide such data, mothers of healthy, full-term infants (30 breast-fed, 12 bottle-fed) maintained diaries, recording each feeding and each episode of spitting and vomiting. Each stool was to be recorded, and the type of stool (formed, pasty, mucus or liquid) was to be noted. Diaries were maintained from nursery discharge to 1 month examination. (Statistical analysis was by Student's t-test or Fisher exact test. two-tailed significance level.) Formula-fed infants were found to have fewer stools/day (2.5±1.5 vs. 3.5±1.4, $p<.05$) and their stools were usually either pasty (62.5%) or firm (25.5%). Although 50.9% of the breast-fed infants' stools were described as liquid, nearly the same proportion (44%) were described as pasty. The consistency of stools was more variable for formula-fed infants than for breast-fed infants. Three or four different stool types were reported for 75% of the formula-fed infants while only 16% of breast-fed infants had more than 2 different stool types. ($p<.001$). Formula-fed infants were more likely to vomit (58% vs. 13% breast-fed, $p<.01$) and to experience greater number of episodes of vomiting/day. (.199±.14 vs. .113±.05, $p<.05$). They also tended to feed fewer times/day (6.7±.95 vs. 7.5±1.7) but this difference did not reach statistical significance.

● **659** HEMATOCRIT STATUS IN WHITE, BLACK AND AMERICAN INDIAN CHILDREN WITH COMPARABLE IRON NUTRITION. Ray Yip, Amos S Deinard and Samuel Schwartz. Dept of Pediatrics and Medicine, University of Minnesota, Minneapolis, Minnesota

Findings from several large scale nutrition surveys in U.S. have found blacks have lower Hgb or Hct values than white (up to 2.6% in Hct), which leads to the suggestion of separate diagnostic criteria of anemia for blacks. In current study, using the case control method, 425 black and 164 American Indian children were matched with equal number of white children for sex, age, and iron nutrition status based on serum ferritin to compare Hct. Black children have a mean Hct 0.7% lower than that of white, matched controls ($p < 0.001$), but no difference exists between American Indian children and their white controls. This finding is consistent with previous series except the magnitude of the Hct difference is the smallest reported. The lower Hct in black children can mostly be accounted for by the calculated incidence of heterozygus hemoglobinopathies which have lower Hct values than normal blacks, i.e. thalassemia trait and sickle cell trait. Since the hemoglobin limiting condition only exists in a subset of black population which resulted in a slight but significant lowering effect on Hgb or Hct for the entire group, the use of the same diagnostic criteria of anemia for all races will enable a uniform detection of nutrition anemia as well as greater diagnostic rate of hereditary hemoglobinopathies. In the case of a black child found anemic, the possibility of factors other than iron deficiency should be considered, especially if there is no significant Hgb or Hct response after a trial course of oral iron therapy.

● **660** HEIGHT AND WEIGHT STATUS OF INDOCHINESE REFUGEE CHILDREN IN COMPARISON WITH U.S. REFERENCE STANDARDS. Ray Yip, Karen N Olness, Austin Indritz and Eric Torjesen (sponsored by P.R. Dallman), Minneapolis Children's Health Center, Minneapolis, MN.

Members of medical team collected height (ht) and weight (wt) measurements from 1,650 children under 12 years of age in Laotian and Cambodian refugee camps and in surrounding villages in Thailand. These ht and wt measurements were transformed to age-specific standard deviation (SD) values based on the U.S. reference data from the 1st Health and Nutrition Examination Survey (1971-74). The mean values and percentages of refugee and Thai children whose measurements fell below -2SD value (the 2.5th percentile) of U.S. reference are listed.

	mean as U.S. SD value			% with values below -2SD		
	Ht/Age	Wt/Age	Wt/Ht	Ht/Age	Wt/Age	Wt/Ht
Laotian (450)	-1.7	-2.2	-1.0	41.3	55.8	30.0
Cambodian (761)	-2.1	-1.7	-0.7	41.7	40.6	11.6
Thai (409)	-2.3	-2.0	-0.7	58.2	44.7	17.1
All (1,650)	-2.0	-1.9	-0.8	45.7	45.8	18.0

The refugee and rural Thai children had similar anthopometric measurements suggesting that their geographic and socioeconomic background is a major factor in the lower ht and wt of the refugee children. This contention is supported by existing growth reference data from Thailand and China which are approximately 1.5 SD lower than the U.S. reference. In evaluating the growth status of Indochinese refugee children against U.S. reference standards, one needs to take into account the lower ht and wt that is characteristic of Southeast Asians. Significant portion of refugee and rural Thai children have subnormal wt/ht ratio which is a more helpful index of undernutrition for these populations.

GENETICS

● **661** CLINICAL MANIFESTATIONS OF INFECTION AND BLEEDING IN GLYCOGENOSIS Ib. D.R. Ambruso, E.R. McCabe, Univ. of Colo. Health Sci. Ctr. Denver; D.C. Anderson, A. Beaudet and D. Mahoney, Baylor Coll. of Med., Houston; I. Brandt, Ind. Univ. Sch. of Med., Indianapolis; J. Keating and B. Brown, Washington U. Sch. Med., St. Louis; R. Matalon, Univ. Ill. Sch. Med., Chicago and T. Roe, USC Sch. of Med., Los Angeles (Spon. by William E. Hathaway).

The initial presentation and clinical course were reviewed in nine patients with glycogenosis Ib. Eight of 9 had a significant incidence of infections including sepsis (in 2 patients), pneumonia (4), abscesses (4), wound infections (2), generalized pyoderma (2), recurrent otitis media (8), periorbital cellulitis (1), and osteomyelitis (1). Oral and anal mucosal ulcers unrelated to the degree of neutropenia were a significant problem in 5/9. S. Aureus and streptococcus were most frequently isolated, but Proteus, E. coli and Pseudomonas were also cultured from infected sites. Eight of 9 subjects exhibited neutrophil counts <1500/cu mm^3. However, seven patients were documented to have normal neutrophil counts during some episodes of infection. Abnormal chemotaxis was found in 5/5 and adherence was decreased in 2/2. Bone marrow examinations were performed in 7 patients, with one reported as normal, 4 demonstrating myeloid hyperplasia and 3 showing a myeloid maturation arrest at various stages of development. Five patients exhibited excessive epistaxis or bleeding from surgical sites. Although all patients had normal platelet counts, bleeding times were abnormal in 3 who were studied. Patients with glycogenosis Ib exhibit an increased incidence of infections and bleeding. Further studies of neutrophils and platelets from these patients will increase our understanding of the metabolic basis for function of these cells in host defense and hemostasis.

● **662** β-THALASSEMIA: DIRECT DETECTION OF MUTATIONS BY RESTRICTION ANALYSIS AND FREQUENCY OF GENETIC COMPOUNDS. Stylianos E .Antonarakis, Stuart H. Orkin, Haig H. Kazazian, Sabra C. Goff, Corinne D. Boehm, Julianne P. Sexton, and Pamela G. Waber, Dept. of Ped., Johns Hopkins Sch. Med. and Harvard Med. Sch. Baltimore and Boston.

We have found a correlation between specific β-thalassemia mutations and haplotypes obtained from seven polymorphic restriction sites in the β-globin gene cluster. Seven different mutations have been identified among 45 Italian β-thal genes; 6 of these were found among 42 Greek β-thal genes. An 8th mutation was found among 4 Turkish genes, and probably 4 new β-thal genes were present among 29 Asian Indian genes. Of the 120 β-thal genes 22 (18%) could be detected directly because either a) the mutation altered a restriction site [HphI (8), RsaI (5), and AvrII (1)] b) the mutation is a deletion (8). The mutation has been identified by DNA sequencing or restriction analysis in 35/122 (29%) of β-thal genes studied. The high correlation between specific polymorphism haplotypes and β-thal mutations allows estimation of the frequency of genetic compounds in affected individuals. Genetic compounds comprise about 85% of Italians and 50% of Greeks and Asian Indians with β-thal. In our sample of 66 affected individuals there are 29 combinations of β-thal genes producing the disease. These data indicate that genetic heterogeneity is prevalent in β-thal leading to a high frequency of genetic compounds in affected individuals, and that prenatal diagnosis of β-thal will usually rely upon linkage analysis of polymorphic restriction sites rather than direct detection of the mutations involved.

Withdrawn Prior to Publication

● **664** GLYCEROL KINASE DEFICIENCY: A X-LINKED DISORDER ASSOCIATED WITH ADRENAL HYPOPLASIA. James A. Bartley, Debra Miller, Univ. of Iowa, Dept. of Peds., Iowa City, Iowa and Edward R. B. McCabe, Univ. of Colorado, School of Medicine, Dept. of Peds., Denver, Colorado. (Spon. by E.Clark)

Glycerol kinase (GK) deficiency has been documented in eight individuals from four families. Hyperglycerolemia and glyceroluria are present in all. Seven of eight GK deficient individuals are males. Pedigree analysis in the family reported by Rose and Haines (J. of Clin. Invest. 61, 163-170, 1978) as well as in the family reported here support X-linked inheritance. This family includes an affected girl (karyotype 46,XX) and boy who are step-first cousins (their mothers are maternal half-sisters). These two patients in addition to the two reported by Guggenheim et al. (Annals of Neurol. 7, 441-449, 1980) exhibit adrenal insufficiency, documented by pathological observation of adrenal hypoplasia in two and by functional testing of glucocorticoid and mineralcorticoid responses in two. The girl died of brain death following hypoglycemia at six months of age. Her fibroblasts have markedly diminished oxidation of C^{14}-glycerol to C^{14}-carbon dioxide (ca. 3% of controls) and a deficiency of GK activity (ca. 6% of controls). These findings are consistent with close linkage of the loci for GK and adrenal hypoplasia on the X-chromosome, but do not rule out the possibility of an etiologic relationship between these associated observations with phenotypic and/or genotypic variability explaining the clinically different families.

● **665** CONSTRUCTION AND SCREENING OF A HUMAN LIVER cDNA LIBRARY, Arthur L. Beaudet, Karla J. Matteson, Tsung-Sheng Su, Charles D. Wendt, and William E. O'Brien, Baylor College of Medicine, Departments of Pediatrics and Cell Biology, Houston.

We have prepared a cDNA library from poly(A)$^+$RNA derived from human liver obtained at surgery. The cDNA was inserted into the PstI site of pBR322 using GC tailing. Recombinants were screened using plasmid selection of mRNA isolated from human or baboon liver, followed by in vitro translation, immunoprecipitation and analysis by SDS gel electrophoresis. As many as 10 recombinants were screened on a single DBM filter disk, and as many as 10 antisera were pooled at the immunoprecipitation step, so that a single lane on SDS gel analysis could represent up to 100 tests. Positive signals were retested with individual recombinants and antibodies to identify each specific cDNA. Studies to date have included antibodies against argininosuccinate synthetase, argininosuccinate lyase, arginase, α_1-antitrypsin, albumin, antichymotrypsin, α_2-HS-glycoprotein, antithrombin III, gC-globulin and apolipoproteins A-I, B and E. After screening 400 recombinants, we have identified the following cDNA clones: >20 for albumin, >8 for α_1-antitrypsin and 4 for apolipoprotein A-I. Identification rests solely on the antibody specificity at the present time. This library should be of general use for isolation of cDNA clones for moderately abundant human liver gene products for which antibodies are available. The α_1-antitrypsin cDNA clones are being used to search for DNA polymorphisms which would be useful for prenatal diagnosis of α_1-antitrypsin deficiency.

● **666** MUCOLIPIDOSIS IV (ML IV): DEFICIENCY OF GANGLIOSIDE NEURAMINIDASE ACTIVITY TOWARD SIALIC ACID-GALACTOSE BUT NOT SIALIC ACID-SIALIC ACID LINKAGES. Yoav Ben-Yoseph and Henry L. Nadler. Wayne State University School of Medicine, Department of Pediatrics, Detroit.

The specificity of ganglioside neuraminidase was examined in fibroblasts from patients with ML IV, their heterozygous parents and controls using mono- (GM_1), di- (GD_{1a} & GD_{1b}) and tri- (GT_1) sialo gangliosides radio-labelled in C_7 and C_8 analogs of their sialic acid residues. The release of sialic acid from all four gangliosides was reduced in the patients fibroblasts (9-34% of control activity) and intermediate levels were found in cells from the obligate heterozygotes (56-74% of control activity). However, the activity in the patients fibroblasts toward GM_1 and GD_{1a} gangliosides which contain only sialic acid linked to galactose was more depressed than the activity toward GD_{1b} and GT_1 gangliosides which contain an additional linkage of sialic acid to sialic acid. Analysis of the reaction products of cell preparations incubated with the various substrates have shown that control fibroblasts catabolized GT_1 ganglioside mainly via GD_{1b} ganglioside, presumably by cleaving first a sialic acid-galactose linkage. In contrast, cell preparations from patients with ML IV converted GT_1 ganglioside mostly into GD_{1a} ganglioside by cleavage of a sialic acid-sialic acid linkage. The apparent K_m values for neuraminidase activities toward GM_1 and GD_{1a} gangliosides were found to be 15-20 times higher in ML IV fibroblasts as compared to those of controls. ML IV appears to be a ganglioside sialidosis due to catalytically defective, sialic acid-galactose specific, ganglioside neuraminidase.

667 MONOCLONAL ANTIBODIES TO THE CYSTIC FIBROSIS (CF) FACTOR AND ITS NORMAL COUNTERPART. Miriam G. Blitzer and Emmanuel Shapira. Tulane Univ. Sch. of Med. The Hayward Genetics Center. Depts. of Peds. and Path. New Orleans.

We recently described the purification of a glycopeptide with molecular weight of approximately 5000 from sera of controls and CF patients. Both appeared to be very similar structurally. The purified glycopeptide from CF patients showed marked ciliary dyskinetic activity, whereas its "normal counterpart" had no apparent biological activity on rabbit tracheal explants. (Pediat. Res 16, March, 1982). In the present study the immunogenic and antigenic properties of the CF glycopeptide and its normal counterpart were compared. BALB/c mice were immunized with one of the glycopeptides and their spleen cells fused with X63NS1/1-Ag-4(NS1) mouse myeloma cells. Six hybridization experiments (3 with each glycopeptide) were performed in which different plating methods and screening assays were evaluated. Although an identical immunization procedure was used, 53 hybridoma cultures producing specific antibodies to the control glycopeptide and only 11 producing antibodies to the CF glycopeptide were obtained. The antibodies from these cloned hybridomas were used to compare serum fractions from controls and CF patients (10 samples in each group). Indistinguishable immunological reactivity (antigenicity) between the controls and CF patients was demonstrated. These findings indicate that, although the CF glycopeptide and its normal counterpart differed markedly in their ciliary dyskinetic activity and in their immunogenicity, they revealed both structural and antigenic similarity.

668 GENE DOSAGE EFFECT FOR PHOSPHORIBOSYLGLYCINEAMIDE SYNTHETASE (GARS) IN A PATIENT WITH DOWN SYNDROME AND NON-ROBERTSONIAN t(21;21) TRANSLOCATION. Cynthia M. Bradley, David M. Cox, David Patterson, and Arthur Robinson. National Jewish Hospital and Research Center, University of Colorado School of Medicine, and Eleanor Roosevelt Institute for Cancer Research, Denver.

The genes for two enzymes involved in separate steps in the purine biosynthetic pathway are on chromosome 21, although the locus of the genes is not fully defined. Cytogenetic and biochemical studies on a family with an unusual translocation of chromosome 21 have provided further information on localization of the GARS locus on chromosome 21. The proband was referred for chromosome analysis to confirm the diagnosis of Down syndrome and was found to have one normal chromosome 21 and a structurally abnormal sub-metacentric chromosome interpreted as a t(21;21) non-Robertsonian translocation, resulting in partial trisomy of chromosome 21q. She was also mosaic for a minute dot-like marker. Cytogenetic studies on the phenotypically normal mother and sibling revealed 47 chromosomes with a small supernumerary bisatellited marker chromosome in addition to the normal karyotype. Cell free extracts from sonicated fibroblasts cultured from the proband and her mother were assayed for GARS activity. The proband's cells had approximately twice the activity of the mother's cells, a result consistent with a gene dosage effect. These results provide evidence that the locus of GARS is closely linked to the genes required for the expression of Down syndrome and is on the segment of the long arm of chromosome 21 which is trisomic in this patient.

669 PARTIAL LIPODYSTROPHY (PL), MESANGIOPROLIFERATIVE GLOMERULONEPHRITIS (MPGN), AND CHROMOSOME ABNORMALITY (8p-). P. Brenholz, L.R. Shapiro, I. Sagel, P.A. Duncan, and P.L. Wilmot. New York Medical College, Westchester County Medical Center, and Letchworth Village, Thiells, New York

Three patients with PL have been evaluated and one of them also had MPGN associated with a 46,XX,del 8 (p21) chromosome constitution. Chromosome abnormality with PL and MPGN has not been previously reported. The few patients with 8p- syndrome in the literature may have been too young to exhibit the findings of PL at the time of reporting.

According to the human gene map, the fibronectin (FN) gene is located on chromosome 8. FN is a cell surface glycoprotein which is found on many normal cells including mesangium. In MPGN, FN is found in excess and C3 complement deposits are demonstrated in the same areas of mesangium. Therefore, the association of 8p- syndrome with PL and MPGN indicates the possibility of a genetically determined abnormal FN production. This may explain the occurrence of MPGN as a result of C3 complement binding to an abnormal FN causing dense deposit disease. An alternate explanation is that the genes for FN and PL are closely linked.

Patients with 8p- syndrome should be followed for possible development of partial lipodystrophy and renal disease because of the probable genetic mechanisms.

670 GENETIC ASPECTS OF THE SPONTANEOUS DIABETIC SYNDROME IN THE RAT. E Colle, RD Guttmann, TA Seemayer. McGill Univ, Mtl Child Hosp & Royal Victoria Hosp, Montreal.

The BB rat spontaneously develops a diabetic syndrome (DM) with hyperglycemia, insulinopenia, and a pancreatic lymphocytic infiltration (PLI) of islets with B-cell destruction. Litter mates may have PLI which involves islets or which occurs only as foci within acinar tissue and around small ducts. 120 control inbred rats did not show this PLI. To investigate the genetics of the syndrome and its relationship to the major histocompatibility complex of the rat, RT1, we crossed BB rats (RT1 u/u) with inbred Lewis (RT1 l/l) or Wistar-Fruth (RT1 u/u) rats. PLI was seen in 13-25% of progeny from both crosses in the F1. In the (Lew x BB) cross, PLI was seen in all three possible genotypes but was more common in animals with 1 RT1 u haplotype derived from the BB. (Odds ratio = 3.8, $p < .05$). Overt insulin-dependent DM occurred only in progeny of the (Lew x BB) in the F2 and subsequent generations. DM and/or PLI was present in at least one parents and some siblings of all DM rats. No RT1 l/l rat developed DM. DM was more common in rats who were RT1 u/u than in those who were RT1 u/l (Odds ratio = 4.0, $p < .05$). The data are compatible with a multigene model in which the susceptibility to PLI is inherited in a dominant fashion. This susceptibility is a necessary but not sufficient component of the diabetic syndrome. Gene products of the RT1 or of genes linked to the RT1 appear to modify expression of the susceptibility. The requirement of other genes is not excluded. This model is similar to human DM which is also associated with gene(s) of the human major histocompatibility complex, HLA.

671 ASSIGNMENT OF THE MOUSE METALLOTHIONEIN 1 GENE (Mt-1) TO CHROMOSOME 8: IMPLICATIONS FOR HUMAN MENKE'S DISEASE. David R. Cox and Richard D. Palmiter, (Spon. by Charles J. Epstein), Department of Pediatrics, University of California, San Francisco, California and Department of Biochemistry, University of Washington, Seattle, Washington.

We have used 16 Chinese hamster x mouse somatic cell hybrid clones to assign Mt-1 to mouse chromosome 8. Mouse MT-1 mRNA was measured by solution hybridization using a cloned mouse MT-1 DNA probe and conditions such that hamster MT mRNA did not hybridize with the probe. Mouse MT-1 mRNA segregated concordantly with mouse glutathione reductase, an enzyme marker for mouse chromosome 8, but showed discordant segregation with enzyme markers for 15 other mouse chromosomes. Karyotype analysis of 8 informative hybrid clones, combined with Southern blot analysis of DNA from these clones, confirmed the assignment of mouse Mt-1 to chromosome 8. Menke's disease (MD) in man and the mottled (Mo) mutation in the mouse, which provides an animal model of MD, are both X-linked degenerative neurologic disorders thought to result from abnormal copper homeostasis. Since abnormal accumulation of copper is associated with an increased amount of metallothionein in both MD and Mo fibroblasts, it has been suggested that MD and Mo are due to a metallothionein gene mutation. Our result demonstrates that a mutation in the mouse MT-1 structural gene or a closely linked regulatory gene is not the primary defect in Mo, and implies that an Mt-1 mutation is not the genetic defect in human MD.

672 MOUSE TRISOMY 16 AS AN ANIMAL MODEL OF DOWN SYNDROME: FORMATION OF VIABLE ADULT TRISOMY 16 ↔ DIPLOID CHIMERAS. David R. Cox, Sandra A. Smith, Teodosia Zamora, Lois B. Epstein, and Charles J. Epstein, Department of Pediatrics, University of California, San Francisco, California.

We have previously shown that three genes assigned to human chromosome 21 are also linked in the mouse and map to mouse chromosome 16. These results suggest that mice trisomic for chromosome 16 may provide an animal model of human trisomy 21 (Down syndrome). Since trisomy 16 mice die before birth, we have aggregated trisomy 16 (Ts16) embryos with diploid (2n) embryos at the 8-16 cell stage to generate viable chimeric mice with cells trisomic for chromosome 16. We have produced nine trisomy 16 ↔ diploid chimeras: five of these Ts16 chimeras were in a group of fetuses sacrificed at 18 days of gestation and four were liveborn. All of the analyzed organs from the Ts16 chimeras, including brain, liver, muscle, kidney, lung, heart, thymus, blood and bone marrow, contained Ts16 and 2n cells. The proportion of Ts16 cells in each organ, as estimated from coat color, enzyme markers, and/or karyotype, ranged from 5-70%, most commonly 20-40%. Of the liveborn Ts16 chimeras, the oldest of which is now 6 months old, two appeared normal, one had unilateral anopthalmos, and one was severely growth retarded. One of the Ts16 chimeras sacrificed at day 18 of gestation had the phenotype of a non-chimeric Ts16 fetus. Our results indicate that it is feasible to generate viable adult trisomy 16 ↔ diploid chimeras which can be used to study the mechanisms by which trisomy 21 in man produces abnormalities of development and function.

● **673** CITRULLINEMIA: PRENATAL DIAGNOSIS OF AN AFFECTED FETUS. Lynn D. Fleisher, Cathy J. Harris, Deborah A. Mitchell, & Henry L. Nadler. Wayne State U. School of Medicine, Dept. of Pediatrics, Detroit, MI and Northwestern U. School of Medicine, Children's Memorial Hospital, Chicago, IL.

Argininosuccinic acid synthetase (ASAS) deficiency, the basic defect in citrullinemia, can be diagnosed in cultured skin fibroblasts. Several laboratories have had difficulties in measuring this enzyme in cultured amniotic fluid (AF) cells due to low and variable activity. We have reported that strict control of tissue culture variables, especially the type of AF cell used and the degree of confluence of at-risk and control cultures, allowed us to diagnose an unaffected at-risk fetus. We have now diagnosed an affected fetus and confirmed this diagnosis after termination of the pregnancy. ASAS activity in cultured AF cells from the fetus at-risk, as measured by ^{14}C citrulline/^{3}H leucine uptake into TCA-precipitable protein,was less than 2% of control epithelioid AF cells (at-risk cells = 0.001, control epithelioid = 0.08 ± 0.04, control fibroblastic = 0.48 ± 0.28). In addition, an increased concentration of citrulline was found in the at-risk AF (0.14 μmoles/ml) as compared to AF from 6 controls and 1 at-risk unaffected pregnancy (trace). The in utero diagnosis was confirmed by assay of ASAS activity in cultured fetal skin fibroblasts (4.4% of control activity). In addition, all 5 fetal tissues studied had significant accumulation of citrulline, whereas control fetal tissues had none. Thus, citrullinemia can be diagnosed in utero if precise control is maintained over tissue culture variables, and the determination of AF citrulline provides important adjunctive evidence of an affected fetus.

● **674** DEFECTIVE CYSTINE EFFLUX FROM LYSOSOME-RICH FRACTIONS OF CYSTINOTIC LEUKOCYTES. W.A. Gahl, F. Tietze, N. Bashan, and J. D. Schulman, NICHD, NIH, Bethesda, MD.

Exposure of intact normal leukocytes to 0.25 mM ^{35}S-cystine dimethyl ester results in intralysosomal ester hydrolysis and mean free cystine accumulation to 2 times the endogenous level of cystinotic leukocytes. Loaded normal and cystinotic lysosome-rich granular fractions (GF) were incubated in 0.25 M sucrose-HEPES, pH 7.0, at 37°C under conditions where lysosomal integrity, assessed by latency of hexosaminidase, was substantially preserved. Serial aliquots were washed, treated with 10 mM N-ethyl maleimide (NEM), and ^{35}S-cystine and ^{35}S-cysteine-NEM analyzed by high-voltage electrophoresis. Half-times (T/2) for ^{35}S-cystine loss from loaded cystinotic GF (80.8 min ± 10.7 SEM, N=12) were much slower ($p < 0.001$) than normal (26.1 ± 1.4, N=13), with heterozygote T/2 intermediate (43.5 ± 3.1, N=8). In contrast, for ^{35}S-cysteine disposal mean cystinotic T/2 was 18.3 min ± 0.9, heterozygote 16.9 ± 0.5, and normal 14.1 ± 0.7. Rate of disposal of ^{3}H-tryptophan (T/2 ~ 27 min) and ^{3}H-methionine (T/2 ~ 18 min) from loaded cystinotic GF was normal. Loading with unlabelled cystine dimethyl ester and serial assay of GF cystine verified that cystinotic GF fail to dispose of cystine. Loss of cystine from normal GF was quantitatively accounted for by cystine recovered in the efflux medium. In preliminary studies, cystine efflux was unchanged by 1 mM NEM, suggesting that its efflux from normal lysosomes may not be mediated by an SH-dependent process nor by prior reduction to cysteine. We conclude that isolated cystinotic lysosomes demonstrate a selective defect in the efflux of cystine, but not of other amino acids examined.

● **675** PERICENTRIC INVERSION OF CHROMOSOME 11 IN A BOY WITH ABNORMAL GENITALIA AND POSSIBLE AUTISM. Lytt I. Gardner, Robert A. Richman, Ernest M. Post, Lawrence P. Gordon, Douglas P. Kalinowski, and Karen J. Sanders. SUNY Upstate Medical Center, Departments of Pediatrics and Pathology, Syracuse, New York.

A thirteen year old white male was noted at birth to have a perineal hypospadias, testes in the inguinal canal, and a bifid scrotum. When evaluated for possible autism at age 4 1/2 years, he was poorly responsive to affection, preoccupied with mechanical objects and lacked expressive verbal skills. At present, he has Tanner stage 4 pubic hair. His penis measures 8 x 2 cm and testes are 11 ml bilaterally. He is considered to have neurologically impaired speech.

Karyotype of peripheral leukocytes was 46,XY, inv(11)(p11q25). Breakage and reunion occurred at band p11 in the short arm and at q25 in the long arm of chromosome 11. The segment lying between these bands was inverted. There was no visible evidence of duplication-deletion recombination with GTG banding. We have found no previous report of abnormal clinical findings in patients with balanced pericentric inversions of chromosome 11 (J Med Genet 17:44, 1980). Position effect related to the inverted segment could explain the clinical abnormalities. This has been postulated in balanced translocations associated with deficits in language acquisition (AJDC 133:1002, 1979). It is also of interest that the interstitial deletion of 11p associated with the aniridia-ambiguous genitalia -mental retardation (AGR) triad (often with Wilms' tumor) is just distal to the present patient's 11p11 break point.

● **676** HYPERGLYCEROLEMIA SECONDARY TO GLYCEROL KINASE DEFICIENCY IN A CHILD WITHOUT NEUROLOGIC DEFICITS. Edward I. Ginns,[1] John A. Barranger,[1] Sharon W. McClean,[1] Ernst Schaefer,[1] Roscoe O. Brady,[1] Richard Young, Stephen I. Goodman[2] and Edward R. B. McCabe[2]. [1]National Institutes of Health, Bethesda, MD. 20205 and [2] Department of Pediatrics, University of Colorado School of Medicine, Denver, Colorado 80262.

This report describes a 7 year old boy with a 3 year history of recurrent episodes of vomiting, acidosis, and coma. Although electroencephalograms at ages 5 and 7 years showed generalized paroxysmal polyspike discharges, no seizure activity has ever been noted. In marked contrast to the clinical histories of previously reported children with glycerol kinase deficiency, the patient's neurologic exam is normal and his Stanford-Binet intelligence scale IQ is 122. Since beginning a low fat diet, no episodes of coma have occurred. Family history is significant for migraine, hypertension and myocardial infarction.

The patient's serum cholesterol, triglyceride, HDL, LDL, VLDL, and apolipoprotein levels (APOA-I, APOA-II, APO-B, and APO-CII) were within normal limits, but serum acid phosphatase was elevated.

Radiochemical assay of skin fibroblast glycerol kinase activity showed the patient's level to be less than 5% of control value. Urine glycerol is markedly elevated. The serum glycerol level of the patient ranges between 30-40 mg/dl, while those of the parents and two younger sibs are within normal limits.

677 A DOUBLE DOSE OF CHROMOSOME REGION Xp22.3 IS NEEDED FOR NORMAL GROWTH IN FEMALES, Wendy L. Golden, Sharon L. Wenger, Dorothy J. Becker and Mark W. Steele, Children's Hospital of Pittsburgh, PA.

The pt. is an 8½ year old white female who weighed 2100 grams when born after a 36 week normal gestation. An occipital encephalocele was repaired at age 2 days; congenital dislocation of both hips was corrected at age 5 mos. The pt's. height and bone age have always measured more than 3 SD below the mean for age. At age 7½ years endocrine workup evaluated thyroid and growth hormones, somatomedin, FSH & LH and all were normal. IQ by Stanford Binet was 70. Other findings were flat nasal bridge, dry facial skin, grade II systolic ejection murmur (with normal peripheral pulses), short 4th & 5th metacarpal bones bilaterally on X-ray. There were no other stigma of Turner's Syndrome. The presence of bilateral Babinskis and poor fine motor coordination suggest that the mental retardation may be a sequelae of the congenital encephalocele. The pt's. parents and female sibling appeared normal.

Chromosome studies on cultured lymphocytes revealed del(Xp22.3) by G-& R-banding and prometaphase techniques in all cells examined. By BUdR technique the partially deleted X chromosome was late replicating in ten of ten cells examined. Chromosome studies of the parents and sib were normal. Xg(a) blood group family study was uninformative. Our data suggest that in females normal growth requires the presence of a double dose of Xp22.3→pter, a chromosome region known to be near at least two other gene loci (Xg & STS) which regularly escape X chromosome inactivation.

678 MS PHENOTYPE, α-1 ANTITRYPSIN DEFICIENCY (AAD) AND NEONATAL LIVER DISEASE, Glenn R. Gourley, Gerard B. Odell, Enid Gilbert, University of Wisconsin Hospitals, Departments of Pediatrics, Pathology, Madison, Wisconsin.

A 35-week, 964-gram, SGA female infant was born to a 30-year-old G_3,P_2 mother by C-section because of pre-eclampsia and suspected growth retardation. On day 2 of life, total bilirubin was 10.7 mg/dl with 0.5 mg/dl "direct." Hemolytic, infectious and metabolic workup was negative. During 8 days of phototherapy the total bilirubin peaked at 11.6 mg/dl. However, the "direct" bilirubin gradually rose to 4.5 mg/dl at 4 weeks of age. A liver biopsy on day 51 of life showed findings consistent with AAD, including PAS^{+} diastase-resistant granules in the periportal area. Electron microscopy showed dilated endoplasmic reticulum containing a granular precipitate. Peak abnormal liver function tests (LFTs) included: GGT 249 U/L (nl < 55), SGOT 73 U/L (nl < 55), serum bile salts 94.7 μM (nl < 10).

	Patient	Mom	Dad	Brother	Brother	Normal
Pi type	MS	SS	M	-	-	M
AA quant. (mg/dl)	95, 152	85, 142	185	188	168	200-400
STIC (mg/ml)	.566	.468	.702	-	-	> .7

(STIC = serum trypsin inhibitory capacity)

LFTs in all other family members were normal. The patient's LFTs were normal by 5 months of age. We are unaware of similar reports of neonatal liver disease related to AAD in patients with the MS phenotype.

● 679 GAUCHER TYPE 1 DISEASE (GD): EVIDENCE FOR MOLECULAR HETEROGENEITY. Gregory A. Grabowski, Evelyn A. Devine, Jack Goldblatt, and Robert J. Desnick, Mt. Sinai School of Medicine, NY.

The physiokinetic properties of the residual acid β-glucosidase (β-Glc) activities were characterized in cultured fibroblasts from Type 1 GD patients from six different ethnic backgrounds. Although the specific activities in all GD fibroblasts were similar (5-12% of mean normal), the apparent Km (for 4-MU-β-glucoside), thermostability (50°C), and electrophoretic (E) mobilities (cellogel) differentiated four groups of molecular defects:

Source	Km (mM)	$T_{\frac{1}{2}}$ (50°C; min)	E Mobility
Normal	2.5	20	N
Group 1			
Ashkenazi	2.5	20	+
Group 2			
Indian	4.0	9	+
Afrikaner	4.0	9	+
Group 3			
Hispanic	4.0	20	+
Cape Colored	4.0	20	+
Group 4			
American Black	7.2	20	+

These data indicate that GD in these ethnic groups result from mutations in the structural gene for β-Glc which differentially alter the kinetic (Vmax or Km), stability and/or charge of the residual activity in cultured fibroblasts. Furthermore, these studies suggest that at least 4 different mutant alleles at the β-Glc locus which result in GD.

680 FAILURE TO THRIVE - A MANIFESTATION OF KLINEFELTER SYNDROME Sue Hahm, Robert W. Marion, George Schwartz, and Harold M. Nitowsky Albert Einstein College of Medicine, Department of Pediatrics, Bronx, N.Y.

Recognition of the typical phenotype of the Klinefelter syndrome, which includes lack of normal virilization, tall stature, eunuchoid body proportions, small testes and gynecomastia, is generally delayed until the postadolescent period. We have observed two boys with failure to thrive, including delay in psychomotor development as well as somatic growth, with onset in early infancy who have a 47,XXY karyotype. Other features include microcephaly, facial dysmorphic features, including micrognathia, flat nasal bridge, large and prominent ears, and biochemical abnormalities consistent with mild renal tubular acidosis in one child. Review of the literature reveals scattered reports of failure to thrive and/or renal tubular acidosis in boys with a 47,XXY karyotype. Although these may reflect chance associations, their frequency suggests that a subset of patients with Klinefelter syndrome can present with failure to thrive as a major manifestation.

● 681 PARTIAL TRISOMY 4p IN A FAMILY WITH A PREVIOUSLY UNDESCRIBED INTERSTITIAL TRANSLOCATION INVOLVING CHROMOSOMES 1 AND 4. H. Eugene Hoyme, Elizabeth F. Allen, and J. Ward Stackpole (Spon. by R. James McKay, Jr.). The Vermont Regional Genetics Center and The University of Vermont College of Medicine, Departments of Pediatrics and Pathology, Burlington, Vermont.

We have recently evaluated two siblings with minor dysmorphic features, including prenatal onset growth deficiency, microcephaly, short palpebral fissures, and hallux valgus. Both manifest mild mental deficiency. Chromosome analysis of the family revealed that the mother was the carrier of an apparently balanced translocation between the short arms of chromosomes 1 and 4. The translocated material from the number 4 was inserted into the 1p36.1 band (46,XX,dir ins[1;4]1pter→1p36.1::4pter→4p12::1p36.1→1qter; 4p12→4qter). Her two affected children had unbalanced karyotypes due to inheritance of the abnormal maternal number 1 and the normal maternal number 4. They are effectively trisomic for the segment 4p12 to 4pter.

Review of the literature reveals few similarities between the patients herein described and those previously reported with partial trisomy 4p, raising question as to the existence of a "partial trisomy 4p syndrome." Clinical variability may be due to the differing corresponding monosomic segments in affected individuals.

● 682 A PERIPHERAL DEFECT IN BIOPTERIN SYNTHESIS: A NEW MUTANT? Stefan Hreidarsson, David Valle, Neil Holtzman, Joseph Coyle, Harvey Singer, Gregory Kapatos, and Seymour Kaufman, Johns Hopkins Hospital, Dept. of Pediat, Baltimore and National Institutes of Health, Bethesda.

A black ♀ with hyperphenylalaninemia, [plasma(pl) phenylalanine (phe)=1336 μM at d 14], had a urine neopterin(N)/biopterin(B) ratio of 85 (nl<5) with 81% of B as BH_4, suggesting a defect in B synthesis. Therapy with po BH_4 lowered pl phe and N, but was stopped when pre-tx CSF B and neurotransmittor metabolites (NT) were found to be normal. Follow-up for 5 months on lo-phe diet shows normal development. CSF B and NT have remained normal despite evidence of continued peripheral BH_4 deficiency.

	Plasma			Urine(μm/mg crt)		CSF (nM)	
	Phe(μM)	N(nM)	B(nM)	N	B	N	B
Lo-phe diet n=4	123.9 ±67.2	239.8 ±98.8	11.8 ±2.6	123.2 ±79.0	1.69 ±1.04	94.4 ±10.5	59.9 ±12.3
Po BH_4,20mg /kg, n=1-3	59.7 ±4.0	92.8 &81.0	133.1 115.8	45.3 ±19.2	57.7 ±55.5	60.1 n=1	112.7 n=1
Po phe,2 mo 100mg/kgx3d	1421.0	975.7	9.5	340.5	2.02	-	-
Po phe,5 mo 100mg/kgx3d	716.0	479.9	6.7	362.9	2.63	-	-
Normal	25-81	32 + 3.6	5.4+ 2.1	25.5+ 11.7	19.6+ 5.6	20-237	12.3-59

Conclusions: This child has adequate CNS BH_4 despite a persistant peripheral defect in N B and, at this age, is unlike previously described B deficient patients. Oral BH_4 increased CSF BH_4 and depressed N levels.

● 683 A SPECIFIC DEFICIENCY OF GLUTARYL-CoA DEHYDROGENASE ACTIVITY IN GLUTARIC ACIDURIA TYPE I (GA). D. Hyman and K. Tanaka; (Intr. by L.E. Rosenberg). Yale University School of Medicine, New Haven, CT.

Patients with GA have greatly increased urinary excretion of glutarate. Their leukocyte and fibroblast sonicates have deficient ability to produce $^{14}CO_2$ from [1,5-^{14}C]glutaryl-CoA, a method which measures the activity of two sequential reactions, dehydrogenation to glutaconyl-CoA, and its decarboxylation. Since GA patients also excrete urinary 3-hydroxyglucarate and glutaconate, it was thought that the glutaryl-CoA dehydrogenase (GDH) activity was normal and the decarboxylase activity deficient. We developed a new assay specific for GDH which measures enzymatic tritium release from [2,3,4-^{3}H]glutaryl-CoA. The K_m of normal GDH for glutaryl-CoA, 5.9 μM, was similar to that reported for the $^{14}CO_2$ assay. Activity from normal fibroblast sonicates in both assays was markedly inhibited by methylenecyclopropylacetyl-CoA (a toxic metabolite of hypoglycin) which inhibits several acyl-CoA dehydrogenases; GDH inhibition was competitive with a K_i near 1 μM. Sonicates from all five GA fibroblast lines examined showed deficient GDH activity (0-15% of control) as well as deficient $^{14}CO_2$ releasing activity (0-5% of control), and all had normal activities of isovaleryl-CoA dehydrogenase. Two GA cell lines showed enzyme activities slightly higher than the other three lines, indicating possible heterogeneity. Since all five GA lines have deficient glutaryl-CoA dehydrogenating activity, urinary glutaconate and 3-hydroxyglutarate in GA patients are not produced via glutaconyl-CoA.

● 684 THE DiGEORGE SYNDROME AND CHROMOSOME 22. R.I.Kelley, E.H. Zackai, B.S.Emanuel, M. Kistenmacher, F. Greenberg, and H.H. Punnett. Children's Hospital of Philadelphia and St. Christopher's Hospital for Children, Philadelphia, Pennsylvania.

The DiGeorge syndrome (DGS) is characterized by parathyroid and thymic hypoplasia/aplasia and cardiac conotruncus or great vessel malformations, usually in patients with mild facial dysmorphia. In three of fourteen patients with DGS whom we have karyotyped (six with banding) over fifteen years we have found identical deletions of the short and proximal long arms of chromosome 22 (22pter→ q11). The remaining long arm material of chromosome 22 was translocated to a different autosome in each with break points 10q26, 3qter, and 20q11. All had classic DGS and few other anomalies despite being, respectively, partial monosomy 10q, partial monosomy 3q, and partial trisomy 20p, in addition to partial monosomy for 22. The chromosome 22 deletion in our patients appears to be identical to that reported by de la Chapelle et al. (Hum Gen 57:253, 1981) in four children with DGS in one family. Several other reported patients with partial or full monosomy for chromosome 22 have had incomplete forms of DGS. To our knowledge, no patient with complete DGS has had a chromosome rearrangement not involving chromosome 22.

Taken together, our patients and other reports suggest that a gene or deletion of genes on chromosome 22, most likely at 22q11, is responsible for some cases of DGS. Our personal experience indicates that the number of patients with DGS and partial monosomy 22 may be significant.

● 685 GERTRUDE KOHN, ELI E. LASCH and ARIEL RÖSLER. Human Genetics and Endocrinology and Metabolism, Hadassah University Hospital, Jerusalem, Israel, and Nasr Children's Hospital, Gaza.

Post-pubertal gender role reversal in male pseudohermaphroditism due to 17 β-hydroxysteroid dehydrogenase deficiency.

A highly inbred Arab kindred with male pseudohermaphroditism due to 17 β-hydroxysteroid dehydrogenase deficiency, extending over 6 generations, is presented. To date, 23 affected individuals, whose ages range from 14 months to 80 years, have been identified. Seven affected individuals were examined in detail and they and their families interviewed. Without exception, they were all raised as females until puberty. All post-puberty affected individuals virilized, had a male distribution of body hair and heavy beard, and a urogenital sinus with enlarged phallus. None had gynecomastia. Puberty was traumatic for all, behavior in school was frequently aggressive and school was often discontinued. Although this disease and its course was recognized and well known within the extended family over several generations, nevertheless, all newborn affected members continued to be raised as females. A few individuals in generations V and VI, on their own initiative and without psychiatric evaluation or help, changed gender role as young adults. Two such patients will be discussed in detail. The inheritance is most compatible with an autosomal recessive disease expressed only in affected males.

● 686 SJOGREN-LARSSON SYNDROME - PRENATAL DIAGNOSIS AND ELECTRON MICROSCOPY. Boris G. Kousseff, Lois Y. Matsuoka, Kurt S. Stenn, John C. Hobbins and Maurice J. Mahoney. Univ. of So. Fl., Tampa, FL, Southern Ill. Univ., Springfield, IL, Yale Univ., New Haven, CN. Departments of Pediatrics, Dermatology, Pathology, Obstetrics, Genetics. (Sponsored by Lewis A. Barness).

Three affected siblings with Sjogren-Larsson syndrome are reported. The eldest sister and the brother were diagnosed at 6½ years and 2½ years of age respectively. The diagnosis was based on their congenital ichthyosis, subsequent progressive spasticity and mental retardation. No environmental factors were identified to account for their symptomatology. Light microscopy of skin biopsies showed hyperkeratosis and papillated epidermal hyperplasia compatible with the syndrome. Electron microscopy revealed the rather unique picture of prominent Golgi apparatus, and increased number of mitochondria within keratinocytes. Also lamellar membranous structures were found within the cells of stratum corneum.

During the subsequent pregnancy of the mother, at 23 weeks gestation a fetoscopy with fetal skin biopsy was performed. Prominent stratum granulosum and orthokeratotic stratum spinosum with densely packed keratin suggested a hyperkeratotic state in the fetus. This was interpreted as indicating Sjogren-Larsson syndrome. The parents decided to have the child. At 34 weeks gestation a liveborn female with congenital ichthyosis but no other major abnormalities was delivered. No scars were present at the sites of the biopsy. Thus, Sjogren-Larsson syndrome became a condition for which prenatal diagnosis is possible.

● 687 MOLECULAR PATHOLOGY OF ACID α-GLUCOSIDASE DEFICIENT VARIANTS. Gundula U. LaBadie, Nicholas G. Beratis, and Kurt Hirschhorn, Mt. Sinai School of Medicine, NY

Residual enzyme in cultured skin fibroblasts from patients with various forms of acid α-glucosidase deficiency (α-GC) could be distinguisned from the normal enzyme and from each other based on their catalytic and immunologic properties. Lysates were prepared at pH 5 or 7 and enzymatic activity was determined. The lysates were subjected to rocket immunoelectrophoresis with or without maltose (M), and the immunoprecipitates were examined for qualitative and quantitative differences relative to control values.

Strain	Enzyme Activity	Enzyme Protein	Immunoreactivity pH 5 (M)	pH 5	pH 7
Control	100%	100%	+	+	+
6 Infantile (CRM-)	1-3%	-	-	-	-
1 Infantile (CRM+)	1-3%	30-50%	±	±	-
1 Juvenile	16-28%	12-28%	+	+	-
2 Adult	9-22%	16-22%	-	+	-
1 Adult (CRM-)	1-3%	-	-	-	-

The residual enzyme proteins in the juvenile and adult forms retained their catalytic properties despite the loss of antigenicity at pH 7. All the residual enzymes, including the catalytically inactive one in the juvenile form, showed normal affinity for maltose and glycogen. These studies demonstrate that the subtypes of α-GD result from a variety of mutations affecting the amount of enzyme detected as well as its catalytic, kinetic and immunologic integrity.

● 688 DISEASES OF COPPER METABOLISM: HISTOCHEMICAL STUDIES OF WILSON'S AND MENKES' DISEASE FIBROBLASTS. Hin-Ching Liu, Wai-Yee Chan and Owen M. Rennert. University of Oklahoma Health Sciences Center, Department of Pediatrics, Oklahoma City.

Wilson's disease (WD) and Menkes' disease (MD) are genetic disorders of copper metabolism. WD is caused by excessive deposition of copper in affected organs resulting in copper toxicosis while MD is caused by defective absorption and utilization resulting in copper deficiency. The genetic abnormality in these two diseases are expressed by cultured skin fibroblasts derived from the patients. Both types of fibroblast cultures demonstrate elevated accumulation of copper. To further identify the functional and morphological consequences of these abnormalities of copper metabolism histochemical studies of fibroblasts have been undertaken. MD cultured fibroblasts showed markedly reduced succinic acid dehydrogenase and amine oxidase activities. Cytochrome oxidase activity was greatly reduced in some cells and almost normal in others. WD cultured fibroblasts showed moderately reduced succinic acid dehydrogenase and cytochrome oxidase activities. Amine oxidase activity was normal when compared to controls. Cytochrome oxidase, a cuproenzyme was variably affected in either MD or WD in spite of the profound abnormality in copper metabolism. Amine oxidase activity measured in these studies included monoamine as well as diamine oxidase which is a cuproenzyme. A significant difference in amine oxidase activities between MD and WD fibroblasts further demonstrates the phenotypic difference between the mutation in these two disorders.

● 689 ASSOCIATION OF ADVANCED PARENTAL AGE WITH THE PRADER-WILLI SYNDROME. Robert W. Marion and Harold M. Nitowsky Albert Einstein College of Medicine, Department of Pediatrics, Bronx, New York

The etiology and pathogenesis of the Prader-Willi syndrome (PWS), characterized by perinatal hypotonia, developmental delay, obesity, and hypogonadism, remain obscure. In recent years, reports of various chromosome abnormalities, including an interstitial deletion of 15q in patients with PWS suggests a chromosomal basis for the disorder. However, the demonstration of a normal karyotype in a substantial proportion of PWS patients suggests etiologic heterogeneity, and possible variability in the clinical, biochemical and epidemiologic correlates of the disorder. Review of parental ages of patients with PWS seen in our clinic (n=11) and reported in the literature (n=34) compared with age and sex-matched controls reveals a significant increase in mean parental age at the time of birth of PWS patients (PWS: maternal age 31.5 ± 6.7 years, paternal age 35.2 ± 6.9 years. Controls: maternal age 27.8 ± 7.4 years and paternal age 28.3 ± 5.5 years). A plot of parental ages of all PWS patients suggests a bimodal distribution, with maternal and paternal age peaks of 26 and 34 and 30 and 38 years respectively. Parental age distribution of PWS patients with a chromosome aberration is shifted to older ages with only a single peak. Etiologic and genetic heterogeneity may account for the inconsistent finding of advanced parental age in PWS in previous reports.

● 690 6-METHYLTETRAHYDROPTERIN ($6MPH_4$) IN THE THERAPY OF A BIOPTERIN SYNTHESIS DEFECT (BSD): EFFECTS ON PHENYLALANINE (PHE) AND NEUROTRANSMITTER (NT) METABOLISM. Roderick McInnes, Seymour Kaufman, Jerry J. Warsh, Glen van Loon, Gregory Kapatos, Sheldon Milstein and Steven Soldin (Spon. by J.A. Lowden) Hosp. for Sick Children, Clarke Inst. of Psychiatry, Dept. of Int. Medicine, Toronto, and NIMH, NIH, Bethesda, MD.

We have evaluated $6MPH_4$, an economical BH_4 analogue effective with aromatic hydroxylases in vitro, in the therapy of a patient with a BSD. On an unrestricted diet (130mg phe/kg/day) $6MPH_4$ (10mg/kg IV) reduced plasma phe from 1.0 to 0.27mM in 3 hr. and 0.40mM at 18 hr. Gastric administration of $6MPH_4$ (20-38mg/kg/day) was also effective: after 11 days of unrestricted diet, plasma phe was 0.19mM. On the 11th day of this study, the $6MPH_4$ level in CSF (60.5ng/ml) was similar to the patient's CSF neopterin level (48ng/ml) and higher than the biopterin level of adult controls (18.6±12.7ng/ml,n=5) and the patient (0.59-0.81ng/ml). $6MPH_4$ did not increase CSF or plasma catecholamines or NT metabolites. NT synthesis in the patient was stimulated by $6MPH_4$, however, since increases were detected in urinary homovanillic acid (from 14 and 50 to 138 and 314μg/24 hr.), 5-hydroxyindolacetic acid (58, 64 to 100, 226μg/24 hr.) and dopamine (209, 216, 236 to 315, 346 μg/gm creatinine). These results indicate that $6MPH_4$ (1) effectively controls the hyperphenylalaninemia of BSD (2) crosses the human blood-brain barrier in the reduced state to produce significant concentrations in the CSF (3) acts as a cofactor in vivo for both tyrosine and tryptophan hydroxylase to increase NT synthesis, and therefore merits further evaluation as replacement therapy in this disease.

● **691** INTENSIVE PLASMA EXCHANGE TRANSFUSIONS IN HUNTER'S SYNDROME. R. Matalon, J.V. Murphy, K. Marquardt, K. Omura, and M. Deanching. Dept. of Peds. Univ. of Ill. Chicago and the Med. College of Wisconsin, Milwaukee.

Plasma exchange transfusion (PET) in the treatment of the mucopolysaccharidoses has been ineffective. This study involved 8 weeks of intensive PETs in order to increase the iduronosulfate sulfatase (IS) level to no less than 35% the normal IS activity. Four patients with Hunter's syndrome were given PETs. The volume of plasma infused at each PET was 50-55 ml per kg. IS activity on the donor's and patient's plasma was performed using tritium labeled disulfated disaccharide prepared following the degradation of heparin by nitrous acid. It was found that 2 PETs were needed per week. The average rise in IS activity following PET was 83.8% (± 10.4) and activity dropped to 43.8% (± 4.0) of normal prior to the next PET. After 8 weeks of PETs, liver and spleen sizes decreased on all patients, as determined by radionuclide studies. Urinary mucopolysaccharides (MPS) dropped in 1 child from 0.24 to 0.08 mg/mg creatinine but there was no significant change in the other 3 children. Liver biopsy in 2 children before and after PET indicated no significant change in MPS despite a slight increase in IS activity in 1 child following PET. These data suggest that PETs in Hunter's syndrome if performed frequently will sustain an adequate plasma IS level.

● **692** ALTERED PROFILES OF SERUM HEXOSAMINIDASE ISOZYMES IN TYPE I GAUCHER DISEASE Sachiko Nakagawa, Selma Kumin, Gay Sachs and Harold M. Nitowsky Albert Einstein College of Medicine, Department of Pediatrics, Bronx, N.Y.

Although reduced acid β-glucosidase activity (β-glu) appears to be the primary enzyme defect in Type I Gaucher disease (GD), previous studies have shown marked elevation of serum acid phosphatase (AP) in GD. We have observed striking changes in the activity and isozyme distribution of serum β-hexosaminidase (hex) in GD, and carrier testing for Tay-Sachs disease may offer a useful approach for the presumptive diagnosis of GD. The mean hex values are 772 ± 183 (nmoles 4-MU/h/ml) for 16 normals (N) 2466 ± 1037 for 6 patients with GD. Total serum hex varies considerably in GD (range: 915-4170) and the level seems to correlate with the clinical severity of the disorder. Serum AP levels are 350 ± 213 (nmoles p-nitrophenol/h/ml) in N and 3364 ± 2250 (1190-6417) in GD. There is a characteristic distribution of the hex isozymes (hex A, I, B) with a significant elevation in hex B, as summarized in Table.

	Percent of total hexosaminidase			
Subject	A	I	B	
Control (16)	77 ± 7.9	17 ± 7.0	6 ± 1.8	
Gaucher (6)	57 ± 6.4	16 ± 4.5	27 ± 4.2	$p < .001$
Juvenile Diabetes (17)	72 ± 6.1	11 ± 4.7	17 ± 4.3	
Pregnant (6)	48 ± 6.3	50 ± 6.2	2 ± 1.8	
Tay-Sachs Carrier (17)	58 ± 5.6	31 ± 5.1	11 ± 2.7	

There are no characteristic alterations of hex or AP in heterozygotes for GD.

● **693** CONGENITAL PROLIDASE DEFICIENCY IN AFFECTED SIBLINGS. Eileen R. Naughten, Susan P. Proctor, J. Thomas Coulombe, Harvey L. Levy, and Mary G. Ampola. Harvard Medical School, Massachusetts General Hospital, State Laboratory Institute, Massachusetts Department of Public Health, and Tufts-New England Medical Center, Boston.

Mendelian genetic disorders may not be recognizable at birth or even early in life, despite the presumed inborn nature of the defect. Non-recognition may result from lack of an appropriate identifying characteristic or from lack of gene expression at that time. When a biochemical marker is identified, however, the phenotype is usually found to be congenital.

Prolidase deficiency is an inherited disorder characterized by severe skin ulcers and iminodipeptiduria. Patients are diagnosed when clinical findings appear in childhood or later years. We detected prolidase deficiency in three sibs because one had iminodipeptiduria on newborn urine screening. Filter paper newborn (3 day) blood and cord blood specimens were recovered and examined for prolidase activity. No activity was detectable in newborn blood from the proband or the two older sibs. Cord blood from the proband had 6.8% of control activity, the residuum possibly enzyme passively transferred from maternal serum. Prolidase activity was detectable in control newborn blood specimens stored up to 4 years but was inversely related to duration of storage (for 9 mos. 3 yrs. and 4 yrs. activity in nmol glycine/disc/hr was respectively 463 ± 103, 142 ± 52, and 15 ± 12).

Prolidase deficiency is expressed at birth and is biochemically detectable by appropriate enzyme analysis in cord blood and newborn blood.

● **694** TRACE METAL METABOLISM IN CULTURED SKIN FIBROBLASTS OF THE MOTTLED MOUSE: RESPONSE TO METALLOTHIONEIN INDUCERS. Seymour Packman and Cynthia O'Toole. (Spon. by Charles J. Epstein). University of California, Department of Pediatrics, San Francisco.

Menkes' kinky hair syndrome is an X-linked disorder of copper (Cu) transport and utilization. An animal model is provided by the blotchy (blo) mouse, mutant at the X-linked mottled locus. Since the defect may reside in abnormal regulation of metallothionein or of its function, we studied the metabolism of Cu, zinc (Zn) and cadmium (Cd) in fibroblasts of the blo mouse. Mutant cells rapidly accumulate added ^{64}Cu to a level 10-fold higher than normal. While the kinetcs of ^{64}Cu uptake are equivalent in mutants and controls, efflux of Cu in mutant cells is impaired. In contrast, the kinetics of ^{65}Zn and ^{109}Cd accumulation are not distinguishible in normal and mutant. ^{64}Cu accumulation was measured in cells exposed to Cd and Zn. In controls there was a 2-3 fold increase in ^{64}Cu accumulation in the presence of Cd, while mutant cells showed no change over baseline mutant levels. A similar qualitative difference was seen between control and mutant cells upon exposure to Zn. Exposure of both cell types to Cd effected no change in ^{65}Zn accumulation. We conclude that the defect in blo cells affects specifically the function of a Cu storage or transport protein, with the metabolism of Zn and Cd unaffected. The differential response of normal and control cells to inducers of metallothionein may be secondary to aberrant function of that specific Cu storage or transport protein, or may reflect altered regulation of a specific Cu thionein.

● **695** MAPPING OF α_1-ANTITRYPSIN LOCUS (PI) TO CHROMOSOME 14 IN RAT HEPATOMA x HUMAN FETAL LIVER CELL HYBRIDS Stephen J. Pearson, Paivi Tetri and Uta Francke Yale University School of Medicine, Dept. of Human Genetics, New Haven, CT.

In order to study the involvement of human chromosomes in the expression of human liver-specific functions, we have produced somatic cell hybrids between a rat hepatocarcinoma cell line and diploid cells from a human fetal liver. The rat hepatoma line was HPRT deficient, and hybrids were selected in medium containing HAT and ouabain. The presence of human liver-specific proteins was analyzed by immunoelectrophoresis techniques applied to concentrated serum-free hybrid culture supernatants. A subset of hybrids secreted an antigen that was immunologically identical to human α_1-antitrypsin (PI). Neither parental line supernatant, nor fetal calf serum, nor normal rat serum reacted with this antiserum. We conclude that interaction of the rat hepatoma genome with that of the human fetal liver cells has activated the human PI locus. In 19 primary HAT-selected and 5 azaguanine back-selected hybrids, human PI production segregated concordantly with chromosome 14. All other chromosomes were excluded by discordant clones. Assignment of the PI gene to chromosome 14 is consistent with data of others localizing the GM immunoglobulin heavy chain gene cluster to this chromosome since family studies have established linkage between PI and GM (at 24 centimorgan with a lod score above 7).

● **696** A NEW FRENCH-CANADIAN FAMILY AFFECTED BY HYPERARGININEMIA. Ijaz A. Qureshi, Jacques Letarte, René Ouellet and Jean Larochelle. Centre de Recherche pédiatrique, Hôpital Ste-Justine, Montréal, and Hôpital de Chicoutimi, Qué.

Hyperargininemia is the rarest syndrome of the hereditary urea cycle disorders. Only seven affected families have been reported, including a French-Canadian family already described by us. We report here another unrelated French-Canadian family in which a newborn male was screened for cystinuria-lysinuria, but has been diagnosed by us recently to be affected by arginase deficiency. Enzymologic and biochemical indices were as follows:

Subject	RBC arginase activity (μmol/g Hb/h)	Plasma arginine (μmol/l)	Urinary arginine (μmol/g creat.)	Urinary orotate (mg/g creat.)
Propositus	0	633	1205	895
Father	569	169	224	1.5
Mother	661	74	199	1.7
Controls(10)	1795 ± 156*	75 ± 17	200 ± 50	1.4 ± 1.3

Both unrelated parents (obligate heterozygotes) as well as propositus showed normal plasma NH_3 values. However, high excretion of orotate in the propositus indicates disturbance in mitochondrial NH_3 metabolism. At 3 years of age, the child showed slight ataxia, normal EMG, epileptic EEG and mental slowing. These results prove that children screened for cystinuria-lysinuria should be tested for arginase deficiency as soon as possible, since early therapy may reverse the progressive neuromuscular deterioration seen in hyperargininemia. *(Mean ± SD)

697 THE INDUCTION OF SISTER CHROMATID EXCHANGES BY ETHANOL IN HUMAN LYMPHOCYTES IN VIVO. Alan L. Shanske, Andrea V. Serotkin and Ernest Lieber,(Sponsored by Philip Lanzkowsky). Sch. of Med. Health Sciences Ctr., SUNY at Stony Brook, Long Island Jewish/Hillside Medical Center and Queens Hospital Center, Dept. of Pediatrics, New Hyde Park, N. Y.

The molecular basis and biologic significance of sister chromatid exchanges (SCE's) is as yet obscure. The analysis of SCE induction has been useful in detecting mutagenic potential. SCE frequency may serve as a useful cytologic marker in the adult alcoholic and in children with the fetal alcohol syndrome (FAS). We have applied our own modification of the flourescence plus Giemsa staining technic to short term lymphocyte cultures established from adult patients admitted to our alcohol detoxification unit and children with the fetal alcohol syndrome attending our developmental clinic. Thus far, we have obtained cultures from 5 children, aged 4 months to 6 years, and 5 adult alcoholics, aged 28 to 48 years and from age and sex matched controls. The cultures were exposed to 3 mcgm/ml of BrdU to obtain chromatid differentiation. A minimum of 25 cells from each individual were scored.

The mean frequency of SCE's in PHA stimulated lymphocytes of children with FAS was 9.01/cell compared to 6.54/cell for controls. The range for patients was 3 to 18 and controls 2 to 16. The mean frequency of SCE's varied significantly ($p < 0.05$). No significant increase of SCE's was observed in our adult patients. We have applied the SCE test as a cytogenetic assay for the mutagenic effect of ethanol on cultured lymphocytes from chronically exposed patients. Preliminary data suggests a drug induced effect in children with the FAS.

698 ENHANCED EXPRESSION OF THE Xq28 FRAGILE SITE IN AFFECTED MALES. Lawrence R. Shapiro, Patrick L. Wilmot, Alena Leff and MaryAnn P. Martino. New York Medical College and Westchester County Medical Center, Valhalla, N. Y., and Letchworth Village D. C., Thiells, New York.

FUdR induction of the Xq28 fragile site has been reported and cited as evidence for folic acid and thymidine inhibition of this fragile site.

The lymphocytes of 8 males affected by this X-linked recessive form of mental retardation were analyzed for the presence of Xq28 fragile sites utilizing the method of Sutherland (Medium 199, 2-5% fetal bovine serum) and a new method utilizing 10^{-6}M FUdR, RPMI-1640 medium and 10% fetal bovine serum in a 96 hour culture.

Medium 199	RPMI-1640 with FUdR
Mean-16% positive Xq28 (range 5-40%)	Mean-38% positive Xq28 (range 15-79%)

No Xq28 fragile sites were found with either method in controls.

Enhanced expression and simplified identification of affected males was possible scoring as few as 20-50 cells with the use of RPMI-1640 with FUdR resulting in direct clinical application.

● **699** HETEROGENEITY OF NIEMANN-PICK DISEASE, TYPE C (NPD-C). Howard R. Sloan, Ohio State Univ. Coll. of Med., Cols. Children's Hosp., Dept. Peds., Columbus, Ohio.

NPD-C is characterized clinically by the onset at age 2-15 yrs. of psychomotor deterioration and chemically by tissue accumulation of sphingomyelin (Sph) and cholesterol (Chol). In this study, Sph, Sph-cleaving activity (Sphase), and Chol were determined in livers (Livs) from 32 patients with forms of NPD: A(15); B(8); C(9). Sph and Chol were elevated in tissues from all NPD patients ($p<.01$). Sph, Chol, Sphase (uns/mg prot/hr), and the rates of formation of Sph and Chol (pmoles/mg prot/hr) were measured in skin fibroblasts (Fibs) from 27 of these patients: A(13); B(7); C(7). Sphase is deficient in NPD-A and B, but not in NPD-C. Tissue accumulation of Sph and Chol is much less in NPD-C than in A or B. Although, for the group, Sphase is not significantly deficient in NPD-C Fibs or Livs ($p=0.45$; 0.49), three patients had low Sphase in Fibs (34, 42, and 51% of normal) and two had low activity in Liv (28 and 47% of normal). In these patients, there was no correlation between Sph or Chol content and Sphase. The rates of formation of Sph and Chol are normal in NPD-C. Classifying patients with modestly depressed Sphase activity as NPD-C is of questionable value; the key to phenotyping an infant remains the clinical course of an affected sibling. The cause of NPD-C remains unknown.

Cond'n	Sphase (Livs)	Sph (%Nl) (Fibs)	Sphase (Fibs)	Sph Form'n (Fibs)	Chol Form'n (Fibs)
Nl (18)	7.7±1.7	100	41 ± 5.8	128±37	82±28
NPD-A	0.3±0.2	270±50	0.2± 0.1	113±31	98±33
NPD-B	0.7±0.4	239±76	0.6± 0.3	138±47	76±30
NPD-C	6.2±2.3	157±28	31 ±10	107±34	67±32

700 THE FATE OF INFUSED ARGINASE IN THE RABBIT. Elaine B. Spector, Huda Cotta, Rita M. Kern, John J. Kanalas and Stephen D. Cederbaum. Univ. of Calif. Los Angeles School of Medicine. Depts. of Ped. and Psych.

Difficulties with the semi-synthethic amino acid limited diet in the treatment of hyperargininemia in arginase deficiency have caused us to explore alternative means of therapy. These studies were performed to determine the feasibility of direct enzyme replacement of arginase, a cytoplasmic enzyme.

Purified rat liver arginase labelled with ^{125}I was injected into two 2.5 kg. rabbits. Circulating enzyme was found only in the plasma and had a half-life of 1.5-5.0 hours. The animals were sacrified at 6.5 and 7.5 hours. Intact arginase was determined by TCA precipitation and validated by immunoprecipitation and SDS polyacrylamide gel electrophoreses.

95% or more of plasma ^{125}I was in arginase, whereas undergraded enzyme represented 40-50% of the total counts in liver, spleen and kidney. These organs contained fewer than 10% of the total counts with approximately equal amounts in each on a per gram basis. Subcellular fractionation placed equal amounts of enzyme in the cytoplasmic and lysosomal compartments. ^{125}I in muscle, brain, lung and heart were largely TCA soluble. The majority of counts were in the GI tract (50%) and urine (10%)and were TCA soluble.

These data suggest that circulating arginase is taken up slowly by liver, spleen and kidney and degraded in the lysosomes. Unless the half-life of enzyme can be increased and the enzyme properly localized,direct enzyme infusion to treat arginase deficiency is not feasible.

● **701** TISSUE CULTURE MODELS OF TWO MAMMALIAN ARGINASE GENE LOCI. Elaine B. Spector, Donald F. Haggarty, Rita M. Kern, Hawley M. Linke and Stephen D. Cederbaum. Univ. of Cal. Los Angeles, Sch. of Med. Depts. of Ped. and Psych.

Studies of normal and arginase deficient patients have shown two arginase isozymes encoded in two structural gene loci. The liver form (LA) contributes > 98% of liver arginase and is absent in hyperargininemia. A second form (KA) comprises 50% or more of arginase activity in kidney, brain and GI tract and is distinguishable from LA by electrophoretic and immunologic methods. It is augmented in hyperargininemia.

Rat hepatoma cell line H4-II-E-C3 (H4) expresses LA. The enzyme is completely precipitated by anti-rat liver arginase antibody and its pK_I of 9.0 is characteristic of LA. Physiologic levels of hydrocortisone (1.0μM) induce LA activity 10-fold to levels comparable to those in rat liver (4 U/mg protein).

Human enbryonic kidney (HEK) and brain (HEB) cells transformed with BK virus establish lines that express arginase at levels comparable to normal human kidney and brain (0.2-0.6 U/mg). The activity is not precipitated by anti-rat liver arginase antibody. The pK_I is 6.2-6.5, characteristic of KA. K_m for arginine, K_i for lysine and ornithine and pH optimum (9.5) are identical for KA and LA and in both tissue culture systems.

The two cell lines provide models in which to study the differential regulation of LA and KA. The ability to induce augmented expression of KA in LA deficiency would represent autoenzyme replacement therapy and may eliminate the need for exogenous enzyme or gene administration.

● **702** SPHINGOMYELIN METABOLISM IN CULTURED FIBROBLASTS FROM NORMAL AND NIEMANN-PICK DISEASE TYPE A PATIENTS. Matthew W. Spence, Dalhousie Univ., Dept. of Peds. and Biochem., and Atlantic Research Centre for Mental Retardation, Halifax, N.S. (Spon. by J. T. R. Clarke)

The metabolism of endogenously and exogenously radiolabeled sphingomyelin was studied in normal and Niemann-Pick Type A (NP-A) cultured fibroblasts. NP-A cells had <4% normal lysosomal sphingomyelinase activity and contained 2-3 x normal amounts of sphingomyelin. However, NP-A cells degraded endogenously [^{32}P] or [^{3}H-choline]-labeled sphingomyelin at normal or near-normal rates when labeled in culture for up to 120 h then transferred to unlabeled medium for a further 148 h. Exogenous [^{3}H-methyl] choline-labeled sphingomyelin was taken up by both normal and NP-A cells, with NP-A cells accumulating 2-4 x more of the labeled lipid. Following removal of labeled sphingomyelin from the medium, cell associated [^{3}H]sphingomyelin decreased in both cell lines, and the label appeared in cellular lecithin, and in free choline and phosphorylcholine (30-70%) and in sphingomyelin and lecithin in the culture medium. Thus, (1) despite a <95% decrease in lysosomal sphingomyelinase activity, NP-A fibroblasts are able to degrade endogenous and exogenous sphingomyelin; and (2) in both normal and mutant cells, the phosphorylcholine headgroup of sphingomyelin is conserved for lecithin biosynthesis. These findings support the concept of a non-lysosomal site of sphingomyelin turnover, possibly in the plasma membrane, with a close relationship between phosphorylcholine turnover in lecithin and sphingomyelin.

703 DUPLICATION OF 5q31→ qter Rawatmal B. Surana*, Chandra M. Tiwary**, Richard D. Landes** & Lillian Ziegler**, (sponsored by Melvin E. Jenkins); Howard University College of Medicine* and U.S.U.H.S.** & W.R.A.M.C.**, Department of Pediatrics* **, Washington, D.C.*, & Bethesda, MD.**

We report a case of duplication 5q31→ qter with renal abnormalities, only 6 other cases have been reported but without renal malformations.

K.K. is the product of a full term uneventful pregnancy, born to a 28 year old Gr 2 Ab 1 Par 0 white mother and 24 year old father. The birth weight was 2,800 g., length 49 cm, o.f.c. 32 cm. Due to dysmorphic features, chromosome analysis was carried out on peripheral blood lymphocyte culture which revealed a karyotype of 46,XX,22q+. Mother's karyotype was 46,XX. The father's karyotype by G-banding was 46,XY,t(5;22)(q31;q13) and proband's karyotype was interpreted as 46,XY,-22,der(22),t(5;22)(q31;q13)pat. Over the past 30 months, she has had recurrent episodes of otitis media and urinary tract infections. Evaluation of the kidneys by sonogram, renal scan and an IVP showed bilateral hydronephrosis and obstruction at the right uretro pelvic junction. On her last examination, at age 22 months, she was below 5th percentile for weight (8.0 kg), length (68 cm) and head circumference (42.5 cm). Other findings were plagiocephaly, ptosis of left eye with antimongoloid slant, hypertelorism, epicanthal folds, beaked nose, low set and malformed ears, hypoplastic philtrum, thin lips, small mouth, high arched palate, right simian crease, bilateral clinodactyly and slight puffyness of feet. The cardiovascular system was normal and the skin showed cutis marmorata. Developmentally, she was functioning at 6-9 mos. level (cognitive) & (gross motor).

● **704** A SIMPLE METHOD FOR DETERMINATION OF PLASMA AND URINARY BIOTIN, Jess G. Thoene, Rahul S. Sanghvi, Rosemary Lemons, School of Medicine, Dept. of Pediatrics University of Michigan, Ann Arbor.

Altered biotin metabolism produces a common clinical presentation including ataxia, alopecia, keratitis and dermatitis. Three separate etiologies are known: 1. A genetic deficiency of biotin holocarboxylase synthetase (BHS). 2. An apparent defect in biotin absorption or transport. 3. Dietary biotin deficiency. Distinguishing groups 2 and 3 from 1 requires measurement of plasma and urinary biotin. The only current method sensitive enough to measure physiologic biotin concentrations requires a bioassay not widely available. We have developed an isotope-dilution assay for biotin utilizing avidin to bind ^{3}(H)-biotin, and nitrocellulose filters to separate bound from free ligand:200λ of urine or plasma ultrafiltrate are mixed with 10λ of ^{3}(H)-biotin (0.41 pmol; 36.4 Ci/mmol), and 30λ of an avidin solution (4 pmol/ml). The tubes are mixed and 225λ of the mixture are then vacuum aspirated through nitrocellulose filters, followed by a 0.6 ml wash of 0.01 M NaAcetate buffer, pH 5.0. The filters are dried and the bound radioactivity determined in a liquid scintillation counter. Known biotin standards prepared in 150 mm NaCl are run simultaneously. A semilog plot of % radioactivity bound versus biotin concentration is linear over the range of 50 to 750 pg biotin. Using this method, the mean urinary biotin excretion for 19 neonates was 118 ± 76 ng/ml creatinine.This agrees with the published range of urinary biotin excretion via the bioassay (4.3 to 95 ng/mg creatinine). Normal plasma biotin concentration by this method was 300-750 pg/ml (bioassay = 200-500).

● **705** DENTAL HYPOPHOSPHATASIA: A GENETIC STUDY. Charles F. Timmons (Spon. by H. N. Kirkman), Univ. of North Carolina Sch. Med., Dept. of Pediatrics, Chapel Hill.

Families of 5 dental hypophosphatasia (DH) propositi (premature loss of deciduous teeth) were compared to maternal and paternal families of a case of lethal, infantile hypophosphatasia (IH). By criteria of low serum alkaline phosphatase (AP) and elevated urinary phosphoethanolamine (PEA), autosomal inheritance was construed in all 7 pedigrees. The gene appears to reduce by 50-70% the basal AP level. A wide normal range of this basal level, however, renders individual carrier screening, out of family context, uninterpretable. In DH families, penetrance for premature loss of deciduous teeth is low. The non-carrier parent of all DH sibships has "low normal" AP, suggesting that penetrance depends on interaction of the DH gene with familial AP levels. As expected, there were no IH cases seen in the DH pedigrees; however, in each IH line, an individual with dental symptoms was ascertained. Acrylamide gel electrophoresis and selective inhibition by amino acids and urea indicate a reduction of bone and liver isoenzymes in some members of each family. No anomalous bands of activity were seen. Electrophoretically isolated serum isoenzymes have to date revealed no kinetic differences between normal, IH carrier, and DH residual activity. These data are in line with the hypotheses that serum AP levels are multifactorial and that cases of dental hypophosphatasia may be manifesting heterozygotes of the severe, autosomal recessive condition.

706 THE 9p- WITH EXCESS OF DIGITAL ARCHES Chandra M. Tiwary* & Rawatmal B. Surana**; U.S.U.H.S. & Walter Reed Army Medical Center, Dept. of Pediatrics*, Howard University College of Medicine, Dept. of Pediatrics**, Bethesda, Md.* & Washington, D.C.**

A partial deletion of the short arm of chromosome 9 is a clinically recognizable cytogenetic disorder. Dermatoglyphic findings when reported have shown an excess of digital whorls. In our case arches were found on 9 digits.

L.L. is a 28 week old Black female born at term to a young couple. During this pregnancy, the mother took some over-the-counter reducing medication. On examination at age 28 weeks, her weight was 6,136 gm, length 59 cm and o.f.c. 41 cm. The other findings were: trigonocephaly, prominent metopic suture, small palpebral fissures, prominent eyes with monogloid slant, hypotelorism, small upturned nose, long philtrum, thin upper lip, microstomia, low posterior hair line, capillary hemangioma in the nape of neck, extra flexian creases on the middle phalanges of third left digit and second and third right digits. Developmentally, she was functioning at four months level. The karyotype was 46, XX,del(9)(p22). Karyotypes of parents and a 3 year old healthy male sib were normal.

Dermatoglyphics revealed axial triradii in t' position, 9 digital arches and an ulnar loop on second right digit. None of the first degree relatives had an excess of digital arches (mother, 8 UL, 2 W; father 8 UL, 1 RL, 1 A; sib 5 UL, SW).

Dermatoglyphics of other 9p- patients need to be studied before excess of whorls can be taken as a characteristic feature of 9p- syndrome.

● **707** BALANCED CHROMOSOME REARRANGEMENTS ARE TWICE AS FREQUENT AS WE THOUGHT. Daniel L. Van Dyke, Lester Weiss, Jacquelyn R. Roberson. Henry Ford Hospital, Medical Genetics and Birth Defects Center, Detroit.

The frequency of balanced chromosome rearrangements (rea) was estimated in studies of consecutive newborns, published 1969-1977. We found 0.4% rea in prenatal genetic studies, about twice the 0.2% observed in the unbanded newborn series ($P < 0.01$). Reciprocal translocations (rcp) and inversions (inv), but not Robertsonian fusions (rob) were more frequent in the prenatal series. Among 1,549 prenatal studies for advanced maternal age, we found 8 rea. Golbus et al and Crandall et al found 15 rea among 4,090 such studies (see Table). Eighteen rea were familial, five de novo, and one undetermined; one subject carried a familial and a de novo rcp. The familial cases had normal outcomes. Two de novo were normal, one abnormal, and two were aborted.

	N	%rob	%rcp	%inv	% total rea
prenatal (banded)	5,840	0.09	0.19	0.12	0.39
newborns (banded)	4,765	0.06	0.10	0.06	0.23
newborns (unbanded)	56,930	0.09	0.09	0.01	0.19

We believe the higher estimates from the prenatal studies reliably approximate the frequencies in the normal population for three reasons. First, chromosome banding was adopted and improved throughout the 1970's, allowing visualization of more rcp and inv. Second, more cells were examined per subject in the prenatal series. Third, because of the perceived consequences of error, amniotic fluid cell karyotypes may be more closely analyzed than those of consecutive newborns.

708 PARTIAL DELETION OF CHROMOSOME 3p DERIVED FROM RECOMBINATION IN AN INDIVIDUAL MOSAIC FOR A DOUBLE PERICENTRIC INVERSION. Brian E. Ward, Edward Goldson, and Arthur Robinson. National Jewish Hospital and Research Center, University of Colorado School of Medicine, and Children's Hospital, Denver.

The advent of high resolution chromosome banding has allowed the discovery of a growing number of subtle but complex chromosomal rearrangements. We here report a child who has both a short arm deletion and a pericentric inversion in one chromosome number 3. This abnormal chromosome arose from a recombinational event in maternal gonadal cells. Recombination occurred between one chromosome 3 which displayed a double pericentric inversion and its normal homologue. The double inversion in chromosome 3 was present in the mosaic state with approximately one-half of the peripheral lymphocytes exhibiting a normal karyotype. The phenotype of the proband is generally consistent with previous reports of duplication-deficiency syndrome of the short arm of chromosome 3, namely, mental retardation, microcephaly, unusual facies and small size. This child has frank seizures of petit mal status with left focal origin and has developed bruxism as well as self-stimulating behavior. The proband's karyotype is designated as 46,XX,-3,+rec(3)(qter→q29::p25→p13::q11→p13::q11→qter)mat. The maternal chromosome constitution is designated as mos46,XX/46,XX,inv(3)(qter→q29::p25→p13::q11→p13::q11→q29::p25→pter). The observation of a mosaic double inversion is, in itself, an unusual finding. The involvement of such a chromosome in a recombination event is truly unique.

709 A PKU CARRIER TEST WITHOUT PHENYLALANINE DOSE LOADING Sharon L. Wenger, Beverly Tenenholz, Jane M. Breck, and Mark W. Steele, Children's Hospital of Pittsburgh, PA.

The best current test for PKU carrier status is the ratio of P^2/T where P is plasma phenylalanine and T is plasma tyrosine after phenylalanine dose loading (reliability is claimed to → 100% by some). The test is cumbersome requiring two venipunctures, and the phenylalanine dosing often produces nausea, dizzyness and occasionally syncopy. Therefore, in order to develop a more benign test 31 adult "controls" (carrier status unknown) and 43 adult obligate PKU carriers were given a standard phenylalanine dose loading test and plasma levels of P, T, & the ratios P/T and P^2/T were determined before and after dose loading. Of all these parameters, the best discrimination between carriers and non-carriers was given by the formula (4.4053 x ln P)-(0.5221 x ln T) -0.6907 where ln is the natural log of fasting plasma P or T. In 92% of our subjects, this formula distinguished between "controls" and obligate carriers with 95% confidence. The test values for the remaining 8% of subjects fell in a "grey" area where their status could not be determined by this or any other of our parameters, singly or in combination. Among 31 "controls", two were classified as PKU carriers by all parameters we evaluated (a frequency compatible with chance). One additional "control" subject classified as a carrier only by our formula could be a misclassification. Among 43 obligate carriers, 3 were classified as non-carriers by our formula, but all 3 carried a variant PKU gene. Our data suggest that ours is a relatively reliable but more benign test for carriers of the classical PKU gene-requiring only a single fasting blood specimen without phenylalanine dosing.

710 MULTIPLE EXOSTOSES, DEVELOPMENTAL DELAY, AND INTERSTITIAL DELETION OF 8Q. William G. Wilson, Harshad Shah, and Herman E. Wyandt (Spon. by Ann Johanson), University of Virginia School of Medicine, Department of Pediatrics, Charlottesville.

We report an 18-year-old female with multiple exostoses, unusual facies, and developmental delay who has an interstitial deletion of 8q. Her physical findings included exostoses of the proximal and distal long bones, severe scoliosis, short stature, microcephaly, prominent ears, a thin nose with squared tip, lax interphalangeal joints, and mild mental retardation. No coning of the phalangeal epiphyses was seen on hand radiograph. Her lymphocyte karyotype, analyzed by G-, Q-, and R-banding, revealed 46, XX, del (8) (pter → q22.8::q24.1 → qter). Both parents had normal karyotypes.

The absence of coned phalangeal epiphyses and the facial appearance were not consistent with the Langer-Giedion syndrome, of which multiple exostoses and mental retardation are features. Three patients with exostoses, mental retardation, and deletions involving 8q have been described. The deleted segments in two patients (Clin Genet 18:142-146, 1980; Hum Genet 58:231-232, 1981) were similar-del (8)(q13 → q22) and del (8)(q21), respectively. The deletion in the third patient (Eur J Pediatr 133:163-166, 1980) was different-del (8)(q24). The deletion in our patient is distinct from those previously reported in patients with exostoses. The similarities in phenotype associated with apparently different deletions of 8q raise the possibility of multiple loci on 8q which are involved in bone formation, the deletion of any of these being associated with similar abnormalities.

HEMATOLOGY AND ONCOLOGY

711 MICROVISCOSITY MEASUREMENT USING A MECHANICAL IMPEDANCE TECHNIQUE. S. Abbasi, L. Johnson, F. Bowen, Univ. of Penn. Sch. of Med., Penn. Hosp., Phila., PA.

Recently there has been increasing interest in the occurence of polycythemia and the hyperviscous state which alters blood flow in small vessels and results in sludging and impaired circulation to vital organs. Hematocrit (Hct) is the most important determinant of blood viscosity (Vis), in addition to temperature and shear rate. Other factors such as RBC deformability, platelet count and protein concentration (globulins, fibrinogen) are also important. Therefore hyperviscosity is better evaluated by actual measurement than by extrapolation from central Hct. The Sonoclot® (Sienco Instruments) is a new portable device for measuring viscosity and the kinetics of blood coagulation. The principle involves measurement of the mechanical impedance imposed on a rapidly vibrating probe (250 Hertz) immersed in whole blood maintained at 37 C. A fixed low shear rate (theoretically approximating zero) is used. 0.05 ml of blood (with or without anticoagulant) is required.

46 normal term infants ≤ 48 hours old with a mean Hct ($\bar{X}$ ± SD) of 55% ± 6.3 (range 41-64%) were found to have a mean Vis ($\bar{X}$ ± SD) of 7.4 ± 1.45 cenipoise (cps). 21 similar infants with Hct ≥ 65% $\bar{X}$ ± SD of 69.5% ± 3.6 had a mean Vis of 10.4 ± 2.2 cps. Four infants with central Vis of ≥ 11 cps were Rx with exchange transfusion. All had Hct ≥ 65%; three were symptomatic. This technique gives highly reproducible, rapid results, which are consistent with other published data. It also provides a continous recording of the kinetics of blood coagulation and would appear to have considerable usefulness in the normal & intensive care nursery.

712 IMBALANCE IN PLATELET-VASCULAR PROSTAGLANDIN SYNTHESIS PRODUCED BY IRRADIATION IN VITRO. Judith B. Allen, Robert H. Sagerman, Marie J. Stuart, Depts. of Pediatrics and Radiology, SUNY, Upstate Med. Ctr., Syracuse, N.Y.

Vascular changes following exposure to radiation include morphological alterations in the vessel intima, vasoconstriction, and the formation of vaso-occlusive thrombi leading to circulatory impairment and regional tissue hypoxia. Since vascular prostaglandin I_2 (PGI_2) is a potent vasodilator and inhibitor of platelet aggregation, and platelet thromboxane A_2 is a vasoconstrictor and platelet aggregator, we evaluated the production of these 2 opposing compounds in control versus irradiated umbilical vascular rings and platelets. In 8 paired experiments following a single dose of 200 rads in vitro, umbilical arterial PGI_2 production (as evaluated by bioassay) was markedly reduced in irradiated vessels (0.18±0.07 ng/mg; 1SEM) when compared to paired normal controls (0.94±0.14; $p<0.001$). A concomitant decrease in 6 Keto $PGF_{1\alpha}$ (the stable end product of vascular PGI_2) was also observed in the irradiated vessels. However, irradiation had no effect on the production of platelet TXB_2 (the stable metabolite of TXA_2). In 7 experiments, mean values of TXB_2 in platelets irradiated up to 2000 rads was 22.0±3.2% when compared to a mean of 21.3 ±3% in paired nonirradiated controls ($p>0.05$). Myocardial infarction has been observed after conventional mediastinal irradiation. In the animal model radiation also acts synergistically with high cholesterol diets to produce severe atheromatous lesions. A decrease in vascular PGI_2 without any concomitant change in platelet TXB_2 may provide an explanation for some of the vascular complications that occur post irradiation.

713 A NON-RADIOACTIVE ALTERNATIVE TO RADIOACTIVE RED CELL (RBC) SURVIVALS. Habib J. Al Sioufi, Richard D. Propper Michael B. Rabinowitz, Lawrence N. Button, Sherwin V. Kevy. (Spon. by David G. Nathan)

Measurements of the survival of RBC in hemolytic anemias of childhood are encumbered by a requirement for radioactive isotopes and/or by the inability to measure the survival of two populations of RBC simultaneously. Therefore, we have devised a method to overcome these problems which takes advantage of modern atomic absorption spectrophotometry. RBC of 5 rhesus monkeys were labeled with 8ug/ml RBC of non-radioactive $Na_2^{52}CrO_4$ and with 0.01 ug/ml RBC of $Na_2^{51}CrO_4$. The disappearances were assayed by atomic absorption spectrophotometry (^{52}Cr) and gamma counting (^{51}Cr). The survival curves were identical, with the tabulated results:

^{51}Cr $t_{½}$ (n=5)	12.6± 1.2 days	(mean± S.E.M.)
^{52}Cr $t_{½}$ (n=5)	12.8± 0.6 days	

These results show that $Na_2^{52}CrO_4$ is non-toxic to RBC and provides an excellent assay of RBC survival without a requirement for radioactivity. Only when dual population studies are required is $Na_2^{51}CrO_4$ necessary. The double labeling procedure permits refined assays to be performed on cohorts of RBC which differ with respect to age, and are, therfore, variably susceptible to hemolysis, in a variety of clinical disorders.

714 REMISSION INDUCTION IN ACUTE NONLYMPHOCYTIC LEUKEMIA (ANLL) WITH LOW-DOSE CYTOSINE ARABINOSIDE (ARA-C). Arnold J. Altman, John J. Quinn, Patricia Pisciotto, David M. Markowitz, Halbert Capuy, Luis Garcia, University of Connecticut Health Center, Department of Pediatrics, Farmington.

Complete remission was successfully induced in an 11 year old ANLL patient using low-dose ARA-C after failure of chemotherapy (CT) utilizing high doses of this agent. Initial CT consisted of two courses of ARA-C, Daunomycin, vincristine, and methylprednisolone; the ARA-C was given by continuous IV infusion at a dose of 150-200mg/M^2/day x 7 days for each course. A bone marrow aspirate (BMA) obtained 17 days after the second course of treatment contained essentially no normal hematopoietic precursors and >80% blast cells. Low-dose ARA-C 0.7mg/kg/day (20mg/M^2/day) by continuous IV infusion was then begun. After 1 week, normal hemopoietic cells were increased and BMA blast count was reduced to 20%; after two weeks, the blast count was <5%. CT was stopped at this point because the patient was pancytopenic, a consequence of marked marrow megaloblastosis. Within one week, the megaloblastosis and pancytopenia had resolved. Repeat BMA 6 weeks later remains in complete remission. A patient with myeloblastic transformation of chronic myelogenous leukemia has also shown a favorable response to low-dose ARA-C and is now back in chronic phase. Neither patient experienced nausea or vomiting; both were treated on an ambulatory basis. The rapid effect and relatively mild toxicity of low-dose ARA-C suggest a noncytotoxic mechanism of action consistent with experimental data demonstrating induction of maturation in ANLL cells (Sachs, L.: Br.J.Haematol. 40:509, 1978).

● **715** RADIOENZYMATIC DETERMINATION OF PLASMA L. DOPA AND ITS METABOLITES IN NEUROBLASTOMA: Carlos S. Alvarado, Bahjat A. Faraj, Vernon M. Camp, Athanasios Verras, Tae H. Kim, and Abdelsalam H. Ragab, Emory University School of Medicine, Department of Pediatrics and Radiology, Atlanta, Georgia.

Neuroblastoma (NB) is a tumor of the neural crest characterized by abnormalities of tryosine metabolism. The purpose of this study was to evaluate plasma L-dopa and its respective metabolites--Dopamine, Norepinephrine and epinephrine in a group of patients with Neuroblastoma. Plasma L-Dopa and its metabolites were measured by a radioenzymatic technic in 12 children with NB and in 12 other children with different malignancies (control group). The average values for Plasma L-Dopa, Dopamine and norepinephrine were 44.8 ng/ml, 420.4 Pg/ml and 1404 Pg/ml respectively in children with NB, as compared to 1.67 ng/ml, 36.6 Pg/ml, and 227 Pg/ml for the control group. Urinary catecholamines were measured in 24 hour urine samples in 10 patients and they were elevated in only 6 patients. However, plasma L-Dopa, Dopamine and Norepinephrine were significantly elevated in 11 of the 12 children with NB. Follow-up determinations of L-Dopa and its metabolites correlated with the clinical course of the patients. Measurement of Plasma L-Dopa, Dopamine and Norepinephrine by this technic is a sensitive marker for the diagnosis and follow-up of children with Neuroblastoma and appears to be more accurate and less cumbersome than measurement of urinary catecholamines.

● **716** DECREASED HYDROXYL RADICAL (·OH) GENERATION AND LACTOFERRIN (LF) CONTENT IN CORD BLOOD NEUTROPHILS (PMNs). Daniel R. Ambruso, Barbara Bentwood, Peter M. Henson, and Richard B. Johnston, Jr., Univ. Colo. School of Med. and Nat. Jewish Hosp. and Res. Ctr., Dept. of Peds, Denver.

We have previously shown that PMNs from cord blood produce normal or increased amounts of superoxide anion but decreased amounts of ·OH compared to adult PMNs. Both myeloperoxidase (MPO) and LF have been shown to enhance ·OH generation. To determine whether the decreased ·OH production by newborn PMNs is related to abnormalities of granule contents or their release, degranulation and the total content of MPO, lysozyme (LYSO) and LF, as well as ·OH production, were measured. Release of LYSO and MPO from 6 newborns after stimulation with opsonized zymosan (OZ) and phorbol myristate acetate (PMA) was not significantly different from adult controls: MPO with PMA, adult 5.7% (mean) vs. newborn 4.8%, with OZ 8.4% vs. 9.9%; LYSO with PMA, 49.6% vs. 42.0%, with OZ, 31.7% vs. 22.0%. Pretreatment with cytochalasin B produced no differences in degranulation between adult and newborn PMNs. Total MPO content was not different (adult ΔOD 2.78 ± 0.26, mean ± SEM, vs. newborn 2.74 ± 0.30, n=6). By contrast, newborn PMNs demonstrated a decrease in total LYSO (ΔOD 0.101 ± 0.010 vs. 0.087 ± 0.010, $p<0.025$), in total LF (87.0 ± 15.0 µg/mg protein vs. 33.2 ± 8.7, $p<0.005$), and in ·OH production (2379 ± 257 pmol ethylene vs. 1590 ± 314 $p<0.005$). These studies suggest that decreased ·OH produced by cord blood PMNs could be related to decreased LF, not to MPO. The changes in granule content involve specific granules and are consistent with a developmental defect or activation and degranulation during parturition.

717 RELATIVE ANEMIA AND IRON DEFICIENCY IN CYSTIC FIBROSIS: THERAPEUTIC TRIALS. Joann L. Ater, John J. Herbst, Stephen A. Landaw, and Richard T. O'Brien. Univ. of Utah School of Medicine, Dept. of Peds. Salt Lake City.

Significant alterations in hematologic function in cystic fibrosis were suggested by the observation that polycythemia was uncommon even among cyanotic patients. To elucidate those factors which influence hematologic equilibrium, 39 stable cystic fibrosis patients were evaluated with CBC, RBC morphology, reticulocyte count, serum Fe and TIBC, serum ferritin, vitamin E, and carboxyhemoglobin assay. Hemoglobins were within low normal range, including 23% who were cyanotic. The majority of patients had evidence of hemolysis, with elevated carboxyhemoglobin values. Hypoferremia was seen in 28%, and serum ferritins were diminished in 59% of patients. The range for ferritin values was 5 to 55 ng/dl. Vit. E (α-tocopherol) levels were less than 5 ng/dl in 33%. These data suggest that some children with cystic fibrosis are relatively anemic, and that iron and vit E. deficiency may significantly contribute to their apparent failure to compensate hematologically for hypoxia. Next 22 patients with either low ferritin, Fe, and/or vit E. were serially given 2 weeks of oral $FeSO_4$ followed by 2 weeks of oral $FeSO_4$ and vit. E. Variable responses to this therapeutic trial were found. Over half the patients had a significant rise in Hgb of greater than 0.6 gm/dl after the month of $FeSO_4$. Those whose ferritin did not rise, did not show a rise in Hgb. Response in relation to vit E. was variable. These results suggest that the cause of the relative anemia in cystic fibrosis is multi-factorial, but Fe deficiency does make a contribution.

● **718** BONE MARROW TRANSPLANTATION (BMT) IN NON LYMPHOCYTIC LEUKEMIA (NLL): LONG TERM SURVIVAL WITH REDUCED AMOUNTS OF TOTAL BODY IRRADIATION (TBI). C.S. August, F.T. Serota, P.A. Koch, G.J. D'Angio and A.E. Evans, University of Pennsylvania School of Medicine, Children's Hospital of Philadelphia, Department of Pediatrics, Philadelphia, PA.

Morbidity and mortality in BMT patients given cyclophosphamide 120 mg/kg (CY-120), and single dose TBI of 1000 rad is considerable, with fatal interstitial pneumonitis occurring frequently. From 1978 to 1980, we treated 10 consecutive patients with NLL in remission (REM) with CY-120 and TBI, 800 rad. The TBI was given as a single dose at a rate of 8 rad/min from a 6 Mev Linear Accelerator. The patients ranged in age from 4 to 18 years. Diagnoses included 6 with acute myelogenous (AML) or myelomonocytic leukemia (AMML) in first REM; 2 with AML in second REM; and 1 with acute monocytic (AMoL) and 1 with acute undifferentiated leukemia (AUL) in first REM. RESULTS. As of 12/1/81, all 6 children with AML or AMML transplanted in first REM survive in complete remission (CR) for 21-42 months. One child with AML in 2nd REM survives in CR at 31 months. The other relapsed and died at 15.5 months. The patients with AMoL and AUL relapsed and died 2.5 and 8 months post BMT. None developed fatal interstitial pneumonia, compared with 3/8 other patients who received 1000 rad single dose TBI as part of their cytoreduction. CONCLUSION. Our data suggest that long term CR may be achieved in children with AML in first remission by performing BMT with less TBI than heretofore deemed possible. The benefit of reduced radiation may be to decrease the incidence of interstitial pneumonia.

719 INVOLVEMENT OF "OTHER" COAGULATION FACTORS IN EARLY ONSET NEONATAL SEPSIS. Dorothy R. Barnard, Robert L. Bortolussi, Alexander C. Allen, Elihu P. Rees, Dora A. Stinson. (Spon. by John F. Crocker). Dalhousie University, Dept. of Pediatrics, Halifax, Nova Scotia, Canada.

Neonates have unique susceptibility to bacterial septicemia. Hemostasis is influenced by the inflammatory process through complement activation and protease release. Six infants were studied at the time of their clinical diagnosis of infection. Coagulation factors affected by granulocyte proteases (FVIII, FXIII, α2 macroglobulin-α2M, α1antitrypsin-α1AT) and coagulation factors which modify host response to infection (fibronectin-FN, acid 1 glycoprotein-AG) were measured.

FVIII antigen/activity ratios were increased when compared with gestational age matched controls ($p<0.005$), perhaps related to endothelial release of antigen concurrent with protease destruction of activity. FXIII was unaffected in these septic infants. Low values of α2M were measured ($p<0.05$). This may reflect the removal of α2M-protease complexes. Levels of α1AT (a slow inactivator of proteases) were elevated ($p<0.005$) - a response in keeping with an acute phase reactant. FN, an opsonin which enhances reticulo-endothelial clearance and protects against vascular microembolism, was decreased ($p<0.005$). Deficiency of FN may delay elimination of bacteria and contribute to pulmonary insufficiency seen in neonatal sepsis. Measurements of the heparin antagonist AG were increased ($p<0.005$) and may be responsible for the heparin resistance found in septicemia.

Cryoprecipitate, with its high levels of FN, may have therapeutic benefit in neonates with early onset sepsis.

● **719** A ONSET AND RAPID PROGRESSION OF BONE DISEASE AFTER SPLENECTOMY IN NON-NEUROPATHIC GAUCHER DISEASE (GD) Scott H. Barnett, Gregory A. Grabowski, Judith S. Rose, Arthur H. Aufses, Jr., and Robert J. Desnick, Mt. Sinai School of Medicine, NY

Hypersplenism in Type 1 GD has been managed by total splenectomy (S). Although several reports have suggested that S accelerated the progression of bone pathology, the question has remained controversial, due to the variable expression of the disease and lack of prospective studies. Insight into this problem was gained from the prospective assessment of a 5 y/o Hispanic male with marked acid β-glucosidase deficiency and severe non-neuropathic GD. Prior to S (performed for severe cardiopulmonary insufficiency secondary to massive splenomegaly), there was no radiographic or nuclear scan evidence of bone pathology. Within three months of S (4.5 kg), the patient was unable to ambulate and there was collapse of T_{10}, T_{12}, L_1 and L_5, bilateral aseptic necrosis of the femoral heads and Ehrlenmeyer deformities of both distal femora. Since the onset of severe skeletal involvement directly followed S, it is likely that these manifestations resulted from enhanced marrow infiltration, by substrate previously destined for splenic deposition rather than from natural disease progression. These findings provide further evidence for accelerated bone involvement following S. Therefore, S in GD should be delayed as long as possible and partial splenectomy should be considered.

720 METHYLATION OF ARABINOSYL CYTOSINE(araC)RESIDUES IN DNA P. Beardsley, M. Klaus(Sp. D. Nathan)Div.Ped.Oncology Sidney Farber Cancer Institute, Boston, MA 02115

Although araC is a major drug in the treatment of pediatric leukemia, its mode of action is unclear. One hypothesis involves fraudulent incorporation of araC residues into DNA, known to occur randomly at deoxycytidine(dC)positions. This presumes araC DNA is in some way functionally abnormal, but direct evidence is lacking. In mammalian DNA 3-5% of dC residues normally undergo methylation, a process thought to control gene expression. We have carried out studies to determine whether araC in DNA undergoes methylation normally. L1210 cells were incubated for 18hr with ^{14}C araC and/or ^{14}C dC added as shown below. DNA was isolated and exhaustively hydrolyzed enzymatically to nucleosides. These were separated by HPLC and the radioactivity of each component determined. The fraction of each nucleoside converted to its methylated derivative is shown:

Addition(10^{-7}M)	$\frac{CH_3\ araC}{araC} \times 100$	$\frac{CH_3dC}{dC} \times 100$
^{14}C araC only	0.77	--
^{14}C dC only	--	4.6
^{14}dC + araC	--	4.5
^{14}CdC + ^{14}C araC	0.80	4.5

Although araC does not influence the degree of dC methylation, araC in DNA is methylated either less or more slowly than dC. AraC DNA thus appears to be abnormal in this regard. This may explain the ability of araC to induce differention.

721 IDENTIFICATION OF ANTIGEN-BEARING PROTEINS: LOCALIZATION OF PL^{A1} ANTIGEN TO GLYCOPROTEIN (GP) IIIa. D.J.S. Beardsley, J.E. Spiegel, M.M. Jacobs, R.I. Handin, & S.E. Lux, Children's Hosp. Med. Ctr., Brigham & Women's Hosp., & Dept. of Pediatrics, Harvard Med. School, Boston, MA 02115

Antibody mediated platelet destruction is a major cause of childhood thrombocytopenia. Advances in the detection and quantitation of platelet antibodies have aided the diagnosis of these disorders, but little is known about the platelet antigens or receptors involved. We describe a method for separating and immobilizing platelet proteins, retaining their ability to bind antibodies specifically. Gel filtered human platelets are solubilized in SDS and separated on polyacrylamide gels. The component proteins are electrophoretically transferred to nitrocellulose paper. After blocking nonspecific binding sites with albumin and gamma globulin, the immobilized proteins are incubated with anti-platelet antiserum. Antibody bound to a specific protein is then visualized by incubation with ^{125}I labeled goat anti-human IgG followed by autoradiography. The PL^{A1} antigen, important in neonatal isoimmune thrombocytopenia (NIT), has been linked by indirect evidence to the 100,000 MW protein, GPIIIa. When PL^{A1} positive platelet proteins are studied as above with serum from a PL^{A1} negative mother of an infant with NIT, the radioactivity binds specifically to a single band of 100,000 MW. No specific binding occurs with PL^{A1} negative platelets or with control serum. These findings provide direct confirmation that GPIIIa contains the PL^{A1} antigen. The technique developed is rapid, is not limited to the study of precipitating antibodies, and should be applicable to other immune mediated disorders.

722 HEMATOLOGIC MANIFESTATIONS OF MUCOCUTANEOUS LYMPH NODE SYNDROME (MCLNS). John W. Bender, Kathy Stiles, Alan R. Cohen (Spon. by Elias Schwartz). University of Pennsylvania School of Medicine and the Children's Hospital of Philadelphia, Department of Pediatrics, Philadelphia, PA.

MCLNS has been reported to be associated with hematologic abnormalities. We have examined the severity and etiology of these changes in 12 patients who met the standard diagnostic criteria of MCLNS. On admission, the mean hemoglobin level was 10.2 g/dl(range 8.4-12.7). A mild to moderate anemia usually persisted throughout the illness and the lowest mean hemoglobin was seen on the 5th to 6th hospital day (mean 8.9, range 5.9-12.0 g/dl). The anemia was normocytic or mildly microcytic. Leukocytosis was usually present on admission (mean 19,500, range 5,000-28,600/mm^3) and increased to a maximum value on the 5th to 6th hospital day (mean 22,700, range 7,900-59,800/mm^3). The mean leukocyte count returned to normal by the 16th hospital day. More than 10% band forms were present in 9/12 patients; myelocytes or metamyelocytes were present in 11/12 patients. The mean platelet count on admission was 438,000/mm^3 (range 160,000-898,000) with a maximum platelet count between the 11th and 16th hospital day. The platelet counts were >1,000,000/mm^3 in 3 patients but were <100,000/mm^3 in 2 patients. Platelet counts, hemoglobin level and WBC were similar in patients with and without cardiac involvement. MCLNS is commonly associated with a mild to moderate anemia, leukocytosis with a marked left shift, and thrombocytosis. The similarity of these changes to those found in other inflammatory diseases suggests a common etiology. The hematologic abnormalities are not predictive of cardiac complications in MCLNS.

723 TRANSCRIPTION AND PROCESSING ABNORMALITIES IN DIFFERENT FORMS OF β-THALASSEMIA. E.J. Benz, Jr., K. Takeshita, A. Scarpa, L. Chan, H. Pearson, and A.K. Ritchey. Yale University, New Haven, Connecticut.

We have studied the molecular basis of β-thalassemia in 20 patients, using recombinant DNA cloning and nucleotide sequence analysis of defective β globin genes, analysis of β globin gene transcription in vivo and in vitro, and/or analysis of the structure and content of abnormal β mRNA species by S_1 nuclease mapping and primer extension techniques. The most common form of β^+-thalassemia (10/19 pts) observed was due to a mutation within intervening sequence-1 (IVS-1), creating an alternative mRNA processing splice site. The anomalous splice site is utilized preferentially, creating an abnormal β mRNA species incapable of translation into β globin; a reduced amount of normal β mRNA is also generated by this gene. The abnormal species accumulates poorly, leaving only the small amount of normally functioning β mRNA. The other patients exhibited either no structurally abnormal β mRNA species or different remnants of IVS-1 or IVS-2. One patient with β^0-thalassemia exhibited abnormal accumulation of β mRNA precursor sequences containing IVS-2, due to a mutation abolishing the normal site for IVS-2 splicing at the 5'-end of IVS-2. In a second patient with β^0-thalassemia, substantial evidence for a primary transcriptional defect has been obtained by studies of mRNA synthesis in vivo, cloning of the defective gene, and transcriptional analysis in vitro. Hb Lepore, a structurally abnormal hemoglobin associated with β^0-thalassemia, is also due to defective transcription.

● **724** **RADIAL IMMUNODIFFUSION: A Simple Technique for Quantitation of Platelet-Associated IgG (PAIgG) in Children.** V. Blanchette, V. Hogan, B. Gormley, E. Hsu, B. Luke and G. Rock. (Intr. by P. Vlad) Ottawa Blood Transfusion Centre, Children's Hospital of Eastern Ontario and University of Ottawa, Ontario, Canada.

Using current techniques elevated levels of PAIgG can be demonstrated in most children with immune thrombocytopenic purpura (ITP); however these techniques are complex, often require large volumes of blood, and are generally available only in specialized laboratories. We have quantitated PAIgG in children with a variety of illnesses using a simple radial immunodiffusion (RID) technique. 0.25 to 1 x 10^8 platelets harvested from 6 to 10 ml of whole blood were solubilized and plated immediately or after storage at -20°C on low level, commercially available, IgG immunoplates*; PAIgG levels were proportional to the size of the immunodiffusion rings and exact values were calculated by reference to a standard curve. In 15 healthy, non-thrombocytopenic children PAIgG values (fg/plt) were 3.3 ± 1.3 (range 1.5 to 6.8). 15 children with normal platelet counts and other hematological disorders also had normal PAIgG values (mean 3.5 ± 1.7). 77% (10/13) children with ITP and thrombocytopenia (mean plt count 37.7 x 10^3/µl, range 10 to 86 x 10^3/µl) had elevated PAIgG values - mean 26 fg/plt, range 6 to 86.4 fg/plt. In 9 of these children parallel testing of PAIgG was performed using the more complex complement lysis inhibition assay and comparable results were obtained in all cases. In only one of 9 children with ITP in remission (plt count ⩾150, x10^3/µl), was the PAIgG level elevated (mean 4, range 1.5 to 7.8 fg/plt). We conclude that this simple technique is of value in the investigation of children with thrombocytopenia and can be readily adapted in most hematology laboratories.

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* LC-Partigen, Behring.

725 **ROLE OF PLASMA EXCHANGE (PE) IN ADOLESCENTS WITH IMMUNE THROMBOCYTOPENIC PURPURA (ITP).** V. Blanchette, V. Hogan, E. Hsu, B. Luke and G. Rock. (Intr. by P. Vlad) Children's Hospital of Eastern Ontario, Ottawa Blood Transfusion Centre and University of Ottawa, Ontario, Canada.

Recent reports suggest that early PE therapy can induce prolonged remissions in some adults with ITP and so avoid the need for splenectomy. We have used intensive PE in the management of three adolescents, ages 15, 16, and 17 years with ITP. Therapy was initiated because of failure to respond to prednisone 1.5 mgm/Kg/day x 4 weeks (1 male, acute ITP) and recurrence of severe thrombocytopenia when steroids were discontinued (2 cases, one male and one female, with chronic ITP for 1 and 2 years respectively). Patients received a mean of 6 exchanges over a 9 day period using peripheral veins for access and fresh frozen plasma as replacement fluid. Single plasma volumes were exchanged (mean 2.5 litres/procedure). Serial measurements were made of platelet-associated immunoglobulin (PAIgG) using a complement lysis inhibition assay. Mean pre-exchange platelet (plt) counts were 31, 16.9 and 16 x 10^3/µl respectively; PAIgG values were markedly elevated in all cases - 77.5, 54, and 100 fg/plt, control value <10 fg/plt. A rapid and complete response was observed in the case with acute ITP (post-exchange platelet count 186 x 10^3/µl and PAIgG level 9 fg/plt) and he has remained in remission for >6 months. In contrast no response was observed in the 2 cases with chronic ITP (post-exchange platelet counts 18 and <10 x 10^3/µl and PAIgG values 43 and 100 fg/plt). Both patients subsequently had complete responses to splenectomy. We conclude that intensive PE therapy is likely not effective in chronic ITP and should not delay splenectomy if clinically significant hemorrhage is present. In acute ITP unresponsive to steroid therapy PE can induce complete remission thus avoiding the need for splenectomy and the risk of post-splenectomy sepsis; this approach merits further study.

726 GENETIC DIFFERENCES IN METHYLCHOLANTHRENE (MC)-MEDIATED IMMUNOSUPPRESSION IN MICE. Jeffrey L. Blumer and Dorothy M. Frank (Spon. by W.T. Speck). Case Western Reserve University School of Medicine, Rainbow Babies and Children's Hospital, Departments of Pediatrics and Pharmacology, Cleveland, Ohio 44106.

Delayed-cutaneous hypersensitivity to 2,4-dinitrofluorobenzene (DNFB) was measured by an ear swelling assay in C57BL/6J (B6) and DBA/2J (D2) inbred mice and their F_1, backcross and F_2 progeny. Treatment with MC (80mg/kg) prior to DNFB sensitization suppressed the ear swelling response (~80%) in B6, F_1 and aryl hydrocarbon hydroxylase (AHH) inducible backcross and F_2 mice but not in D2 or non-inducible backcross or F_2 mice. Similar observations were made with four additional AHH-inducible and four non-inducible strains of mice. This immunosuppressive response to MC showed the same dose-dependence as AHH induction in responsive mice. Induction of AHH activity by β-naphthoflavone prior to MC treatment resulted in a shift of the dose-response curve for suppression to the left. Thus an ED20 dose of MC was converted to an ED80 dose. Phenobarbital pre-treatment had only a moderate effect on MC-mediated immune suppression. This suggested a requirement for an induced form of the enzyme in the immunosuppressive response. Finally the immunosuppressive response to MC could be completely blocked by prior administration of α-naphthoflavone suggesting a requirement for MC metabolism in the production of the immunosuppressive response. These results suggest a strong positive correlation between carcinogen-mediated suppression of cell-mediated immunity and aromatic hydrocarbon responsiveness in mice. (Supported by American Cancer Society Grant.)

727 LYMPHOCYTE (LPC) GLUTATHIONE-S-TRANSFERASE (GST) ACTIVITY AND INDUCIBILITY IN ACUTE LEUKEMIA. Jeffrey L. Blumer, Margaret Pellack-Walker and Rebecca Dunn (Spon. by W.T. Speck). Case Western Reserve University School of Medicine, Rainbow Babies and Children's Hospital, Departments of Pediatrics and Pharmacology, Cleveland, Ohio 44106.

Aggregate GST activity was measured in LPC sonicates using CDNB as the substrate. The activity in LPC from leukemic children in remission was indistinguishable from that found in cells from unaffected individuals averaging 70 to 120 nmol/min/mg. LPC GST activity was compared to that found in human liver cytosol. While enzyme specific activity was 5 to 7-fold higher in liver, the GST activities in the two tissues were identical with respect to pH, ionic strength and substrate concentration dependence as well as thermal inactivation. The response of GST activity to exposure to various antioxidant compounds was studied in LPC cultured in the presence and absence of mitogens. The antioxidants studied were BHA, BHT, ethoxyquin (E) and α-tocopherol (AT). Culturing in the presence or absence of mitogen had little effect on GST activity. In the absence of mitogen antioxidants were without effect. In the presence of mitogen all four compounds caused a dose-dependent increase in GST activity in cells from non-leukemic individuals. The maximal increase was 2 to 3-fold and the order of potency was AT>E>BHA>BHT. BHA was tested for its ability to induce GST activity in cells from leukemic children in remission. At doses of 5 to 10 μM which results in maximal GST induction in normal cells no increase in activity was observed. These results suggest that the cytoprotective enzyme GST is inducible in human cells and that leukemic children are deficient in this response.

● **728** PREDNISONE THERAPY FOR CHILDREN WITH ACUTE IDIOPATHIC THROMBOCYTOPENIC PURPURA (ITP): RESULTS OF A RANDOMIZED CLINICAL TRIAL. George R. Buchanan and Christine A. Holtkamp, University of Texas Health Science Center at Dallas, Southwestern Medical School, Department of Pediatrics, Dallas.

The efficacy of corticosteroids in childhood acute ITP is controversial and has not been evaluated in a controlled randomized study. We examined the value of prednisone (2 mg/kg/day for 14 days with subsequent tapering and discontinuation by day 21) in 27 children with newly diagnosed ITP. Patients were randomized to receive either prednisone or placebo. Platelet count, bleeding time (a test of the integrity of the platelet-microvasculature interaction), and clinical bleeding tendency (scored on a 0-4+ scale) were determined before (day 0) and six times following initiation of drug therapy (days 1-2, 3-5, 7, 14, 21, and 28). Patients in the steroid and placebo groups were similar with respect to age, sex, initial platelet count and bleeding score, duration of bleeding symptoms, and history of antecedent infection. There were no statistically significant differences between the two treatment groups in any of the three parameters except on day 7 of therapy when children receiving prednisone had higher platelet counts and lower bleeding scores than those receiving placebo. Bleeding score and bleeding time generally correlated with the platelet count. Prednisone did not influence bleeding time or clinical bleeding score independent of its effect on platelet count. We conclude that prednisone does not improve hemostasis or reduce bleeding tendency in childhood acute ITP except transiently at the end of one week of treatment.

729 INTP WITH NORMAL PLATELET ANTIBODY. James B. Bussel, Margaret Hilgartner, Richard Aster NYH-CUMC Div. Ped. Hem/Onc., N.Y., N.Y., S.E. Wis. Blood Ctr., Milwaukee, Wis.

Isoimmune Neonatal Thrombocytopenia (INT) is diagnosed in thrombocytopenic newborns when the mother has a normal platelet count & maternal/fetal platelet antigen incompatibility and/or a maternal serum antiplatelet activity against paternal plts is demonstrated. In 3 term infants we obtained fetal & maternal platelet counts & Platelet associated immunoglobulin (PAIG) determinations and the above mentioned INT studies. The plt antibody titers were obtained on days 4 to 8 of life when platelet counts were still <40,000. All 3 mothers had normal platelet counts and normal PAIG.

PAIG:	INFANT #1			NL INFANT #2			NL INFANT # 3		
	PLA_1	PL^{E1}	$HLA\text{-}A_2$	PLA_1	PL^{E1}	$HLA\text{-}A_2$	PLA_1	PL^{E1}	$HLA\text{-}A_2$
MOTHER	+	+	-	-	+	+	-	+	-
FATHER	+	+	-	+	+	-	+	+	+

CYTOTOXICITY/INDIRECT IMMUNOFLUORESCENCE of mothers serum to father platelets: -/- +/ND +/+

The results were unexpected. Since infant #1 was the only one of the 3 with increased PAIG, we expected him to be the only one with INT instead of the only one without it. Either there is antibody mediated damage to the megakaryocytes by anti PLA^1 such that there is a lag time between antibody clearance and a rise in platelet count, or lightly sensitized platelets with anti PLA^1 are immediately cleared by the newborn RES. Both hypotheses would help explain the 14% mortality with INT.

● **730** IV IgG FOR CHRONIC ITP. James B. Bussel, Elizabeth Smithwick, Charlotte Cunningham Rundles, Robert Inman Robert Kimberly, Irving Schulman & Margaret Hilgartner NYH-CUMC Div. Ped. Hem/Onc., N.Y., N.Y., MSKCC, N.Y.,N.Y., Hospital for Special Surgery, N.Y.,N.Y. and Stanford Medical Ctr. Palo Alto, Cal.

Two children with chronic ITP were treated with Swiss Red Cross i.v. Gammoglobulin (IgSRK). Platelet counts rose only to 40 to 80,000 on prednisone & imuran for 6 months despite normal platelet associated immunoglobulin (PAIG);prednisone could not be tapered. Both patients received 0.4 gm/kg/day IgSRK: platelet counts rose to over 400,000 within 1 week. Prednisone & imuran were discontinued and both patients had platelet counts greater than 100,000 5 weeks after the last infusion. 1. IgG rhogam coated Cr^{51} labelled autologous red cell clearance was used to determine splenic phagocytic function. Both patients had ½ life prolonged to 300% of baseline 1½ hours after the 4th day of i.v. IgSRK infusion; the ½ life was 200% at 2 weeks and only back to baseline at 4 weeks. 2. The IgG levels rose dramatically during the infusions and then slowly returned to low normal over the ensuing 2 to 3 weeks; however, both patients had a polyclonal IgM increase to over 200% of baseline in the week after the infusion was completed with subsequent return to baseline. ANA & RF were negative. 3. Multiple PAIG values were within normal limits. 4. Other studies include serial lymphocyte stimulation, T & B cells with monoclonal evaluation of helper/suppressor subsets, in vitro antibody synthesis with the plaque assay, and immune complex and complement determinations.

● **731** MONONUCLEAR PHAGOCYTE DYSFUNCTION IN CHILDREN WITH SICKLE CELL DISEASE. Robert Chilcote, Barbara Jones, (Spon. Lawrence M. Gartner), Pritzker School of Med., Univ. of Chicago, Wyler Children's Hosp., Dept. Peds., Chicago

Though patients with HbSS are susceptible to salmonella infections, the factors responsible for this immunologic defect are incompletely understood. As salmonella are facultative intracellular parasites of mononuclear phagocytes and do not produce peroxide, we examined monocyte superoxide (O_2^-) production, a factor expected to influence oxygen dependent bacterial killing. We obtained blood from stable children with HbSS, HbSC, and controls and separated mononuclear cells in Ficoll-Hypaque. Monocytes were incubated with cytochrome C and zymosan opsonized by control serum. O_2^- dependent cytochrome C reduction was calculated from the change in OD at 550 over 30'. Unstimulated patient and control monocytes produced similar amounts of O_2^- (1.0 vs. 1.9 ± 0.5 nmol per 10^6 monocytes, N=19, p=0.2). However, stimulated HbSS patient monocytes produced significantly less O_2^- than did controls (13 ± 2 vs. 18 ± 2 nmol per 10^6 monocytes, N=19, p <0.001). Suppression of O_2^- production could not be correlated with splenic function as measured by the presence or absence of Howell-Jolly bodies or the "pit count." Patients with HbSC who have less severe problems had intermediate deficiency (16 ± 2, N=3). On the other hand, monocytes from patients with HbSS chronically hypertransfused to HbS values <15% produced normal amounts of O_2^- (17 ± 2, N=6). These results indicate that HbSS patients have a defect in monocyte O_2^- production and that the defect is acquired, not genetic.

732 FIVE CASES OF CONGENITAL LEUKEMIA. Jen-Yih Chu, Dennis M. O'Connor, & Gordon B. Gale, St. Louis University, Cardinal Glennon Memorial Hospital for Children, Department of Pediatrics, St. Louis, Missouri.

Five newborn infants developed leukemia at the age of 1 day, 2 weeks, 8 weeks, 2 days, and 9 days (cases 1-5 respectively). No chromosomal abnormalities were noted in routine peripheral blood cytogenetic studies. There were several unusual features of clinical interest. Two infants were diagnosed as acute myelomonocytic leukemia (cases 3,5). The other 3 cases were initially considered to be undifferentiated leukemia from morphological & cytochemical studies. Agar culture from peripheral blood of case 1 suggested a myelogenous leukemia. The original peripheral undifferentiated cells of case 2 became more differentiated monocytic cells & monocytes also appeared in cerebrospinal fluid after treatment. However, case 4 later had two short periods of spontaneous regression of leukemia with the clinical course consistent with acute lymphocytic leukemia (A.L.L.) later. Three patients had prominent skin nodules & 2 out of 4 male patients presented with testicular disease. Two patients had CNS disease at the time of diagnosis and one had an isolated CNS relapse at the age of 22 months (case 4). Case 1 died at 2 days of age. Case 2 died at 5.5 weeks with prolonged marrow suppression following vincristine & prednisone induction therapy. Cases 3 & 5 had prolonged remissions with 6-thioguanine & cytosine arabinoside. Case 3 died at 22 months with pneumonia & relapse & case 5 is still in remission at 27 months of age. Case 4 responded to treatment with A.L.L. regimens & is in remission at the age of 36 months.

733 THE ROLE OF OXYGEN IN THE TERMINATION OF THE GRANULOCYTE OXIDATIVE BURST. Harvey J. Cohen and Margaret E. Chovaniec, University of Rochester School of Medicine & Dentistry, Strong Memorial Hospital, Department of Pediatrics & Cancer Center, Rochester, NY

In order to determine the role of oxygen and its metabolites on the activation and inactivation of the membrane bound superoxide (O_2^-) generating oxidase, we stimulated guinea pig peritoneal cavity granulocytes (PMN) under aerobic and anaerobic conditions and examined activity as a function of time. With a soluble stimulant phorbol myristate acetate (PMA), membrane enriched particles from PMN generated similar maximal NADPH dependent O_2^- production under aerobic (43.5 ± 2.2 nmol O_2^-/min/mg pro) and anaerobic (38.4 ± 2.4 nmol O_2^-/min/mg pro) conditions. However, under aerobic conditions activity fell over 120 minutes with a pseudo first order rate constant or .0283 min^{-1}. Under anaerobic conditions, there was no significant change in oxidase activity for up to 120 minutes. NADPH dependent O_2^- production after 120 minutes was 36.8 ± 1.5 nmol O_2^-/min/mg pro for anaerobic stimulation, compared with 1.7 ± 0.3 nmol O_2^-/min/mg pro for aerobic stimulation. Neither cytochrome c, cyanide, superoxide dismutase, catalase, nor benzoate could prevent aerobic inactivation. NADPH dependent O_2^- production is phagocytic vesicles made from pmn which had ingested opsonized lipopolysaccharide coated oil droplets for 5 minutes was equivalent under aerobic (19.9 ± 2.5 nmol O_2^-/min/mg pro) and anaerobic (23.2 ± 4.6 nmol O_2^-/min/mg pro) conditions. However, inactivation of the oxidase occurred to the same extent under both aerobic and anaerobic conditions. We conclude that for PMA but not for opsonized particle stimulated cells, inactivation of the oxidase is dependent entirely on oxygen or an internally generated oxygen metabolite.

734 ARE THE FUNCTIONAL ABNORMALITIES OF NEWBORN PLATELETS ASSOCIATED WITH ALTERATIONS OF MEMBRANE GLYCOPROTEINS? Donald G. Corby, Thomas P. O'Barr, and Ellen E. Swanson, Fitzsimons Army Medical Center, Department of Clinical Investigation, Aurora, CO.

Membrane glycoproteins have been strongly implicated in certain platelet-associated hemostatic phenomena, i.e., adhesion, aggregation, and secretion. As part of our continuing evaluation of the platelets of the newborn infant, washed intact platelets prepared from samples of platelet-rich plasma, obtained from EDTA-anticoagulated whole blood taken from the umbilical vein at delivery or the antecubital vein from normal adult volunteers, were solubilized in 2% sodium dodecyl sulphate, reduced with dithiothreitol, and electrophoresed on 7.5% polyacrylamide gels using the discontinuous buffer system of Laemmli. Gels were fixed, and stained with periodic acid-Schiff's reagent or Coomassie blue. Distribution of glycoproteins was measured by scanning densitometry at 525 nM. In both newborn and adult platelets, ten identically-migrating peaks ranging in molecular weights from 50,000 to 185,000 were observed. Analysis of apparent molecular weights revealed all major membrane glycoproteins to be present in both platelet populations. In conclusion, these studies indicate that the functional abnormalities found in the platelets of newborn infants cannot be attributed to qualitative or quantitative alterations in membrane surface glycoproteins.

● **735** ABNORMAL REDUCTION OF CIRCULATING ERYTHROPOIETIN LEVELS IN NEPHROPATHIC CYSTINOSIS. Brian J. Corden, Laurence Corash, Eugene Goldwasser, and Joseph D. Schulman. National Institutes of Health, Bethesda, MD and University of Chicago, Chicago, IL.

Individuals with the Fanconi syndrome due to nephropathic cystinosis regularly develop substantial anemia many years before progressing to renal failure. The mechanism of this anemia is unexplained. In 7 male and 3 female cystinotics with mean age 5.5y ± 2.3 S.D. (range 2.4-8.1) with mean serum creatinine 1.4 ± 1.2 (range 0.54-4.5), the mean Hgb was 11.1 ± 2.0 (range 7.6-14.2). Reticulocyte counts were inappropriately low for the degree of anemia. Patients were not Fe or folate deficient and there was no evidence of hemolysis. Serum erythropoietin determined by radioimmunoassay was markedly decreased in all cystinotics: mean 7.4 mU/ml ± 2.4 (range 4-10). Two males ages 7.5 yrs and 8.6 yrs with Fanconi syndrome unrelated to cystinosis (Lowe's syndrome) had no anemia and serum erythropoietin of 47 and 36 respectively. Normal adult erythropoietin levels in this laboratory average 21 ± 6. The anemia of cystinosis is thus consistently associated with low concentrations of circulating erythropoietin. We speculate that kidney cystine accumulation may impair renal erythropoietin production. Disappearance of anemia in cystinosis after renal transplantation suggests that, in contrast, cystine deposits do not grossly impair marrow responsiveness to erythropoietin.

736 IMPAIRED CARBOXYLATION AND SYNTHESIS OF PROTHROMBIN PRECURSOR IN LIVER DISEASE. James J. Corrigan, Jr., Monette Jeter, and David L. Earnest. University of Arizona Health Sciences Center, Departments of Pediatrics and Internal Medicine, Tucson, Arizona.

Prothrombin (factor II) precursor is synthesized by the liver and converted to biologically active protein by a carboxylase-vitamin K dependent reaction. Since both the inactive and active proteins are antigenically similar, methods using antibody to factor II measures both. The difference between total immunoreactive protein (II-Ag) and the active fraction or coagulant activity (II-CA) in plasma represents the inactive precursor. Eight patients with acute and 29 with chronic liver disease (LD) were studied and compared to 11 warfarin treated patients and 50 normal controls. Reduced II-CA (< 50% of normal) and II-Ag (< 52% of normal) was noted in 96% and 62%, respectively, of the 24 cases with moderate to severe LD. Also, II-Ag levels exceeded II-CA (normal, < 11% difference) in 66% of these patients. In contrast, in mild LD II-CA and II-Ag was abnormally reduced in 0% and 13% respectively. There was no case of reduced II-Ag in the warfarin group although all had reduced II-CA and excess II-Ag. Conclusion: Reduced synthesis as well as impaired carboxylation of prothrombin precursor are important factors contributing to the coagulopathy of patients with moderate to severe hepatocellular disease. The data also suggest that measurement of circulating levels of prothrombin immunoreactive protein may provide an excellent indication of hepatic synthetic capacity.

737 DEFECTIVE CANDIDACIDAL ACTIVITY BY NEUTROPHILS (PMNs) DURING THE REMISSION PHASE OF ACUTE LYMPHOBLASTIC LEUKEMIA (ALL). Lourdes F. Cruz, James R. Humbert, Ganesh N. Deshpande. State University of New York at Buffalo and The Children's Hospital of Buffalo, NY.

The reason for the propensity toward fungal infections among children with ALL, particularly during remission, is unclear. PMN phagocytic and cidal activity was therefore evaluated in 25 children with ALL during remission, and 32 healthy adult controls using a modification of the histochemical supravital method of Pantazis for Candida albicans. Mean and SEM are reported for 30' and 90' of incubation time:

	Controls (32)		Remission (25)	
	30'	90'	30'	90'
Phagocytosis**	201 ± 13	230 ± 8	185 ± 12.8	208 ± 10.2
Killing***	9.4 ± 0.8	28.9 ± 1.2	6.4 ± 0.7*	21.6 ± 1.8*

* $p < 0.02$ when compared to controls ** candida/100 PMNs
*** percent candida killed

Eleven patients with low candidacidal values did not differ from the other 13 patients with regard to age, sex, presence or type of chemotherapy, and hematologic values. They did differ significantly ($p < 0.01$) in duration of chemotherapy (33 vs 22 months); there was also a significant inverse relationship between duration of chemotherapy and candidacidal activity ($p < 0.05$). During remission, ALL patients develop a defect in PMN candidacidal activity, which may be due to the cumulative effect of chemotherapy agents. This could account in part for the susceptibility of ALL patients toward fungal infections.

738 LEUKEMIA IN TRISOMY 21: PROGRESSIVE OR TRANSIENT? P.A. deAlarcon, J.Goldberg and J.Allen (Spon. by J.A. Stockman III). Depts. Ped. and Med. MIBH, Cooperstown and Depts. Ped. and Med. SUNY, Upstate Med. Ctr., Syracuse, N.Y.

Patients (pts.) with Trisomy 21 may develop unusual leukemoid reactions that are difficult to distinguish from acute myelogenous leukemia. We studied 2 infants presenting with blast forms in the peripheral blood (PB) and bone marrow (BM). ST had hepatosplenomegaly, a platelet count (plt.) of 80,000/dl, white blood cell count (WBC) of 20,100/µl, hemoglobin (HGB) 15.1 gm/dl, PB differential cell count (diff) included 36% blasts and BM revealed 17% blasts. Six mos. later SD had no clinical manifestations of leukemia and the BM contained 0.2% blasts. JR presented with failure to thrive, petechiae, hepatomegaly, HGB 10.6 gm/dl, plt. 32,000/dl, WBC 7,800/µl, diff. included 34% blasts, and BM disclosed 12% blasts. The clinical course was progressive and JR died 12 mos. later of infection. A double layer agar culture technique was employed to evaluate granulopoietic progenitor cells (CFU-GM). Cultures of 10^5 BM cells obtained from 20 normal donors yielded 70-100 clusters and 12-69 colonies. Cultures of 10^5 BM cells from ST formed 2 clusters and 4 colonies at diagnosis and 13 clusters and 6 colonies at recovery. Cultures of 10^5 BM cells from JR failed to form any colonies or clusters. The growth pattern of BM CFU-GM observed in these 2 pts. appeared to correlate with the clinical course. BM cells from JR failed to grow in vitro and JR had progressive disease, while BM cells from ST displayed a normal in vitro growth pattern and ST recovered. Thus, the CFU-GM assay may be useful in predicting clinical outcome in pts. with Trisomy 21 who manifest leukemoid reactions.

739 **PHYSIOLOGIC ANEMIA OF THE NEWBORN: EVIDENCE AGAINST SERUM INHIBITORS OF ERYTHROPOIESIS. Pedro A. de Alarcon and James A. Stockman, III, Depts. Ped. and Med., MIBH, Cooperstown, and Dept. of Ped., SUNY, Syracuse, N.Y.**

During the first few months of life the hgb. concentration of the newborn decreases to a level which would be considered anemia at any other age. The mechanisms controlling this so-called "physiologic anemia" are not clearly defined. One mechanism which has been previously suggested is the presence of a serum inhibitor of erythropoiesis. The in vitro colony assay of hematopoietic progenitor cells affords the opportunity to test this hypothesis. We studied the effects of serum from five 6 wk. old term infants (TI) and from 5 cord blood (CB) samples on the circulating peripheral blood late erythroid progenitor cells (burst forming units erythroid=BFU-E) in the plasmaclot assay. All serum samples were tested using mononuclear cells from the peripheral blood of a single normal laboratory volunteer (C). Tests were carried out with and without the addition of 4 µ/ml of sheep erythropoietin (EPO). Maximum growth of BFU-E was achieved with $4x10^4$ cells per micro well and 4 µ/ml EPO. There was no growth of BFU-E in the absence of EPO. Maximal colony growth of BFU-E in the presence of TI serum was 97.6±47.6 colonies. Maximum colony growth in the presence of C serum was 80.4±36 colonies. Peripheral blood BFU-E in the presence of CB serum showed maximum colonies of 53.2±45 with the C serum showing 42.3±30.7 colonies. No inhibitory effect of TI serum or CB could be demonstrated at any cell or EPO gradient. This study provides evidence against the presence of a serum inhibitor of erythropoiesis as a mechanism involved in the "physiologic anemia" of the newborn.

740 IMMUNOLOGIC AND CLINICAL IMPLICATIONS OF EXTRAMEDULLARY RELAPSES IN CHILDHOOD ALL. N.Dunn, E. Russell, N.McWilliams, H. Maurer, T. Mohanakumar. Medical College of Virginia, Departments of Pediatrics and Surgery, Richmond.

Reactivity of nonhuman antisera to human leukemic cells may influence therapy by providing more sensitive means of detecting sub-clinical residual disease. This additional information may be particularly helpful in seemingly isolated episodes of extramedullary leukemic relapses (EMR).

12 children with ALL in bone marrow(BM) remission, have experienced 20 EMR episodes. Normal appearing marrow lymphocytes obtained at the time of EMR were tested against anti-sera defining leukemia associated antigens (LAA) and human Ia-like antigens and found to be reactive to 1 or both in 11/20 (55%) instances (50% LAA +,50% Ia+). In contrast, 0/20 morphologically normal marrow specimens on 20 patients in complete, continuous remission demonstrated reactivity.

All EMR's were treated locally and, in most instances, with brief intensification of systemic chemotherapy. Three patients remain disease-free 3+-17+ mos following a single EMR. 6 patients have had a BM relapse (med. 21 mos after EMR). The other 3 patients have had more EMR episodes but remain in BM remission, 3+-52+ mos following the first EMR.

We conclude that extramedullary relapse is frequently not an isolated event. This is evidenced in >50% of patients immunologically, by the ability to detect abnormal surface antigens on marrow lymphocytes and clinically, by the generally poor ultimate outcome. Therefore, we recommend that EMR be treated with both systemic intensification and local therapy.

741 SERIAL EVALUATION OF HEXOSAMINIDASE ENZYME PATTERNS IN CHILDHOOD LEUKEMIA. N.L. Dunn, E. Whalen, R.Z.Eanes, T. Mohanakumar(Spon. by H.M. Maurer), Depts. of Pediatrics and Surgery. Medical College of Virginia, Richmond.

Certain enzyme/isoenzyme patterns in childhood leukemia may be useful in the differential diagnosis, outcome prediction and detection of subclinical residual disease. The lysosomal hydrolase, hexosaminidase, is one of the enzymes currently under close scrutiny.

Serial peripheral blood lymphocyte samples from 23 leukemic children have been analyzed for total hexosaminidase activity and isoenzyme profiles. Total enzyme activities were virtually identical at diagnosis (48.5 nm/mg cell protein/minute) and during remission (48.3), while column chromatography revealed an elevated I isoenzyme peak (defined as as I/A peak ratio ≥ 0.2) in certain initial leukemic samples:

Type of Leukemia	# With Initial I/A ≥0.2
ALL, null cell, cALL+	7/12
ALL, null cell, cALL-	3/3
ALL, null cell, cALL unknown	0/3
ALL(T or B cell), AML	0/5

Elevated initial I/A returned to low levels(med 0.11,range 0.06-0.16)during remission. Two patients with high initial values have relapsed in the marrow. The I/A rose above baseline remission levels in both these patients.

We conclude from our data that hexosaminidase isoenzyme patterns may be useful as a tumor marker of childhood leukemia.

742 BLUNTED LIPOXYGENASE RESPONSE OF THE ASPIRIN TREATED TURKEY THROMBOCYTE. Stanley Einzig, Gundu H.R. Rao, Kasthuri R. Reddy, Barbara K. Borgwardt, Nancy A. Staley, George R. Noren, James G. White, University of Minnesota Hospitals, Department of Pediatrics, Minneapolis.

Aspirin (ASA) inhibition of platelet (P) cyclooxygenase (CO)results in a fully compensatory increase in lipoxygenase (LP) products of arachidonic (AA) metabolism. The effect of ASA on AA metabolism of the nucleated avian thrombocyte (Thb) is unknown. ASA was given (60 mg/kg, PO) to 8 white turkeys (Nicholas) ages 75-205 days. At 3,24,48,72, and 168 hr after ASA, Thb rich plasma was incubated with ^{14}C-AA and the percent conversion to thromboxane B_2 (TBx), 12L-hydroxy-5,8,10-heptadecatrienoic acid (HHT), and 12L-hydroxy-5,8,10,14-eicosatetrainoic acid (HETE) was determined using thin layer radiochromatography. Normal human P were examined.

	TBx(%)	HHT(%)	HETE(%)	AA(%)
P-con (n=4)	31.4±1.1	15.9±1.9	40.9±3.4	12.0±3.6
Thb-con (n=8)	55.4±0.6*	16.1±2.0	6.5±1.0*	22.0±4.0
3 hr (n=8)	4.1±0.7	5.6±0.6	14.1±1.4	75.9±1.9
72 hr (n=5)	29.4±4.4	11.7±1.0	10.0±1.0	48.9±4.8
168 hr (n=4)	56.9±3.2	19.7±3.9	8.2±1.5	15.0±2.9

Mean ± SE: *P<0.01, unpaired t-test, Thb-con vs. P-con (control). Like human P, ASA transiently inhibits CO products (TBx, HHT). The limited ability to increase HETE production suggests that; 1) ASA may have a partial inhibitory effect on Thb LP, or 2)HETE production may be relatively "fixed" at a low level which is poorly responsive to ASA modulation of Thb CO. Thus, the turkey Thb may be a useful model for defining the relative roles of LP and CO pathways in cardiovascular physiology.

743 CHEMOTACTIC ENHANCEMENT OF NEUTROPHIL MEDIATED CYTOTOXICITY. Denis English and John N. Lukens, Vanderbilt University School of Medicine, Nashville.

Stimulation of neutrophil oxidative metabolism is associated with the release of free radicals which are potentially injurious to neighboring cells. To determine if chemoattractants exert a regulatory influence on neutrophil cytotoxic responses, neutrophils and target cells were preincubated with chemoattractants and subsequently exposed to 5ng/ml phorbol myristate acetate. Cytotoxicity was determined by assaying ^{51}Cr release from prelabeled target cells and by measuring changes in small ion permeability. Both myeloid leukemia K562 cells and freshly isolated mononuclear leukocytes were used as target cells. Two types of chemoattractants were studied; those which stimulate neutrophil oxidative metabolism at concentrations higher than those required for chemotaxis (C5a, FMLP) and those which do not stimulate neutrophil oxidative metabolism at any concentration (casein, unheated serum). At low concentrations, the former chemoattractants strikingly enhanced PMA-stimulated cytotoxicity. In contrast, chemotactic concentrations of casein and serum failed to augment the cytotoxicity of stimulated neutrophils. Cytotoxicity enhanced by different concentrations of FMLP correlated with the rate of superoxide release and with the degree of chemiluminescence, but not with the extent of superoxide release. We conclude that cellular processes activated during initial encounters of neutrophils and certain chemoattractants enhance subsequent cytotoxic activity. These processes may contribute to tissue damage at sites of inflammation.

744 THE RELATIONSHIP OF STIMULATED NEUTROPHIL ADHERENCE TO EXOCYTOSIS OF SPECIFIC GRANULES. Denis English and John N. Lukens, Vanderbilt University School of Medicine, Nashville, TN

Neutrophil hyperadherence stimulated by phorbol myristate acetate (PMA) was characterized by assessing the attachment of labeled cells to plastic surfaces. PMA failed to stimulate adherence in the presence of N-ethyl maleimide, 2-deoxyglucose, or at low temperatures. However, adding these inhibitors to adherent cells, or exposing adherent cells to $0^{o}C$ for extended times, failed to effect surface detachment. These results suggest that an activity energy consuming process was involved in the initiation but not the persistance of adherence. That adherence was mediated by an intracellular factor was further supported by a close correlation between lysozyme release and the degree of adherence under a variety of conditions. Thus, inhibitors and suboptimal temperatures consistently affected adherence and enzyme release to the same extent. Further the kinetics of stimulation of adherence closely paralleled the rate of lysozyme release at each concentration of PMA tested. On the other hand, adherence, but not lysozyme release, was completely inhibited by omission of Mg^{++}. However, the neutrophil adherence factor, extracted from specific granules, was also found to require Mg^{++} for expression of activity. These results support the hypothesis that a preformed Mg^{++} dependent intracellular factor is integrally involved in the process of neutrophil adherence.

745 NEUROPSYCHIATRIC CORRELATES OF SOMNOLENCES SYNDROME. C. Erickson, P. Trautman, D. Shaffer, R. Gould. Sponsored by M. Katz Columbia University College of Physicians and Surgeons, The Babies Hospital, Department of Pediatrics, New York, NY 10032

This study was conducted to determine whether prophylactic irradiation of the central nervous system for acute lymphocytic leukemia (ALL) causes cognitive, psychological, or neurological dysfunction in children who developed somnolence syndrome. The sample consisted of 35 children between the ages of 5 and 14 years, who had ALL diagnosed no less than six months before the study began and who had no relapses, or signs of CNS leukemia. The children were divided into a somnolent and a nonsomnolent group. There were no significant differences between these groups in sex, age at diagnosis, proportion who received more than 2000 rads, or psychological disturbances in the parents, as determined by a standardized psychiatric symptom inventory (BSI). We noted no significant differences between the groups with regard to 1) cognitive functioning, as measured by WISC-R intelligence quotients and PIAT reading scores, 2) symptoms of psychological abnormalities as measured by the Achenbach Child Behavior Checklist and the Achenbach Teacher Report, or 3) seizures, as an indication of a neurological dysfunction. The results of the behavior checklists do, however, indicate that, as a group, the leukemic children in this study have a significantly higher rate of psychopathology than does the general population

746 ACTIVATION OF OXIDATIVE AND ARACHIDONIC ACID METABOLISM IN NEUTROPHILS BY RESPIRATORY SYNCYTIAL VIRUS (RSV)-ANTIBODY COMPLEXES: POSSIBLE ROLE IN DISEASE. Howard S. Faden, Tej N. Kaul, Pearay L. Ogra. State University of New York at Buffalo, Children's Hospital of Buffalo, Department of Pediatrics, Buffalo, N.Y.

The effect of RSV-antibody complexes on the metabolism of ficoll-hypaque separated human neutrophils was determined by examining the generation of luminol-dependent chemiluminescence, superoxide, and thromboxane B_2 (a product of arachidonic acid metabolism with bronchoconstrictive activity). Incubation of neutrophils with RSV-antibody complexes resulted in a significant increase in chemiluminescence production. The increase in chemiluminescence appeared to be due to 1. active phagocytosis of RSV-antibody complexes as evidenced by its inhibition with cytochalasin B ($p<.001$) 2. increased superoxide production as evidenced by its inhibition with superoxide dismutase ($p<.001$). The generation of superoxide was confirmed by specific analysis in a superoxide dismutase inhibitable ferricytochrome C reduction assay. Of particular importance was the observation that RSV-antibody complexes induced the release of significant quantities of thromboxane B_2 from neutrophils as determined by a radioimmune assay. These data document the release of superoxide and thromboxane B_2 upon ingestion of RSV-antibody complexes by neutrophils. It is proposed that oxygen radicals and products of arachidonic acid metabolism may, in part, mediate the pathogenesis of RSV infection through direct tissue damage and bronchoconstriction.

747 LONG TERM CULTURE OF TWO "TRANSITIONAL" B CELL LINES-THE EFFECT OF IN VITRO CHEMOTHERAPEUTIC AGENTS ON LEUKEMIC CFU OF "TRANSITIONAL" B CELLS AND T CELLS. Harry Findley, Max Cooper, Richard Ray, and Abdelsalam H. Ragab, Emory University School of Medicine, Atlanta, GA, and The Univ. of Alabama, Birmingham, Alabama, Departments of Pediatrics.

We have successfully established two leukemic cell lines from children with acute lymphocytic leukemia (line 207 and 697). These cell lines were positive for the common-ALL antigen (CALLA), the HLA-DR antigen, and for cytoplasmic and surface u heavy chains. Line 697 was positive for Ebstein--Barr virus (EBV). Line 697 carried a marker chromosome which was also present in the patients' fresh leukemic cells. Phenotypically, both cell lines appear to be arrested in a transitional stage of development between Pre-B and B cells. Both cell lines formed colonies (leukemic CFU) in agar and methylcellulose. We performed in vitro drug testing on two cell lines--line 697 and a T cell line (KT-2) kindly provided to us by Dr. Stephen Smith (University of Kansas). The drugs were also tested on "normal" bone marrows. Sensitivities to prednisolone, vincristine, methotrexate, adriamycin and bactrim were determined using a clonal assay in which leukemic lymphoblasts and CFU-GM formed colonies in methylcellulose medium. Normal CFU-GM were more resistant to prednisolone, methotrexate and adriamycin than were the leukemic cells. Line KT-2 (T cell) was more sensitive to Bactrim than line 697 (transitional B cell). This assay for leukemic CFU may be useful for in vitro drug testing. To the best of our knowledge, this is the first report of a "transitional" B leukemic cell line.

748 AN ASSAY OF PLURIPOTENT AND UNIPOTENT HUMAN HEMATOPOIETIC STEM CELLS: CLINICAL APPLICATIONS. Melvin H. Freedman and E. Fred Saunders, Univ of Toronto, Hosp for Sick Children, Div of Hematology, Toronto, Canada.

A unique culture method has been developed which profiles 4 classes of hematopoietic stem cells in 1 culture plate. Marrow or peripheral blood cells were cultured in methylcellulose with 2-mercaptoethanol, erythropoietin, and PHA-LCM. Pluripotent stem cells formed colonies containing granulocytes, erythrocytes, macrophages, and megakaryocytes (CFU-GEMM). The plates also contained colonies of specific cell type from BFU-E, CFU-C and CFU-M. When replated, single CFU-GEMM gave rise to secondary CFU-GEMM confirming self renewal. Control marrow (n=22) yielded means±SD of 17±12 CFU-GEMM, 136±77 BFU-E and 145±67 CFU-C/2 x 10^5 cells plated, 3-4 fold higher than values in peripheral blood. Changes in numbers of CFU-GEMM correlated closely with changes in BFU-E ($r=.77$) but not with CFU-C. In Fanconi's anemia CFU-GEMM were markedly decreased indicating a defect in the pluripotent stem cell. In aplastic anemia the dynamics of reconstitution of all progenitor classes could be demonstrated after marrow transplantation. In red cell aplasia serum inhibitors specific for BFU-E could be documented. In Diamond-Blackfan anemia both decreased BFU-E and CFU-GEMM were seen suggesting a defect earlier in hematopoiesis than previously suspected. In osteopetrosis there were 10 fold increases in blood CFU-GEMM, BFU-E, and CFU-C. This novel assay gives an overview of the relationship between pluripotent and committed stem cells using 1 procedure and is applicable to studies of hematopoiesis at its earliest stages.

● **749** TRANSIENT RED CELL APLASIA OF CHILDHOOD: VARIED PATHOGENESIS. Melvin H. Freedman and E. Fred Saunders, Univ of Toronto, Hosp for Sick Children, Div of Hematology, Toronto, Canada.

Transient red cell aplasia ("erythroblastopenia") is a unique disorder of previously healthy children characterized by profound erythropoietic failure with preservation of other hematopoietic lines, and spontaneous recovery without recurrence. The mechanism of anemia in 4 pts was studied in vitro at the time of diagnosis by assessing BFU-E in methylcellulose cultures. Marrow from pt 1 yielded normal numbers of colonies (13 BFU-E/10^5 cells plated vs controls, 18 BFU-E±10/10^5) that markedly declined when autologous serum or IgM was added to the cultures (4 BFU-E/10^5 and 0 BFU-E/10^5, respectively), but remained unchanged with added autologous IgG or peripheral blood mononuclear cells (PBMC). Pt 2 had 30 BFU-E/10^5 which were completely abolished on addition of autologous serum or IgG, but were unchanged with IgM or PBMC. Marrow from pt 3 yielded 1 BFU-E/10^5 with standard plating techniques, but produced 59 BFU-E/10^5 when plated after fractionating the cells on an albumin density gradient. PBMC from pt 3 suppressed BFU-E growth (from 44 to 20/10^5) but serum had no effect. Pt 4 had 11 BFU-E/10^5 that increased with added autologous serum and remained unchanged with autologous PBMC. We conclude that the red cell aplasia in pts 1, 2 & 3 was due to suppressed erythropoiesis via IgM, IgG, and cell-mediated inhibition, respectively, and in pt 4 by a non-immune mechanism. Whereas transient red cell aplasia has a uniform clinical presentation, there are at least 4 pathogenetic mechanisms that can be detect in vitro.

● **750** GROWTH, MORPHOLOGY, AND CHEMOTHERAPEUTIC RESPONSE OF MEDULLOBLASTOMA (MBT) IN ATHYMIC MICE. H.S. Friedman, S.H. Bigner, S.C. Schold, Jr., D.D. Bigner, (Spon. by J.M. Falletta). Department of Pediatrics and Pathology, Duke University Medical Center, Durham, N.C.

A permanent human MBT cell line (TE-671) was subcutaneously transplanted into athymic nude mice (BALB/c), producing progressively growing subcutaneous tumors. Tumors were serially passed, with growth stability occurring after 3 generations. Mean latency from transplantation to 500 MM^3 tumor volume was 22.4 + 4.4 days. Mean doubling time was 4.92 + 1.7 days. Histologically they contained small round cells with high N/C ratios, high mitotic rates, perivascular pseudorosettes, focal necrosis, and no change in serial passage. Chromosome analysis at passage 19 revealed a near tetraploid chromosome count. There were multiple marker chromosomes including a 4q+, 9q+, 17p+ and Gq-, each present in duplicate. At the first and seventh nude mouse passages the same 4 marker chromosomes were identified.

Groups of randomly assigned mice were treated with antineoplastic compounds at 75% of the LD_{10} by the i.p. route when the median tumor volume exceeded 200 MM^3. Response was assessed by per cent regressors, mean treated vs. control tumor volumes (T/C) and difference in days to 1000 MM^3 tumor volume (T-C):

	T-C	p value	T/C	p value	Regressions	p value
AZQ	3.3	<.025	.505	<.01	0/5	>.05
MTX	2.8	>.05	.79	.004	0/9	>.05
BCNU	1.4	>.05	.82	>.05	1/10	>.05
Procarb	.825	>.05	.82	>.05	2/8	>.05

This xenograft system allows characterization of human MBT in vivo and permits determination of chemotherapeutic sensitivity.

751 MACROCYTOSIS AND HODGKIN'S DISEASE. H.S. Friedman, J.E. Wagner, T.R. Kinney, J.M. Falletta, W. Hannan, R. Neuberg, J.A. Stockman III, Depts. of Peds. Duke Univ. Med. Ctr. Durham, N.C., and SUNY, Syracuse, N.Y.

Macrocytosis is commonly observed in children with malignancy. This may be either a consequence of the disease process or its treatment. A study was undertaken to determine whether macrocytosis was seen in association with Hodgkin's disease (HD) and what the significance of this finding might be. Twenty three children (<16 yrs) with varying stages of HD were studied throughout the course of their illness. Macrocytosis was not present in any child at the time of diagnosis. The mean MCV was 77.5 fl with 28% of the children 2 S.D. <mean for age for MCV. This initial microcytosis had no apparent etiology and was felt to represent the anemia of chronic disorders. In a group of adults with HD matched for stage, 10% of subjects also demonstrated microcytosis. None had macrocytosis. There was no relationship between MCV at diagnosis and disease stage. By 6 mos. from the start of therapy 80% of the children exhibited MCV's >2 S.D. above normal mean MCV for age. Macrocytosis was noted in 4/4 patients with S-IVB disease treated with chemotherapy (MOPP) alone and in 13/15 subjects with S-II-III disease treated with chemotherapy and radiation. Subjects treated with irradiation alone did not exhibit macrocytosis. Following cessation of therapy macrocytosis persisted in 9/15 subjects for 1 to >6 years. These data indicate that macrocytosis may occur during the course of treatment of H.D. as a result of chemotherapy, not the disease itself or radiation. The reason for the persistance of macrocytosis in some subjects and its relationship to risk of second malignancy requires further study.

752 SEVERE CONGENITAL NEUTROPENIA WITH UNIQUE FEATURES OF DYSGRANULOPOIESIS. Aruna K. Garg, Alton L. Lightsey, Richard W. Parmley, Harold M. Koenig, William L. Marsh, William J. Thomas, Baruch Wallach, Laurence A. Boxer, Departments of Pediatrics, Naval Regional Medical Center, San Diego and Oakland, California, University of Alabama, Birmingham, University of Indiana Medical School, Indianapolis.

Congenital dysgranulopoietic neutropenia (CDN) is a recently proposed entity that describes a small subgroup of children with clinically severe neutropenia. We followed and studied a 3-year-old female with neutropenia (<500/mm^3) and recurrent severe infections in whom repeated marrow evaluations revealed large (30-50 um) multinucleated promyelocytes to polymorphonuclear cells with as many as 4 to 16 nuclei or nuclear lobes respectively. In addition to the nuclear endoreduplication, ultrastructural and cytochemical evaluation of these cells demonstrated abnormalities in granule genesis and centriole structure. Concomitantly, immunoperoxidase staining indicated that many of the granules were devoid of lactoferrin but not lysozyme. In vitro proliferation studies from blood and marrow mononuclear cells revealed normal to increased thymidine labelling, normal numbers of colony-forming cells and normal colony stimulating activity. These findings support ineffective myelopoeisis and provide a cause for the neutropenia. Serum folate, B_{12} and lysozyme levels were normal. Conceivably, the marked nuclear and cytoplasmic abnormalities in this patient could be secondary to abnormal centriole directed microtubule function, resulting in this unique example of CDN.

● **753** INFECTION IN CHILDREN WITH SICKLE CELL DISEASE Marilyn H. Gaston, John M. Falletta, Joel I. Verter, Doris L. Wethers, Robert Chilcote, Shelton Landesman for the Cooperative Study of Sickle Cell Disease

It has been recognized for many years that children with sickle cell anemia have a significant mortality rate in early life due to Streptococcus pneumoniae. This important problem was examined by the Cooperative Study of Sickle Cell Disease which involves 21 institutions nationwide investigating the clinical course of sickle cell disease.

Two hundred ninety-five children with SS disease less than three years of age were prospectively evaluated for: a) the development of severe bacterial infection (i.e., bacteria cultured from CSF, blood, pleural fluid or lung tissue); b) splenic function (i.e., the presence of vesiculated rbc; and c) whether they had received prophylactic penicillin or vaccination for Streptococcus pneumoniae.

There were 16 severe pneumococcal infections per 253.89 person years for an overall incidence rate of 6.3 per 100 person years. Ten of 13 patients had abnormal splenic function, as evidenced by vesiculated rbc >3%, near the time of the infection. Most importantly, six of the 16 children died, for a striking mortality rate of 37.5%.

These data underline the continuing problem and deleterious effects of Streptococcus pneumoniae in children with sickle cell anemia with no apparent change in the trend of survival in recent years.

● **754** PROPHYLACTIC USE OF TRIMETHOPRIM-SULFAMETHOXAZOLE (T-S) IN CHILDREN WITH ACUTE LYMPHOCYTIC LEUKEMIA (ALL). Allen M. Goorin, Brenda J. Hershey, Richard D. Gelber, George R. Siber, Kerrie Flynn, Stephen Sallen and Myron J. Levin. Children's Hospital Medical Center, Sidney Farber Cancer Institute, Boston, MA.

Children receiving anthracycline-containing chemotherapy for ALL were randomized to a double-blind trial comparing T-S to placebo. The following trends were observed:

	T-S	PLACEBO
Patient Number	27	28
Infectious Episodes	78	93
Bacteremia	1	5
Acute Otitis Media	2	18
Oral Candidiasis	8	1

The number of episodes of URI, pharyngitis, pneumonia, enteritis, urinary tract infection, cellulitis and unexplained fever were similar in both groups. E. coli resistant to T-S occurred frequently in the stool of both groups, but other gram-negative rods resistant to T-S occurred in 5/14 patients on T-S vs 0/14 on placebo. Pseudomonas was not found in either group. The geometric mean neutrophil nadir was 150 in the T-S group and 251 in the control group. No significant delay in chemotherapy occurred because of T-S. We conclude children receiving aggressive chemotherapy for ALL and prophylactic T-S had fewer episodes of otitis media and bacteremia without serious toxicity.

755 THE IMPACT OF S.C. DESFERRIOXAMINE IN THALASSEMIA - A FOUR YEAR TRIAL. Patricia J.Giardina,Robert W.Grady Margaret Hilgartner, Kathryn Ehlers, Joseph Graziano & Alicejane Markenson. NYH-CUMC Div. Ped. Hem/Onc., N.Y.,N.Y. & Columbia-Presbytrian Med. Center Div.Ped Hem/Onc.,N.Y.,N.Y.

The effect of DFO administered over 8 hours as a s.c. infusion has been evaluated over the course of 48 months in 63 hypertransfused thalassemic patients aged 5 to 20 years. Groups based on age, lifetime transfusions at the start of DFO therapy were assessed. 53/63 patients have complied with therapy using DFO 4 or more days per week. Iron balance was approached in most young children and negative balance achieved in nearly all the older children and young adults. With time a number of patients initially in negative balance exhibited decreased urinary iron excretion and approached positive iron balance suggesting depletion of a chelatable iron pool, drug resistance or decreased drug efficacy. Serum ferritin, SGOT & SGPT which initially decreased in each group subsequently plateaued. Liver biopsies evaluated for histopathological changes and quantitative iron content showed no significant qualitative progression of disease & a significant decrease in quantitative iron was noted in many cases. Cardiac studies revealed a decrease in arrhythmias in younger patients as compared to an age-matched untreated group prior to DFO therapy. Nonetheless, cardiac failure is still the main cause of death. The average age at death rose from 18 to 20 years. Decreased skin pigmentation persists as does the alleviation of arthropathies. No drug toxicity has occurred. Thus, the efficacy of s.c.DFO is strongly suggested.Further trials are needed to determine the full extent of its usefulness.

● **756** ADENOSINE DEAMINASE (ADA) ACTIVITY IN BONE MARROW MONONUCLEAR CELLS: A MARKER OF MINIMAL DISEASE IN T-CELL LEUKEMIA/LYMPHOMA. Bertil E. Glader, Michael P. Link, Michael D. Amylon, and Karen Backer. Department of Pediatrics, Stanford University School of Medicine and Division of Hematology/Oncology, Children's Hospital at Stanford, Palo Alto, California.

Since mononuclear cell ADA activity (mean EU/mg protein ± SD) is markedly elevated in T-cell leukemia (140 ± 39, 9 patients) compared to normal 4.8 ± 1.1, 25 controls, we examined whether ADA activity could be used to detect small fractions of malignant cells in the presence of normal lymphoid cells. We observed that ADA activity could discriminate normal mononuclear cells (4.9 ± 1.2) from mixtures of normal mononuclear cells containing 5% malignant T-cells (9.4 ± 1.2). In addition, adenosine deaminase activity in normal peripheral blood mononuclear cells (4.9 ± 1.2) was markedly increased (15.0 ± 3.2) when a small fraction of malignant T-cells (equivalent to 2% of peripheral blood leukocytes) was added to whole blood before mononuclear cell separation. Lastly, ADA activity in normal bone marrow mononuclear cells (5.6 ± 1.5) also was increased (14.1 ± 3.1) when a small fraction of malignant T-cells (equivalent to 1% of marrow nucleated cells) was added to normal bone marrow before mononuclear cell separation. Current evaluation of bone marrows for residual disease in lymphoid malignancies is limited by the lack of a specific morphologic marker of the malignant cell. Based on the data reported here, measurement of ADA activity in lymphocyte enriched populations from "normal appearing" bone marrows or peripheral blood may be useful in the detection of minimal T-cell disease.

● **757** INHIBITION OF TRANSPLANTED HUMAN OSTEOSARCOMA (HOS) TUMORS IN ATHYMIC MICE BY HUMAN INTERFERON (HuIFN). Lowell A. Glasgow, Kenneth M.Kosak, Douglas K.Kelsey. Univ. of Utah Sch. of Medicine, Dept. Pediatrics, Salt Lake City.

HuIFN is being evaluated as a potential therapeutic agent for human malignancies. Unfortunately clinical trials are being initiated with minimal background data from preliminary studies in animal models. We developed an experimental model utilizing the sc transplantation of HOS cells into athymic mice. Prior to treatment in vivo, the growth of HOS cells in culture were shown to be inhibited by lymphoblastoid HuIFN (512u-94%, 32u-63%, 8u-36%). In contrast a human melanoma cell line was resistant to the antiproliferative effect of HuIFN (500u-10%, 32u-0, 8u-0). In athymic mice HuIFN administered sc for 7d completely prevented or inhibited the growth of HOS tumors (control-35 tumors/35 mice, 50,000u-2/30, 25,000u-1/12, 12,500u-4/12, 6,250u-4/6). The in vitro resistance of the melanoma cells was also reflected in vivo (control-6/6, 100,000u-5/6, 50,000u-6/6, 25,000u-6/6).

The mechanism thru which HuIFN exerts its antitumor activity in vivo remains only partially defined. Because of the species specificity of IFN, we postulated that HuIFN would only express antiproliferative activity in the mouse. This was confirmed by the demonstration that in vitro HuIFN augmented human (21% specific ^{51}Cr release to 75%), but not murine NK cell activity; activated human monocytes to be cytotoxic for HOS cells, but failed to activate murine macrophages. In summary, the in vitro sensitivity of the tumor cells was reflected in vivo and the antitumor activity of HuIFN in this model appeared to be due to a direct antiproliferative effect on the human tumor cells.

● **758** A PROSPECTIVE STUDY OF EVOKED POTENTIALS (EPs) IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA (ALL). Daniel G. Glaze, Donald H. Mahoney, Jr., Robert P. Borda, and Donald J. Fernbach. Baylor College of Medicine, Houston, Texas 77030. (Spons. by Alan K. Percy)

Central nervous system (CNS) prophylaxis is an accepted component of treatment of children with ALL and it is important to evaluate the long-term neurological sequelae of this therapy. Brainstem auditory evoked potentials (BAEPs) and visual evoked potentials (VEPs) were evaluated serially from time of diagnosis in children with ALL: Group 1, prophylactic cranial irradiation and intrathecal (IT) methotrexate; Group 2, prophylactic IT chemotherapy alone. BAEPs showed no significant abnormalities. At diagnosis VEPs to diffuse flash (FVEPs) or pattern reversal stimuli were abnormal in 12/13 patients (Pt), Group 1; and 15/27 Pt, Group 2. The findings suggested dysfunction of visual pathways or of higher cerebral centers. Following the initiation of prophylactic CNS therapy, 7/13 pt, Group 1, and 8/27 pt, Group 2, the FVEPs showed an overall increase in amplitude consisting of relative suppression of early components and enhancement of longer latency components and had the appearance of regression of the VEP to a more immature pattern. One year after diagnosis these FVEPs had not normalized and no pt. had developed CNS leukemia. These findings indicate a significant occurrence of functional damage to visual pathways or higher cerebral centers in patients with ALL receiving presymptomatic CNS treatment. This study suggests that the VEP detects a preclinical CNS abnormality and that it may be useful in the subsequent clinical evaluation of CNS prophylaxis therapies.

759 THE COMBINED USE OF 2,3-DIHYDROXYBENZOIC ACID AND DESFERRIOXAMINE IN IRON CHELATION THERAPY. Robert W. Grady, Patricia J. Giardina and Margaret W. Hilgartner. Div. Ped. Hemat/Onc. New York Hosp. Cornell Med. Ctr. N.Y.

2,3-Dihydroxybenzoic acid (2,3-DHB), an iron-chelating agent has been shown to have an additive effect with desferrioxamine (DFO) in hypertransfused iron overloaded rats. 2,3-DHB in humans is both effective and non-toxic. Its efficacy combined with s.c. DFO in thalassemic patients was assessed. Nine thalassemic patients on low iron diets were studied for 15 days while receiving s.c. DFO at 20mg/kg. as an 8-hour nightly infusion. 100 mg/kg of 2,3-DHB was given orally with meals during the latter 8 days. Daily urine & stool collections from the last 5 days of each trial period were compared for changes in iron content. 2/9 patients experienced gastrointestinal discomfort and were given antacids during which time iron excretion decreased. In 7/9 patients the mean urinary iron excretion increased from 15.6 to 20.0 mg/day as a result of combination therapy while fecal excretion increased from 15.9 to 17.2 mg/day. Unlike previous studies where 2,3-DHB was used alone, the major increase in iron excretion occurred in the urine. Thus, combined use of the two drugs appears to cause an increase in the total iron excretion. It is suggested that the combination would be of use in patients who are good compliers to DFO therapy.

760 **Haemophilia A is caused by sex linked congenital lack of clotting factor VIII. In current treatment of haemophilia A, concentrated human factor VIII plasma is administered intravenously for hemorrhagic episodes. Although oral useful therapy has been desired and oral ingestion of factor VIII entrapped in liposomes has been attempted, there is some problem in acquiring antibodies against F VIII.**

Kanpo (Japanese traditional medicine), transmitted from China in the seventh century and modified in Japan since then, recentry attracted increasing attention in modern medicine in Japan because of its effectiveness without side effects. The extract of Huang-chieh-tu-tang (HLCT) is one of the Kanpo medicines consisting of four medical herbs, Corptis sp., Scutellaria baicalensis, Gardenia jasminoides and Phellodendrom amurense, which has been believed to possess antiinflammatory and hemostatic effects. HLCT was clinically very effective for bleeding episodes in haemophilia A so that both in vivo and in vitro experiments were done. Extract of HLCT was given orally 0.15g/kg to a patient with severe haemophilia A. Plasma concentration of factor VIII rose from less than 1% to 41% one hour after oral administration. APTT also shortened from 102"9 to 70"9. In vitro experiment, HLCT revealed to have activities of factor VIII, IX and X at concentrations around 0.08%.

761 TWO-DIMENSIONAL ELECTROPHORESIS (2-DE) OF CELL PROTEINS IN CHILDHOOD LEUKEMIA. Samir M. Hanash, David G. Tubergen, Ruth M. Heyn, James V. Neel, Louis Sandy, Gloria S. Stevens, Barnett B. Rosenblum and Karen N. Springstead, University of Michigan Medical School, Ann Arbor and Denver Children's Hospital, Denver CO.

We have investigated the potential of 2-DE to identify differences in the protein patterns of various types of childhood leukemia. Solubilized proteins in normal lymphocytes and in blast cells from children with acute lymphoblastic (ALL) or myelogenous leukemia (AML) were electrophoresed using Andersons' ISODALT system. Protein spots were visualized with Coomassie staining followed by a modification of Merrill's silver staining technique. Approximately 1000 spots were routinely visualized in individual gels. Various spots gave characteristic shades of color from blue to yellow red and brown. Identical patterns were observed in multiple runs of the same sample. Initial Analysis included the 400 major spots in the gels. Analysis was facilitated by cytocomputer imaging of specific constellations of spots. A total of five spots were present in all five AML samples and consistently non-detectable in ten ALL samples including seven non-T, non-B and three T-cell ALL. Four spots were present in ALL but not in AML samples. Five spots were present in ALL samples but not in normal lymphocytes. It is concluded that 2-DE is a useful tool for the delineation of characteristic protein patterns in leukemia. The 2-DE approach could be used to identify a protein basis for monoclonal antibody specificity and to systematically search for key antigenic differences between cell types for monoclonal antibody production.

762 ABNORMAL PHAGOCYTIC AND BACTERICIDAL PROPERTIES OF NEUTROPHILS (PMNs) IN SICKLE CELL DISEASE (SCD). James R. Humbert, John H. Githens, Depts. of Pediatrics, State University of New York and The Children's Hospital, Buffalo, NY and University of Colorado Health Sciences Center, Denver, CO.

Conflicting data exist regarding PMN functions in SCD. We investigated the phagocytic and bactericidal activity of PMNs toward Staphylococcus aureus 502 A in 44 SCD patients (31 SS, 13 SC) and 35 healthy adults (Tan's technique). Results (mean ± SEM) are expressed as % of surviving extracellular (EB) or intracellular (IB) bacteria, compared with the initial bacterial inoculum, after a ½ and 2 hours incubation. (P value: patients vs controls. NS: not significant).

	30'	P	120'	P
a) Phagocytosis (EB)				
controls	20.0±2.7(13)		4.5±0.4(35)	
SS	27.2±3.4(39)	< 0.05	8.1±1.6(31)	< 0.05
SC	32.7±6.4(13)	NS	8.7±1.3(13)	< 0.001
b) Killing (IB)				
controls	0.6±0.2(13)		1.3±0.2(35)	
SS	2.2±0.5(29)	< 0.001	1.8±0.3(31)	NS
SC	2.5±0.6(13)	< 0.01	2.6±0.6(13)	< 0.01

Paraffin oil particles were ingested equally well by SCD patients and controls (Stoessel's 5' test). The bactericidal defect was present in 19/42 patients at 30', but only 2/44 patients at 120'. After long interactions of particles and PMNs a phagocytic defect appears in patients with SS and SC disease while the initial bactericidal defect improves. These data are compatible with partial activation or oxidant stress of PMNs in SCD patients.

763 EVALUATION OF ANEMIA AND HEMOGLOBINOPATHIES IN SOUTHEAST ASIAN REFUGEE (SEA) CHILDREN. Deborah Hurst, Barbara Tittle, Klara Kleman, Stephen Embury*, Bertram Lubin, Bruce Lyon Mem. Res. Lab., Children's Hosp. Med. Ctr., Oakland, CA and *San Francisco Gen. Hosp., San Francisco, CA.

Over 250,000 SEA refugee children will have entered the U.S. by 1982. To identify the hematologic disorders in this population, we screened 274 children and found the following results:

Phenotype by Isoelectric Focusing	Cambodian	Laotian	Vietnamese
Hb AA	29 (10)	78 (28)	65 (24)
Hb E trait	19 (7)	23 (8)	
Hb EE	8 (3)	4 (2)	0
Hb Eβ^0-thal	0	3 (<2)	0
β-thal trait (↑A_2)	2 (1)	1 (<1)	8 (3)
α-thal trait (gene mapping)	4 (2)	19 (7)	11 (4)
Anemia (↑FEP)	29 (10)	23 (8)	9 (3)

MCV's and Hb's of normal (AA) SEA children did not differ significantly from age-appropriate values established in this country. Children with E trait and EE had Hb's which did not differ from normal. E trait MCV's were 10-15% below normal for age, but increased with age parallel to the normal values. Homozygous EE and E-β-thal resulted in markedly reduced MCV's (50-60 fl). A subgroup of children with E trait in combination with α-thal trait had less than 27% Hb E, and/or MCV less than 62 fl. Anemia but not percent Hb F and E distinguished EE from E-β-thal. This information should prove useful to pediatricians who are faced with the care of SEA patients.

764 SYNOVECTOMY FOR RECURRENT HEMARTHROSIS IN HEMOPHILIACS WITH HIGH-LEVEL INHIBITOR. Raymond J. Hutchinson, John A. Penner, Robert N. Hensinger. (Spon. by Robert P. Kelch). The University of Michigan Medical School, Ann Arbor.

Recurrent hemarthrosis with resultant synovial thickening and joint damage is a common affliction of patients with severe hemophilia A (factor VIII < 1%). Synovectomy to remove the diseased synovium and thereby reduce the likelihood of recurrent hemorrhage has not been attempted often in hemophiliac patients with a high-level inhibitor (≥ 5 Bethesda Units). Two patients with severe hemophilia A and high-level inhibitor (68 BU and 10.5 BU respectively) underwent synovectomy while receiving anti-inhibitor coagulant complex (Autoplex). The first patient received two doses of 28 units/kg each, immediately before and during the surgery, with maintenance continued at 40-60 units/kg/dose for 9 doses over 5 days. The second patient received a dose of 63 units/kg before and one of 77 units/kg after the surgical procedure. Maintenance was continued at 40-60 units/kg/dose for 20 doses over 6 days. Recurrent bleeding occurred on the 10th and 8th postoperative days in the two patients, necessitating further therapy. Blood loss during the surgery was estimated at 150 ml for patient 1 and 932 ml for patient 2. The boys received 4 and 9 units of packed red blood cells respectively during the intra- and postoperative periods. Side effects of therapy included headache and perhaps low-grade fever. Neither patient developed thrombocytopenia or hypofibrinogenemia, nor clinical signs of thrombosis. Synovectomy is possible in severe hemophiliacs with high-level inhibitor using Autoplex at 40-60 units/kg/dose, with doses given at 6-8 hour intervals for a minimum of 10 days.

765 LINEAR GROWTH ABERRATIONS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA (ALL). Raymond J. Hutchinson, Mary J. Waskerwitz, Nancy J. Hopwood, University of Michigan Medical School, Ann Arbor, MI 48109.

In order to assess the effects of ALL and its therapy upon linear growth, growth curves were plotted for 72 surviving children and adolescents diagnosed with ALL between the years 1972-78. All of these patients received systemic chemotherapy, including daily steroids during induction therapy, and central nervous system (CNS) radiotherapy. Seventeen patients experienced a transient growth deceleration during therapy, but all regained their losses. An additional 17 patients demonstrated marked growth deceleration from which they have not recovered. Linear growth velocities ranged from 0-3.8 cm/year during the period of deceleration. This group serves as the basis for the rest of the reported data. Twelve of these patients are off therapy from 8 mos to 5 yrs, while 5 remain on. In 3 patients the growth deceleration was probably secondary to normal postpubertal changes. In 2 patients it appeared to be temporally related to administration of a second course of CNS radiotherapy. The remaining 12 patients exhibited deceleration beginning early in therapy. Five of the 12 patients have both standing and sitting heights falling below the 3rd percentile. The type of CNS radiotherapy administered (cranial vs craniospinal) did not appear to influence growth outcome differently. All 17 patients have normal thyroid studies (T4, TSH), and 5 of the more severely affected patients had growth hormone assays performed which were normal. Although the etiology is unclear, growth deceleration is common in children with ALL during anti-leukemic therapy, with a persistent effect seen in 19% of this group.

766 CYTOGENETICS IN 8 CONSECUTIVE PEDIATRIC CASES OF ACUTE NON-LYMPHOCYTIC LEUKEMIA (ANLL). Susumu Inoue, Michael Tyrkus, Yaddanapudi Ravindranath, Children's Hospital of Michigan and Wayne State University School of Medicine, Detroit, MI. 48201.

Initial cytogenetic analysis of leukemic cells seems to be an independent prognostic indicator in adult ANLL. Patients with no normal karyotypes at the time of diagnosis had significantly shorter survival period than those with normal metaphases. The t(8q;21q) without sex chromosome loss indicated good prognosis. We examined the initial karyotypes of 8 consecutively studied children with ANLL during the last 6 months. All 8 patients had at least 20% of metaphases with normal karyotypes. Five patients two with 46XX only, one with t(8;21), one with the 18p- and one with a monosomy 7 are alive and in remission. All of them had typical M1 and M2 morphology. An 8 month old girl with hemohistiocytic leukemia (normal karyotype) and a 7 year old girl with initial erythroleukemia-like picture with very large platelets (1-2 times as large as a red cell) preceding progressive increase of monoblasts (46XX in 85% and monosomy 10 in 15% of cells) failed to achieve remission and died. The 8th patient, an 18 month old girl with monomyelocytic leukemia with bilateral orbital chloroma had t(8;21). She was not treated and died. The type of cytogenetic abnormalities in childhood ANLL appears to be similar to that seen in adults. In this small series, the morphological and clinical factors were more useful in predicting the outcome than cytogenetic data per se.

767 RESPONSE OF PLATELETS TO EPINEPHRINE IN THE NEWBORN INFANT. EVALUATION USING A NEW MICRO AGGREGOMETER L. Johnson, M. Grous, S. Abbasi, Univ. of Penn. Med. Sch. Pennsylvania Hospital, Dept. Peds., Philadelphia, Pa.

We report the feasibility of doing platelet aggregations on only 45 lambda of platelet rich plasma (PRP) using the Sienco Dual Channel Aggregometer. (90 lambda is required if the platelet count is ⩽150,000.)

The 45 lambda of PRP are diluted 4 fold with phosphate buffered saline to which 20 lambda of aggregating agent is then added. Results can be reported as presence or absence of 1st and 2nd phase aggregation and as percent aggregated for each phase. Blood is collected into a polyethylene micro centrifuge tube calibrated at the 1.5 mark and containing 150 lambda of 3.8% citrate. Heel stick blood can be used providing the heel is warmed and coated with a thin film of vaseline and a free blood flow is obtained. Results are highly reproducible and agree precisely with duplicate assays using a larger sample size.

In agreement with previous reports, we have found the great majority (80%) of newborn infants with birth weights ⩽2000 gm have platelets which are unresponsive to epinephrine as an aggregating agent. The remainder (20%) show a response of low magnitude. Aggregation with adenosine diphosphate (ADP) is also impaired, but not to as great an extent. Term infants show similar but less striking trends. In all birth weight groups, an increasing responsiveness to epinephrine is seen with increasing age, the majority of aggregation assays being positive by age 3 weeks.

768 PROPHYLACTIC EXCHANGE TRANSFUSION THERAPY AND SERUM FERRITIN IN SICKLE CELL DISEASE. Gungor Karayalcin, Robert Festa, Ashok Shende, David Chung, and Philip Lanzkowsky. Sch.of Med.,Health Sciences Ctr.,SUNY at Stony Brook and Long Island Jewish-Hillside Med.Ctr., Dept. of Pediatrics, New Hyde Park, N.Y.

Serum ferritin levels were determined in 14 patients with homozygous sickle cell anemia who were on partial exchange transfusion therapy (SS+Tx) for 1 to 3 years. The ferritin levels were compared to 14 age-matched non-transfused patients with sickle cell anemia (SS) and to 10 patients with B-thalassemia major (B-Thal) who had received a similar volume of blood by packed red cell transfusion (45±17 units for SS+Tx vs. 51±25 units for B-thal, P:NS).

	Control	SS	SS+Tx	B-Thal
Number	14	14	14	10
Age (Years)	13.4±4.8	13.4±4.8	13.4±4.8	7±3.8
S.Ferritin (ng/ml)	23±7.6	276±169	1210±626	2180±104
Significance (P)		< 0.0005	< 0.0005	< 0.005

The SS patients had significantly higher serum ferritin levels than age-matched nonanemic controls. The SS+Tx patients showed a marked increase in ferritin levels compared to non-transfused SS patients, but lower levels than B-thal patients. The data suggests that partial exchange transfusions result in hemosiderosis but the transfusional iron load may be less than that produced by packed cell transfusions. For this reason SS+Tx patients should be monitored for iron overload and chelation therapy may be indicated in these patients for prevention of transfusional hemosiderosis.

769 MODULATION OF NEUTROPHIL (PMN) FUNCTIONS BY ALPHA-1 ANTITRYPSIN (AAT). A.J. Khan, H.E. Evans, M. Varghese and P. Khan, Dept. of Ped. Jewish Hosp. and Med Ctr/ SUNY Downstate Medical Center, Brooklyn, NY

ATT has been shown to suppress the function of B lymphocytes. We studied the effect of AAT on phagocytic Index (CI) and chemotactic index (CI) of PMNs derived from 10 healthy subjects. PI was determined by incubating PMN and latex particles with and without AAT. Chemotaxis was performed with a modified Boyden's technique. PMN were placed in the upper compartment with and without AAT and chemotactic factor(s) in the lower. Ratio of migrated to total cells represented CI. In separate experiments Hank's solution with and without AAT was placed in the lower compartment to determine chemo-attractive index (CAI). Mean (± 1SD) CI, CAI and PI are presented (table). Concentration of 500 mg/dl decreased the PI ($P<0.01$) and suppression was inversely dose related ($r=0.89$, $P<0.02$). CI decreased and CAI increased progressively with 100 to 500 mg concentrations ($r<0.79$ and $P<0.05$ in each instance AAT in ≥ 200 mg/dl concentration decreases PMN function. Comparably high concentrations of AAT, as occurs in malignancies including leukemia may contribute to the well known defects of PMN function and increased susceptibility to infection. Defective CI appears to be due to AAT acting as a chemotactic factor.

AAT mg/dl	N	CI	CAI	PI
0	5	76(14)	16(4)	31(10)
100	5	59(12)	20(4)	29(14)
200	5	44(10)	30(7)	--
500	5	28(7)	44(6)	16(7)
1000	5	32(8)	44(10)	16(9)

770 FINE NEEDLE ASPIRATION BIOPSY OF MASS LESIONS IN PEDIATRIC PRACTICE, K.R.Kini, Sudha R. Kini, R. P. Warrier, J. Martin Miller, Joel I. Hamburger, (Spon. by Lester Weiss). Henry Ford Hospital, Dept. of Pediatrics, Detroit.

Percutaneous fine needle aspiration (FNA) biopsy of mass lesions is a reliable technique. This technique is easily performed by using a 22 to 25 gauge needle. For deep seated lesions, the procedure is performed under the guidance of fluoroscopy, CT scanning, or ultrasound. The aspirated material is stained by the Papanicolaou method.

We have examined over 4,000 fine needle aspirates of thyroid nodules of which 53 were from 50 children and adolescents. Sixteen aspirates were from tumors of miscellaneous sites from 15 patients, ranging from 18-months to 18-years of age. Of 53 thyroid aspirates, 12 papillary carcinomas, 2 follicular carcinomas, 2 Hurthle cell tumors, 2 follicular adenomas were cytologically diagnosed and confirmed histologically. Of 16 miscellaneous aspirates, the following cytologic diagnoses were made: 1 malignant sacrococcygeal teratoma, 1 Wilm's tumor, 2 rhabdomyosarcoma, 1 metastatic thyroid carcinoma and 1 leukemic infiltrate. These were also confirmed histologically.

With adequate cellular material, the fine needle aspiration biopsy offers a high degree of accuracy. Malignancy not only can be diagnosed but typed accurately. Prompt chemotherapy can be initiated in advanced malignancies. A preoperative diagnosis helps in planning proper surgical therapy. A benign diagnosis in many instances may prevent unnecessary surgical procedures.

771 IMPROVED PROGNOSIS OF SEVERE APLASTIC ANEMIA IN BLACK CHILDREN TREATED WITH ANTI-LYMPHOCYTE GLOBULINS Dahlia Kirkpatrick, Neena Kapoor, Michael Sorell, Robert Dinsmore, Richard J. O'Reilly and the MSKCC Transplant Service

Severe aplastic anemia is associated with a 70-80% mortality in patients treated with supportive care, with or without androgens. While marrow transplantation is a preferred option, clear improvement in survival in all patient groups has not been achieved. In particular, Elfenbein et al. have recently documented poor transplant results in Black patients with aplasia. Over the past two years, we have treated 15 patients with severe aplastic anemia with either anti-thymocyte or anti-thoracic duct lymphocyte globulin. Of these patients, 10 are alive 2-36 months post treatment (Median= 12 months). Of 5 Caucasian patients, only 2 are alive, and only one has enjoyed a partial remission of his disease. In contrast, of 7 Black patients treated, 5 have achieved complete hematologic remissions. Five patients are surviving. One patient died of sepsis during treatment; another died of an accident while in complete remission 9 months post therapy. These preliminary results suggest the possibility that Black patients may be at particular risk for "autoimmune" forms of aplastic anemia responsive to this form of immunosuppressive therapy.

● **772** ACCELERATED DEVELOPMENT OF BLOOD COAGULATION BY CORTISOL IN THE LAMB FETUS. C. Thomas Kisker, Jean E. Robillard, David P. Bohlken. University of Iowa College of Medicine, Department of Pediatrics, Iowa City, IA 52242

Blood coagulation factor activities are dependent upon gestational age as shown in both premature infants and in chronically catheterized fetal lambs. Eight sets of chronically catheterized twin lamb fetuses were studied to determine if cortisol would accelerate the development of blood coagulation. One twin from each pair was infused intraperitoneally with cortisol (2 mg/ 0.8 cc/hr for 48 hrs) while its twin sib was infused with normal saline (0.8 cc/hr). Changes in coagulation factor activities measured before and after the infusions were analyzed using a paired T test. Significant differences between cortisol infused (c) and saline infused (s) sibs were apparent: blood cortisol +31.8 pg/dl (c), +2 pg/dl (s), p=0.001; Factor II +16.6% (c), +2% (s), p=0.006; Factor V +54% (c), +18.2% (s), p=0.002; Factor VII +24% (c), +0.1% (s), p=0.01; Factor X +26% (c), -1% (s), p=0.001; Factor XII +9.4% (c), +1.4% (s), p=0.025. No differences were seen with fibrinogen +24 mg% (c), +21 mg% (s); Factor VIII +2% (c) +9% (s); Factor IX +12% (c), +4% (s) or Factor XI -4.2% (c), +1.8% (s). Betamethasone at 15 mg/day for 2 days given to pregnant ewes resulted in changes in fetal coagulation factors similar to those observed when lambs were given cortisol directly (Factor II +14%, Factor V +58%, Factor VII +31%, Factor X +22%, Factor XII +10%). Results indicate that cortisol accelerates the development of blood coagulation and suggest that coagulation factor activities might be improved by giving betamethasone to mothers at high risk for premature delivery.

● **773** *HEMATOPOIETIC DYSPLASIA AND MARROW HYPOCELLULARITY IN CHILDREN: A PRE-LEUKEMIC CONDITION.* *Nathan L. Kobrinsky, Richard D. Brunning, Norma K.C. Ramsay, Diane C. Arthur, William Krivit, Mark E. Nesbit. University of Minnesota, Minneapolis, Minnesota 55455*

Seven children with Hematopoietic Dysplasia (HD) were identified by morphologic criteria. The bone marrow and peripheral blood findings in these children were characterized by progressive marrow hypoplasia, proteinaceous debris in the marrow interstices, megaloblastoid changes in the erythroid and myeloid lines, and peripheral macro-ovalocytosis. Six patients had major constitutional abnormalities. Six developed pancytopenia. Three developed myelogenous leukemia at 13, 47 and 100 months after presentation. Three have expired from leukemia (2) or intracranial hemorrhage (1). Chromosome studies of blood and bone marrow demonstrated a clonal abnormality involving the B,C and E groups in 3/5 cases. CFU-Cs were uniformly decreased in 5/5 cases, even prior to the onset of leukopenia in one case. Incomplete and/or transient responses to pyridoxine (1/4), folic acid (3/4), androgens (1/4), and steroids (3/3) were noted. No responses to B_{12} (0/3) or to ATG or other immunosuppressive therapies (0/4) were noted. One child has been successfully reconstituted by bone marrow transplantation. Children with HD differ morphologically and clinically from adults with "the pre-leukemic syndrome" by manifesting marrow hypocellularity and constitutional abnormalities. Both groups are at high risk for the development of progressive pancytopenia and myelogenous leukemia. Unlike Fanconi anemia, these children respond poorly to androgens and steroids. Results of bone marrow transplantation in one of the patients are encouraging.

774 CONGENITAL MACROCYTIC ANEMIAS OF MICE AND MEN. Harold M. Koenig and Louis K. Diamond, Naval Regional Medical Center, Oakland and University of California, San Francisco, Department of Pediatrics.

Three forms of congenital macrocytic anemia (CMA) have been defined in mice. One form can be cured only by transplantation of intact marrow and is due to a hematopoietic microenvironment defect. The other forms can be cured by transplantation of hematopoietic cells from the spleen, marrow or fetal liver and are due to intrinsic defects of erythroid progenitors in which either an early or a late arrest occurs in the cells maturation process. Diamond-Blackfan Syndrome (DBS) is a CMA of humans in which steroids repair the anemia in many patients. In this study the clinical course of 8 children with DBS was correlated with the ability of their bone marrow mononuclear cells to form erythroid colonies in methyl cellulose culture. One child did not respond to steroids but produced large numbers of erythroid colonies in culture. This child may have a defect in the hematopoietic microenvironment. Three children maintained satisfactory hemoglobin levels on low dose alternate day steroid therapy and produced normal numbers of erythroid colonies in culture. Four children required higher doses of steroids to maintain satisfactory hemoglobin levels and produced low numbers of erythroid colonies in culture. The latter two groups of children may have intrinsic defects of their erythroid progenitor cells in which a maturation arrest occurs at different stages of the cells maturation process. Correlation of clinical course with erythroid colony forming ability provides additional understanding of the defects in DBS.

775 DEOXYNUCLEOSIDE METABOLISM IN T/B HYBRID LYMPHOBLASTS: Joanne Kurtzberg and Michael S. Hershfield, Spon. by John Falletta, Departments of Pediatric Oncology and Medicine, Duke University Medical Center, Durham, N.C. 27710.

2'-Deoxycoformycin (dCF), a potent inhibitor of adenosine deaminase (ADA), has been effective in the treatment of T-cell, but not B-cell leukemias, a finding that appears to be related to the ability of T, but not B-lymphoblasts to trap deoxyadenosine (dAdo) as dATP. Both increased ability of T-cells to phosphorylate dAdo, and of B-cells to degrade deoxyribonucleotides could explain this distinction. However, differences in activities of dAdo kinases and cytoplasmic deoxyribonucleotidase in T- and B-cell lines are not sufficient to account for the 100-fold difference in their capacity to accumulate dATP. To further evaluate the basis for this phenomenon we have developed human B-cell/T-cell hybrid cell lines, and evaluated 1) sensitivity to the cytotoxic effect of dAdo, 2) ability to accumulate dATP, and 3) ability to degrade intracellular dATP after expansion of this pool by prior incubation with dAdo. We fused CEM(T) cells with either WI-L2 (B) cells, or with a double mutant derived from WI-L2 that lacked both enzymes necessary to phosphorylate dAdo (adenosine and deoxycytidine kinases = AK^--dCK^-). The concentration of dAdo required for 50% growth inhibition of CEM, WI-L2, and several CEM/WI-L2 hybrids were respectively, 0.35μM, 45μM, and 15-35μM. The hybrids were intermediate in their capacity to accumulate dATP, and in their capacity to catabolize an expanded dATP pool. CEM/AK^--dCK^- hybrids were resistant to dAdo. Our results thus far indicate that "B-ness" is dominant over "T-ness", and are consistent with the opertion in B-cells of a mechanism, possibly enhanced nucleotidase activity, that diminishes the ability to accumulate dATP from dAdo.

776 EVIDENCE FOR A TIGHTLY-LINKED SPECTRIN LATTICE IN RED BLOOD CELLS (RBC) OF NEWBORN (NB) MAN. Stephen A. Landaw, Susan C. Rathbun, and Robert L. Guancial. VA and SUNY-Upstate Medical Centers, Syracuse, New York.

Prior studies implicated a tightly-linked membrane in the NB rat as responsible for decreased deformability and survival (Ped. Res. 14:536,1980).To test for a similar change in human NB RBC, we studied spectrin extractability by 1mM EDTA (pH 8,37°C,25min) from fresh RBC ghosts of normal adults and from cord blood of normal fullterm NB. We also studied solubility of Triton X-100 (0.5%,30min,0°C) treated ghosts in cyanate-free urea (0.25-1 M). Washed Triton shells were suspended in buffer to an optical density(OD) of 0.4 at 360nm. Aliquots were added to urea and rate of change of OD determined (OD units/8min). Results were:

	NEWBORN RBC	ADULT RBC	p
Unextracted Band I,Fresh RBC(%)	18.1 ± 9.1	4.5 ± 1.6	.001
" " " ATP-depleted	36.9 ± 10.5	20.2 ± 3.9	.001
Solubilization Rate, 0.25M Urea	.033 ± .012	.055 ± .006	.01
" " " 0.5 M "	.054 ± .024	.086 ± .020	.001
" " " 1.0 M "	.146 ± .060	.209 ± .043	.01

Band I comprised 48% of total spectrin (Bands I&II) in both NB & adult RBC prior to extraction, and the ratio of spectrin to Band III was 95-96% for both. Results show that Band I is less extractable from both fresh and ATP-depleted NB RBC ghosts, and that the Triton cytoskeletons are less dissociable in urea for NB RBC at all concentrations of urea tested. We thus conclude that the RBC membrane cytoskeleton is more tightly linked in the RBC of newborn man, leading to its altered deformability & survival.

● **777** PLASMA LACTOFERRIN REFLECTS GRANULOCYTE ACTIVATION IN VIVO Joseph A. Lash, Thomas D. Coates, Robert L. Baehner, and Laurence A. Boxer. Indiana University School of Medicine, James Whitcomb Riley Hospital for Children, Department of Pediatrics, Indianapolis.

Formyl-Met-Leu-Phe (FMLP) causes polymorphonuclear leukocytes (PMN) to secrete and become "sticky" in vitro. We related these events to FMLP-induced neutropenia. FMLP was intravenously administered to anesthetized rabbits in doses ranging from 0.01 ug to 1.0 ug. Controls received phosphate-buffered saline (PBS). Blood pressure (BP), heart and respiratory rate (RR), arterial gases and pH were monitored. At intervals over one hour following injection, blood samples were obtained for absolute PMN count (AGC) and plasma lactoferrin (PLF), a constituent of PMN specific granules. High and intermediate doses of FMLP caused a dramatic but transient decrease in BP, and increase in RR. Prior to FMLP infusion, PLF levels were 6.4 ± 4.1ug/ml and AGC were 2,008 ± 1,229 (mean ± S.D.). There was a positive linear correlation between AGC and PLF prior to injection of FMLP (R^2=0.74,$p < .01$). At one minute after FMLP injection, the percent change in AGC decreased as an exponential function of dose to as low as 10% of baseline (R^2=0.86, $p < .01$) and PLF increased as an exponential function of dose to as high as 30ug/ml (R^2=0.84,$p < .01$). Thus FMLP-induced neutropenia is associated with increased levels of PLF suggesting that PMN are induced to degranulate, aggregate and manifest increased adherence to microvasculature. Furthermore the rise in PLF can be employed as a marker of PMN activation in vivo.

778 BEHAVIORAL TREATMENT FOR CONTROL OF CHEMOTHERAPY-RELATED NAUSEA AND VOMITING IN CHILDREN AND ADOLESCENTS WITH CANCER. Samuel LeBaron and Lonnie Zeltzer. (spon. by Charles Grose). The Univ. of Texas Health Science Ctr., Department of Pediatrics, San Antonio, Texas.

The effectiveness of behavioral treatment (beh. Rx) for control of nausea and vomiting was evaluated in our study of pediatric cancer patients (pts.). Twenty-eight pts. prospectively rated their nausea and vomiting, and the extent to which these symptoms "bothered" them (i.e., made them sad, worried, or physically uncomfortable) and disrupted their daily routines (e.g., school, peers, etc.). Pt. compliance with data gathering was 100%. Thirteen of these pts. (46%) reported minimal vomiting and 8 had vomiting but died or terminated their chemotherapy. The remaining 7 pts. rated their symptoms during a mean of 2.7 chemotherapy courses before and 4.4 courses following beh. Rx. Courses were matched for drug types and dosages for each pt. Drugs included adriamycin, cytoxan, vincristine, high-dose methotrexate, 5-Azacytidine, Ara-C, and L-asparaginase. Beh. Rx was designed to reduce anxiety, distract the pt., encourage positive expectations, reward "well" behavior, reduce rewards for "sick" behavior, and induce relaxation. Mean course ratings for each pt. were derived for baseline and for post-intervention time periods and were analyzed by paired t-tests. Following intervention, reductions were obtained in nausea ($p<.03$), vomiting ($p<.05$), "bother" ($p<.05$), and "disruption" ($p<.025$). We conclude that behavioral techniques can reduce vomiting and disability associated with intensive regimens of chemotherapy.

779 DEFORMABILITY, GEOMETRY AND MECHANICAL PROPERTIES OF NORMAL NEONATAL RED BLOOD CELLS. Otwin Linderkamp, Herbert J. Meiselman, Paul Y.K. Wu, Franklin C. Miller. Univ. of So. CAlif. Sch. of Med., Depts. Physiol. & Biophys., Peds., Obstet. & Gynec., Los Angeles.

Neonatal red blood cells (RBC) are less filterable and have a shorter life-span than adult RBC, suggesting that neonatal RBC are less deformable. We have studied cellular deformability of RBC by means of a counter rotating Rheoscope (D) and by measuring the pressure (Pt) required to aspirate whole cells into micropipettes with internal diameters of 3.3μm. Smaller pipettes were used to study geometric properties: viz, volume (V), surface area (SA), excess surface area beyond that required to enclose the cell volume (ESA), and mechanical properties: viz,elastic shear modulus (μ), time constant of viscoelastic recovery (tc), membrane viscosity (η=μxtc)., of RBC. Results from 10 neonatal (N) and 10 adult (A) blood samples were:

	D(τ=50 dyn/cm²)	Pt(mmH₂O)	SA(μm²)	V(fl)	ESA(%)
N	0.40+0.04	1.32+0.89*	151.6+23.2*	106.8+22.7*	39+9
A	0.42+0.07	0.72+0.38	134.3+13.5	88.4+12.8	39+8

	μ(10-3dyn/cm)	tc(sec)	η(10-3dyn sec/cm)	
N	5.4+1.3	0.138+0.026	0.75+0.20	*p< 0.05
A	6.0+1.1	0.121+0.023	0.73+0.18	

Significant differences were found only in Pt, RBC surface area and volume, while the membrane mechanical and geometrical properties were similar in both groups. There were significant positive relationships between Pt and V in individual blood samples. Increased Pt of neonatal RBC may be a result of their larger V.

● **780** DIAMOND BLACKFAN ANEMIA (DBA): HETEROGENEITY OF THE BLOCK IN ERYTHROID PROGENITOR (EP) MATURATION. J.M. Lipton, D.G. Nathan, and M. Kudisch. Children's Hospital Medical Center, Sidney Farber Cancer Institute and Dept. of Pediatrics, Harvard Medical School, Boston, MA 02115.

We have previously demonstrated that adults and children with steroid resistant DBA exhibit low to absent bone marrow EP colony growth in culture. However, DBA is usually sensitive to steroids suggesting that EP may be present in many newly diagnosed patients. To evaluate this possibility we measured EP frequency in the plasma clot cultures of marrows of 10 newly diagnosed or relapsed steroid resistant patients who were not receiving steroid therapy. 5 of 6 newly diagnosed patients (age 2-8 mos.) had normal or nearly normal marrow EP derived colonies, and all 5 responded promptly to steroid therapy. One had low EP and failed to respond. In contrast, 4 steroid resistant patients (age 13-64 mos.) had reduced to absent EP derived colonies that were in 2 cases stimulated to develop in reduced numbers only after addition of T cell derived burst promoting activity (BPA) to the culture medium. This requirement for BPA suggests immaturity of the residual EP population. These results show that DBA is a heterogeneous disorder at the progenitor level. Some patients exhibit blocks in EP maturation between CFU-E and erythroblasts and have normal EP numbers. Others have blocks between CFU-S and BFU-E, lack EP and fail to respond to steroids. Responsiveness to steroids may therefore relate to the level at which EP maturation is impaired.

781 Influence of Progenitor Maturity & Environmental Factors on Fetal Hemoglobin(HbF)Synthesis in Simian Marrow. J.M.Lipton,J.David,R.Mackiis,P.K.Pettis&D.G.Nathan Dept. of Ped., Harvard Medical School, Boston, MA & Dept. of Medicine, N.Y.U. Medical Center, N.Y. To determine if fetal hemoglobin accumulation in erythroid cells is controlled by the level of progenitor maturity from which these cells derive or by environmental factors acting on erythroblasts, we measured the growth characteristics and, by radio ligand-immunoassay the proportions of HbA and HbF in normal adult rhesus monkey marrow erythroid colonies cultured in plasma clots. Pooled CFU-E colonies contained 3-12% HbF while pooled BFU-E colonies contained 25-45% HbF. A subpopulation of CFU-E was found to form colonies in the absence of added erythropoietin(epo). These "highly epo responsive cells" (HERCs) produced small colonies with no HbF. These findings, show that simian bone marrow contains a hierarchy of erythroid progenitors which differ in globin gene expression(decreasing HbF with increasing maturity)in the colonies to which they give rise. The HbF:HbA ratio in BFU-E and CFU-E derived colonies increased in proportion to the level of crude epo in cultures, whereas burst promoting activity influenced the HbF:HbA ratio in BFU-E derived colonies only. Thus the ability to express maximal HbF in progenitor derived erythroid cells is influenced by environmental factors and progenitor maturity. We propose that erythrocytes produced in normal steady states are derived from the most mature progenitors, whereas increased HbF production in stress results from the direct differentiation of immature progenitors. HbF synthesis may be further influenced by epo and BPA action on erythroid precursors and/or progenitors.

782 LITHIUM CARBONATE (Li) THERAPY FOR NEUTROPENIA OF GLYCOGEN STORAGE DISEASE (GSD) TYPE IB. Donald H. Mahoney, Jr., Donald C. Anderson, and Arthur L. Beaudet, Department of Pediatrics, Baylor College of Medicine Houston, Texas 77030.

A clinical trial of Li therapy was undertaken in a 5-year-old boy with GSD, Type IB, variable neutropenia, and neutrophil dysfunction. Prior to therapy, absolute granulocyte numbers (AGN) ranged: 234-774/mm^3. Neutrophil function and assays revealed diminished random motility (30% of control value) and directed migration (45% of control values), by modified Boyden technique; diminished bipolar configuration change; absence of enhancement of adherence properties and distribution of surface adhesive sites with conditions of chemotactic stimulation. Colony-stimulating activity (CSA) production of patient (PT) and control (C) mononuclear cells (MNC), +/- Li at 1 meq/L, was studied using standard agar clonogenic assays and reported as colony-forming units in culture (CFUc) per 1 x 10^5/ml normal bone marrow cells. The PT was started on Li therapy at 50 mgm q 8 hours, with escalating doses. AGN >1000/mm^3 was observed by one week and remained so for the study period (8 weeks).

C - MNC		PT - MNC		No Therapy	Li Therapy	Serum Li
CSA	CSA + Li	CSA	CSA + Li	PT - AGN	PT - AGN + Li	(meq/L)
152±6	146±9	104±5	205±14	504±381	2480±1491	0.46±0.38

Neutrophil function assays, tested on two occasions during Li therapy, failed to improve. Because of problems with intermittent nausea, vomiting, anorexia, one episode of mild diabetes insipidus (serum Li = 1.35 meq/L) and compliance, this study was terminated.

● **783** THE ROLE OF COAGULOPATHY IN NEONATAL INTRACRANIAL HEMORRHAGE (ICH). Marilyn M. McDonald, Michael L. Johnson, Carol M. Rumack, Mary Anne Guggenheim, Beverly L. Koops, Wm. E. Hathaway. University of Colorado School of Medicine, Departments of Pediatrics and Radiology, Denver.

This study of the role of coagulopathy in the onset or progression of ICH followed 50 inborn infants (≤33 weeks gestation) prospectively from birth. Clotting studies were obtained within 4 hours of birth and daily for the first 72 hours. The onset and progression of ICH was documented with bedside ultrasound every 8 hours. Hypocoagulability was initially present in 15 of 20 infants who developed significant hemorrhagic complications and in 5 of 30 infants who did not (χ^2 <.001):

Initial Abnormalities		Severe ICH	No ICH	Significance
fibrinogen	<150 mg/dl	43%	0%	<.01
platelets	<150 x 10^9/l	29%	7%	<.05
micro-clotting time	>135 seconds	33%	10%	<.05
antithrombin III	<20% adult	44%	9%	<.05

No significant differences were seen in the bleeding time, $\bar{m}$ = 5.2 minutes (ICH) vs. 4.3 minutes (no ICH), the monomer test (positive in the majority of both groups) or the prothrombin time, $\bar{m}$ = 18.9 seconds (ICH) vs. 18.7 seconds (no ICH). Serial clotting studies done on the second and third days of life were not significantly abnormal or different in both the ICH and no ICH infants. Gestational complications that were related to both initial hypocoagulability and ICH were premature labor and chorioamnionitis; fetal distress was most related to hypocoagulability. In conclusion, early coagulopathy is frequently seen in premature infants who develop ICH.

● **784** OPTIMAL DURATION OF THERAPY IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL). Denis R. Miller, Sanford Leikin, Vincent Albo, Harland Sather & Denman Hammond. Childrens Cancer Study Group (CCSG), Los Angeles, Ca. 90031.

Determination of the optimal duration of maintenance therapy is important in ALL to minimize potential late effects. Previous CCSG studies showed a significantly higher relapse rate in patients (pts), particularly males, whose therapy was discontinued after 3 years of complete continuous remission (CCR). In CCG 141, pts in CCR for 3 yrs. were randomly assigned to 1 of 3 regimens: A = discontinue (DC) therapy; B = reinduction then DC; C = continue maintenance for 2 more years then DC. 235 boys had bilateral open wedge testicular biopsies; 21 (8.9%) with occult disease were not randomized. Of 880 pts entered on study, 490 (56%) were in CCR at 3 yrs. Of the 310 pts randomized (R), 100 were in Reg. A, 103 on Reg. B, and 107 on Reg. C. Of the 157 nonrandomized (NR) pts, 94 received Reg. A, 5 Reg. B, and 58 Reg. C. 23 pts were randomization exceptions. 226 pts (161 R, 65 NR) have been followed for 5 yrs or more in CCR. Disease-free survival (DFS), hematologic remission (HR), and extramedullary relapses were not statistically significantly different in R and NR pts on Reg. A, B, and C. The death rate was higher in pts on Reg. C but the differences were not significant. Of 34 first adverse events (FAE) 22 occurred in males, 12 in females (p=0.03). Off therapy (Reg. A & B) 17/23 FAE were in males. Nine of the 11 pts on Reg. C with FAE (5 males, 6 females) have died; 5 after BM relapse and 4 unrelated to relapse. In conclusion, 3 years of maintenance therapy in pts in CCR appears adequate, but boys have a higher relapse rate than girls.

785 HEMATOLOGIC/GENETIC DISORDERS OF SE ASIAN REFUGEES Carlos M. Monzon, E. Omer Burgert, Jr., Virgil F. Fairbanks, and Stephen O. Elliott-Mayo Graduate School of Medicine, Mayo Clinic, Department of Pediatrics, Rochester, MN

Resettlement introduced many Indochinese to the US. Of 561 persons (136 families) studied there were 258 Tai Dam, 160 Khmer, 35 Hmong, 82 Lao Loum, and 26 ethnic Vietnamese. Tables I & II show gene frequency for G-6PD def., α-Thal, β-Thal, and Hb E.

Table I Gene Frequencies

	n*	G-6PD
Khmer	85	0.30
Viet	13	0.38
Hmong	15	0.33
Lao Loum	17	0.18
Tai Dam	54	0.18

*n=no. of unrelated male

Table II Gene Frequencies

	N*	Hb E	α-Thal$_1$	β-Thal
Khmer	138	0.17	0.04	0.0
Viet	22	0.00	0.11	0.0
Hmong	60	0.00	0.06	0.0
Lao Loum	66	0.21	0.06	0.0
Tai Dam	206	0.06	0.07	0.04

*N=no. of chromosome studied.

Among 184 unrelated males 27% had G-6PD def. Hb E is common in Khmer and Lao Loum but thus far none is found in Viet and Hmong. The Tai Dam show β-Thal-minor, and they have a predictive prevalence for severe thalassemic disorders (β-Thal major and E/β-thalassemia) of 6/1000. This prevalence is about 10X that of Italians and Greeks. Although microcytosis (Tab. III) is in 199 (35%), Fe Def. was infrequent; & Hb E & α-Thal were more frequent.

Table III Cause of Microcytosis

	n	Fe Def (%)	Hb E (%)	α-Thal$_1$ (%)	β-Thal (%)
Khmer	62	7	27	5	0
Viet	5	0	0	19	0
Hmong	4	9	0	2	0
Lao Loum	36	4	40	5	0
Tai Dam	92	6	10	8	9

786 CORD BLOOD GRANULOPOIETIC PROGENITOR CELLS (CB-CFU-C's): EFFECT OF FETAL AND MATERNAL FACTORS. Ronnie W. Neuberg, David A. Clark, Jack Goldberg, Eileen M. Willcox, Lorraine A. McGuire (Spon. by James A. Stockman, III). Depts. of Pediatrics and Medicine, SUNY Upstate Medical Center, Syracuse, NY

CB-CFU-C's of 25 newborns (18 normal full term, 4 infants of diabetic mothers (IDM), 2 preterm infants and 1 infant of a mother treated for acute leukemia (AL) during pregnancy) were evaluated using a double layer agar culture technique. Normal full term CB yielded a mean of 1425 colonies/ml. The number of CB-CFU-C's was not influenced by mode of delivery, apgar scores, or CB total WBC, absolute neutrophil count (ANC) or hemoglobin. The mean CFU-C/ANC ratio was 0.41. Cultures of CB obtained from IDM's formed a mean of 2700 colonies/ml with a CFU-C/ANC ratio of 0.72. Cultures of CB from 2 preterm infants yielded less colonies (200/ml) than observed in normals. A 34 wk gestation infant, born to a woman receiving chemotherapy for AL was also evaluated. The number of CB-CFU-C's from this infant was not significantly increased (3210/ml) but the ratio of CFU-C's/ANC (2.68) was well outside the range determined for normal full term or preterm infants. Thus, CB-CFU-C's were not affected by the various maternal and newborn parameters examined. Preterm infants may have lower numbers of CFU-C's/ml in CB, however, this was not statistically significant in our small group of patients. The data on the infant born to the mother with AL suggest that when marrow suppressive agents are given to a pregnant female, they may affect fetal hematopoiesis.

● **787** NEUTROPHIL DYSFUNCTION WITH GIANT LYSOSOMES AND DEFECTIVE RESPIRATORY BURST ACTIVATION. P.E. Newburger, J. Robinson, K. Pryzwansky, & G. Vawter (Spon. by J.B. Hanshaw). Univ. Massachusetts Medical Center, Worcester; Harvard Medical School, Boston; Univ. North Carolina, Chapel Hill.

We describe a patient whose peripheral blood neutrophils (PMN) and bone marrow precursors (beyond promyelocyte) contained multiple large azurophilic granules. There were also giant granules in eosinophils, basophils, melanocytes, renal tubules, thyroid, and neurones. Immunofluorescent staining with fluoroscein- and rhodamine-conjugated antibodies to 1^{o} and 2^{o} granule markers showed virtually all of the PMN granules to be fusion products containing both markers. Electron microscopy showed the granules to be large peroxidase-containing lysosomes. Only rare normal 1^{o} and 2^{o} granules were present. Superoxide generation in response to opsonized zymosan(OZ) was 7.3 nmol/min/10^{6} cells (control 8.9); but in response to phorbol myristate acetate(PMA), only 2.2(control 9.4). Nitroblue tetrazolium slides showed dye reduction in response to OZ by 90% of PMN (control 91%) and to PMA by 22% (control 99%). Degranulation was normal, as was ingestion of opsonized particles. Killing of Staph. Aureus was 60% at 90 min incubation (control 92%). PMN cyclic AMP content was 4 pmol/10^{7} cells (control 3.1). In order to determine whether these characteristics derived from the cells' genetic program or their environment, the patient's bone marrow was grown in long term culture. PMN produced in vitro demonstrated the same morphology and normal cAMP level as those in vivo. These studies describe a new disorder of PMN; the structural similarity to, but biochemical differences from, Chediak-Higashi Disease indicate the probably heterogeneity of mechanisms for the same morphologic abnormality.

788 MALIGNANT POSTERIOR FOSSA TUMORS OF CHILDHOOD-ENDOCRINE FUNCTION-STATUS POST RADIATION AND CHEMOTHERAPY. S.E. Oberfield, J. Pareira, J.C. Allen, B. Jereb, L.S. Levine, D.R. Miller, M.I. New, The New York Hospital-Cornell Med Ctr, and Memorial Sloan-Kettering Cancer Ctr, New York NY 10021.

Eleven patients (6 male, 5 female) who had received standard neuraxis radiation with (n=7) or without (n=4) chemotherapy for treatment of posterior fossa tumors (medulloblastoma (n=10), ependymoma (n=1)), had hypothalamic-pituitary target organ axis evaluation at 3-53 months after completion of treatment. The age range at initiation of treatment was 3 7/12-23 8/12 yrs and age range at time of evaluation was 4 1/12-24 1/2 yrs. The radiation treatment consisted of approximately 3600 rads to the neuraxis with a 1500 rad boost to the posterior fossa. The approximate mean radiation dose to the hypothalamic-pituitary region and thyroid gland were 3600 and 2300 rads respectively. In 9/11 patients the skeletal age was within one year of the chronological age. Growth hormone reserve was deficient in 5/11. Somatomedin C was decreased for age in 2/9 patients. Cortisol response to insulin-induced hypgolycemia was inadequate in 1/7. TSH response to TRH testing was performed in 9 patients and was normal in 3, compatible with 1^{o} thyroid dysfunction in 5 and suggestive of hypothalamic dysfunction in 1. One patient developed abnormal thyroid function 12 mos after an initially normal evaluation. Since endocrine evaluation was not obtained prior to therapy, we cannot be certain that the decribed abnormalities were a consequence of treatment. However our results argue that children who have received CNS radiation for malignant posterior fossa lesions should have continued evaluation to allow for early detection of hormonal deficiencies and institution of appropriate replacement therapy.

789 HLA HISTOCOMPATIBILITY BETWEEN PARENT AND AFFECTED CHILD IN FANCONI'S ANEMIA. Richard J. O'Reilly, Marilyn S. Pollack, Arleen D. Auerbach, Neena Kapoor, Dahlia Kirkpatrick, R.S.K. Chaganti, Bo Dupont. Memorial Sloan-Kettering Cancer Center, New York, New York 10021

Fanconi's anemia is a genetic disorder characterized by congenital malformations, abnormal chromosomal instability and progressive marrow failure. Inheritance patterns suggest an autosomal recessive disorder but with genetic heterogeneity. Histocompatibility studies were performed on 11 patients with Fanconi's anemia documented by clinical and cytogenetic findings. Parental consanguinity could be established in only 1 case. Nevertheless, by virtue of parental sharing of HLA haplotypes, 6/11 patients were found to be HLA-A,B identical to either the mother (5 cases) or the father (1 case). Of these 6 patients, 5 were also shown to be HLA-D identical to one of their parents. An additional patient, found to be HLA-D compatible with his mother, was mismatched only for an HLA-B specificity. Patients did not exhibit common HLA phenotypes, nor was an abnormal frequency of any phenotype observed. That the disorder is not linked to HLA, is suggested by the identification of normal heterozygotes for this disorder among the patients' HLA-matched siblings. The higher incidence of histocompatibility between Fanconi's anemia patients and their parents is not explained. Materno-fetal histocompatibility is known in animals to influence fetal growth and hematopoietic development. Whether such compatibility affects the clinical expression of the genetic defects of Fanconi's anemia remains to be determined.

790 PROGNOSTIC FACTORS THAT PREDICT THE RESPONSE OF PATIENTS WITH HISTIOCYTOSIS-X TO THYMIC EXTRACT (SUPPRESSIN) THERAPY. Michael Osband and Philip Lavin, Boston U Med Ctr and Sidney Farber Cancer Ins (Spon. by J. Alpert)

We have reported (NEJM 304:146) that approximately 60% of histiocytosis-X patients will respond to therapy with suppressin (thymic extract), a derivative of calf thymus that induces suppressor T-cells. We studied 4 factors to see whether they could predict patient response: 1)clinical stage, 2) # of T-cells with H2 type histamine receptors (H2R+ cells), 3) ratio of T-cells with H1 receptors (helper cells) to those with H2 receptors (suppressor cells)(H1R+:H2R+), 4) induction of H2R+ suppressor cells by incubation in suppressin. In this study, 13/20 patients responded to suppressin (65%). The responding patients were from all clinical stages, and stage was not useful as an indicator. The other 3 factors were all significantly predictive of response to suppressin therapy. These data indicate that those patients who are characterized by low numbers of H2R+ suppressor cells, a high helper to suppressor cell (H1R+:H2R+) ratio, and increased suppressor cells after incubation in suppressin, may constitute a biologically distinct subset of patients who are immunologically abnormal. Perhaps suppressin therapy should be limited to use in these patients.

factor	# responders/ # treated	p value
# H2R+ cells		
low	11/13	<.02
normal	2/7	
H1R+:H2R+		
high	11/13	<.02
normal	2/7	
in vitro induction of suppressors		
yes	12/12	<.0001
no	1/8	

791 CORD BLOOD POLYMORPHONUCLEAR LEUKOCYTE AGGREGATION Ronald S. Oseas, Eric M. Toloza and Michael E. Miller. UCLA School of Medicine, Harbor-UCLA Med.cal Center, Dept. of Pediatrics, Torrance, Ca.

In vitro aggregation of cord blood or neonatal polymorphonuclear leukocytes (PMN) has not been fully evaluated. Using a spectrophotometric aggregometer/recorder system, we studied the responses of cord blood PMN(CPMN) to soluble chemotactic and their metabolic and divalent cation requirements. Using n-formyl-methionyl-leucyl phenylalanine(FMLP),adult PMN exhibited a dose dependent response of 19cm^{2} at 2 x 10^{-9}M, 23cm^{2} at 2 x 10^{-7}M and 29cm^{2} at 2 x 10^{-5}M. CPMN also had a dose dependent response of 20cm^{2}, 25cm^{2} and 30cm^{2} respectively. Pre-incubation with cytochalasin B (CB) resulted in a potentiation of the aggregation responses of both adult PMN and CPMN. Optimal aggregation occurred in the presence of both Ca^{+2} and Mg^{+2}. CPMN stimulated by FMLP after incubation with CB in media devoid of divalent cations demonstrated an aggregation response (28cm^{2}) whereas the adult PMN did not (20cm^{2}). The glycolytic inhibitors 2 deoxyglucose and KCN blunted the aggregation responses of both CPMN and adult PMN by 50%. The mitochondrial toxins NaF and Iodoacetate had no effect on aggregation. Stir bar rate also did not affect the amplitude of aggregation of the CPMN or adult PMN. Unlike recently reported deficient aggregation response of CPMN, these studies show similarities in the metabolic requirements and aggregation responses of adult and CPMN, while a significant difference in divalent cation requirements is demonstrated when CPMN are rendered secretory with CB.

792 A MICROMETHOD OF POLYMORPHONUCLEAR LEUKOCYTE AGGREGATION. Ronald S. Oseas, Eric M. Toloza and Michael E. Miller. UCLA School of Medicine, Harbor-UCLA Medical Center, Dept. Pediatrics, Torrance, Ca.

Polymorphonuclear (PMN) leukocytes become chemotactic, degranulate, and aggregate upon stimulation with soluble chemotactic factors such as n-formyl-methionyl-leucyl-phenylalanine (FMLP). We have devised a modification (micro) of the in vitro spectrophotometric aggregation assay of Craddock et al requiring as little as 5×10^5 PMN per sample. Quantitation of FMLP induced aggregation was accomplished using a polar planimeter and demonstrated a dose dependent effect of $17cm^2$ at 2×10^{-9}M, $23cm^2$ at 2×10^{-7}M and $29cm^2$ at 2×10^{-5}M in the macro method. A response of $19cm^2$, $29cm^2$ and $36cm^2$ was seen using the micromethod. PMN rendered secretory with cytochalasin B (CB) 2.5µg/ml resulted in potentiation of the aggregation response with FMLP 2×10^{-7} of 35% in the microassay and 45% in macroassay. Correlation between both assays on both secretory (r_s=.96) and non secretory (r_{ns}=.85)PMN was high. In both the macro and micro assays aggregation was blunted by the glycolytic metabolic inhibitors 2 deoxy-d-glucose (1mM) and Iodoacetate (1mM) by 50%. No suppression of the aggregation response was seen with the mitochondrial toxins NaF and KCN. Divalent cations (Ca^{+2} and Mg^{+2}) were required for an optimal aggregation response to FMLP. The amplitude of the FMLP induced aggregation was not affected by changes of stir speed from 300 to 1200 RPM. Reduced cell numbers, sample size, and quantitation allows the use of aggregometry studies of the PMN in the pediatric population and neonatal PMN which are known to be functionally deficient.

793 ACUTE LUNG SYNDROME DURING NARCOTIC THERAPY OF PAINFUL TRUNCAL CRISIS IN SICKLE CELL DISEASE Judy Palmer, Karen J Auchinleck, J Lawrence Naiman Temple University School of Medicine, Department of Pediatrics St. Christopher's Hospital for Children, Philadelphia

Acute respiratory disease (ARD) is a common problem among children with sickle cell disease (SCD), and is especially prevalent during painful truncal crisis (PTC). We have observed in patients hospitalized for PTC with normal initial physical and radiographic chest examinations, the development 2 to 4 days later of an acute lung syndrome (ALS) characterized by fever, tachypnea, and infiltrates on chest radiograph. This delayed ALS accounted for 23% of all cases of ARD occurring in patients hospitalized for pain, and was limited to those with trunk pain. To identify possible etiologic factors, we compared the 12 PTC/ALS admissions with the 22 other admissions of the same 10 patients for PTC without ALS. There were no significant differences with respect to age, antecedent URI, admission findings (temp.,resp. rate, WBC and diff.), isolation of bacterial pathogens, or antibiotic administration. Slightly more fluids were received during PTC/ALS admissions. Narcotic administration was compared by assigning analgesic equivalent units according to established analgesic ratios, and a narcotic score was calculated for the first 48 hours of treatment. The mean narcotic score (± SE) for PTC/ALS admissions was 21 (± 4) as compared to 6 (± 1) for those PTC admissions not associated with ALS ($p < 0.0005$). The association of ALS with PTC and high narcotic score suggests hypoventilation as an etiologic factor in the development of this common, possibly preventable, complication of painful crisis.

● **794** BONE MARROW ABNORMALITIES IN LEUKEMIA REMISSION PATIENTS OFF CHEMOTHERAPY. Elliott R. Pearl and Hernan Sabio (Spon. by T. Kelly) Univ. of Virginia Medical Center, Univ. of Virginia Hospital, Dept. of Pediatrics, Charlottesville, VA 22908

Pre-B cells comprise a fraction of bone marrow lymphoid cells that contain cytoplasmic IgM heavy chain but lack detectable surface immunoglobulin (sIg). Considerable evidence suggests that they are the immediate precursors of B lymphocytes. Using immunofluorescence techniques, we analyzed the proportion of lymphoid cells, B lymphocytes and pre-B cells in marrow aspirates from children with acute leukemia in long-term remission and off of all chemotherapy. Control marrows were from healthy adults and from children with disorders not involving bone marrow. Results are expressed as mean ± S.D. percent of lymphoid cells.

	sIgM+ B cells	pre-B cells	pre-B/B cells
Patients (n=14)	21.4 ± 8.1	43.0 ± 15.5	2.10 ± 0.58
Controls (n=23)	19.7 ± 11.5	4.4 ± 3.3	0.31 ± 0.29
p value	> 0.5	< 0.001	< 0.001

The proportion of pre-B cells correlates positively with B cells in the patients ($r=0.7$, $p<0.01$) but not in controls ($r=0.2$, $p<0.2$). The abnormalities persist for more than 2 years and do not relate to time following cessation of chemotherapy. These results suggest that a disordered maturation sequence early in B cell development may persist in these patients. Such a defect could be either intrinsic or extrinsic to the marrow microenvironment.

795 SPLENIC FUNCTION IN SICKLE CELL DISORDERS. Howard A. Pearson, John Falletta, Robert Chilcote, Rita Bellevue, Edmund Sullivan, and Jennifer Horton. Yale University, Duke University, University of Chicago, and University of Illinois Schools of Medicine, Jewish Hospital of Brooklyn, New Haven, Durham, and Chicago.

For the Cooperative Study of Sickle Cell Disease

As part of our national study of the clinical course of sickle cell diseases, splenic function has been systematically assessed in more than 1000 patients with various sickling disorders. Blood was collected in the 27 individual centers, fixed in buffered 3% glutaraldehyde, and shipped to a central lab for enumeration of percent pocked RBC using interference phase-contrast microscopy. In HbSS disease, a rapid and progressive increase in pocked RBC was seen after 6 months of age. Although there was considerable individual variability, most patients had >3% pocked RBC after 1-2 years of age. A pocked RBC percentage of >3-5% correlated with functional hyposplenia by ^{99m}Tc scans. 14 children who developed severe bacterial infections had high percentages of pocked RBC. Patients with SC disease had slight impairment of splenic function which did not progress with age. Distinctly different patterns of splenic function were seen in patients with Hb Sβ° and those with Hb Sβ$^+$ thalassemia. Hb Sβ$^+$ thalassemia approximated SC disease, while Hb Sβ° thalassemia resembled HbSS. These patterns provide insights into splenic function in the various sickling disorders. They may also assist in formulation of management strategies for anticipation and prevention of serious bacterial infections in these patients.

796 **RHABDOMYOSARCOMA (RMS) OF THE MIDDLE EAR IN CHILDREN: A REPORT FROM THE INTERGROUP RHABDOMYOSARCOMA STUDY (IRS), 1972-1980.** **R. Beverly Raney, Jr., Walter Lawrence, Jr., Harold M. Maurer, Robert D. Lindberg, William A. Newton, Jr., Abdelsalam H. Ragab, Melvin Tefft, and Mary Foulkes, for the IRS Committee of the CCSG and POG. Children's Hospital Cancer Research Center, Philadelphia, PA 19104.**

32 patients (pts) with middle-ear RMS were treated on IRS protocols (J Pediatr Surg 10:977; 15:371) with radiotherapy (RT) and VAC ± adriamycin. The median age at diagnosis (dx) was 5 yr.; 17 were male and 15 female. One pt had microscopic residual tumor (Group II) after grossly complete removal. 24 pts had gross residual local tumor (Gp. III) after biopsy (20 pts) or mastoidectomy (6 pts). 7 pts had distant metastases at dx (Gp. IV). Currently 14/25 pts (56%) with localized sarcoma continue in relapse-free survival (RFS) at 1-5.7 yr. after dx (median, 2 yr.). Only 1/7 Gp. IV pts is in RFS. 17 pts relapsed at 0.3-6.6 yr. after dx (median, 0.6 yr.); 15 died. Sites of initial recurrence included the meninges (7 pts), distant metastases or local regrowth (4 pts each), regional recurrence (1 pt), or contralateral glioma (1 pt). Outcome was also influenced by signs at dx indicating risk of meningeal tumor: intracranial extension (ICE), petrous bone erosion (BE), or cranial nerve palsy (CNP). RFS rates were 0/6 pts with ICE, 4/9 with BE, 5/8 with CNP, and 6/9 without meningeal risk signs. The addition of cranial RT and intrathecal drugs, begun in 1977, appears to prevent meningeal relapse in 80% of high-risk pts. We conclude that current treatment programs can often cure pts with middle-ear RMS, formerly a universally fatal disease.

797 CIRCULATING PLATELET AGGREGATES IN NEWBORN INFANTS: Sudha Rao, Arvind Shukla, Raymond Olesinski and D. Vidyasagar. Abraham Lincoln School of Medicine, University of Illinois Hospital, Department of Pediatrics, Chicago, Illinois.

Platelets from normal newborn infants demonstrate impaired aggregability to "in vitro" testing when compared with platelets from normal adults. In order to determine if "in vivo" platelet aggregability is altered in newborn infants, we determined the circulating platelet aggregates (CPA) and the microthrombus index (MI) in 20 normal newborn infants between 1-7 days of age (mean age 1½ days) by the method of Wu and Hoak. Mothers of infants chosen were not on any antenatal medications. 20 normal adults were used as controls. CPA% in the infants ranged from 0-35% which was slightly higher than the adult CPA range of 0-25%. The CPA% (mean ± SEM) for the infants was 8.02 ± 5.34 and 10.38 ± 3.98 for the adults. There was no significant difference between the two groups. The MI ranged from 0.5-1.5 in the infants as compared to 0.4-1.3 in the adults. The MI (mean ± SEM) was 0.89 ± 0.39 for the adults and 0.919 ± 0.053 for the infants. Again, there was no significant difference between the two groups. There was no apparent correlation between either sex, race or age and the CPA%.

We conclude that although "in vitro" platelet aggregability is impaired in newborn infants, platelet aggregation "in vivo" is apparently adequate. There is no evidence of hyperaggregability "in vivo" (suggestive of endogenous activation) to account for the decreased aggregability "in vitro".

798 HEMOLYTIC ANEMIA ASSOCIATED WITH SEVERE MICROCYTOSIS, ELEVATED INTRACELLULAR CALCIUM (Ca) AND LOSS OF SPECTRIN. Yaddanapudi Ravindranath and Robert Johnson. (Spon. by S. Inoue). Children's Hospital of Michigan; Departments of Pediatrics and Biochemistry, Wayne State University School of Medicine, Detroit, MI.

This report concerns a 12 month old black female infant with hemolytic anemia. Hb values range between 8.0-9.0 gms.%, Hct 19%-27% and retic counts 20-36%. Despite the high retics MCV ranged from 46-63 u^3. Osmotic fragility was markedly increased. Peripheral smears showed extreme microspherocytosis, poikilocytosis and fragmentation of red cells - a morphology resembling that of hereditary pyropoikilocytosis. However, thermal sensitivity could not be demonstrated with by incubating the red cells for up to 6 hours at 45°C or by measurement of circular dichroism of separated spectrin at 220 nm. Intracellular electrocyte determinations showed markedly increased Ca and slight lowered K (see table). SDS gel electrophoresis of the membrane polypeptides demonstrated a relative lack of spectrin as measured by densitometric scanning of Coomassie Blue stained gels.

	Ca (nmol/G Hb)	K (umol/G Hb)	Spectrin (% of total stability)
Patient	173	245	25
Mother	40.1	287	39
Father	18.4	273	35
Normals	15	278-294	38± 2.3 (N=7)

Severe sphering and fragmentation are probably secondary to the membrane instability induced by the loss of spectrin. The exact relationship of the high intracellular Ca to spectrin is unclear.

● **799** RANDOM AND DIRECTED CELL MOTILITY IN ACUTE LEUKEMIC LYMPHOBLASTS - CORRELATION WITH Fc-IgM RECEPTOR (Fc-IgMR) EXPRESSION Gregory Reaman, Jane Zaloudek, & Sanford Leikin. George Washington Univ., Children's Hospital National Medical Center, Department of Hematology/Oncology., Washington, D.C.

In an attempt to demonstrate biological explanations for factors which appear to have prognostic importance in children with acute lymphoblastic leukemia (ALL), we compared the random and directed motility of leukemic cells from 32 pts. with ALL (4 T cell, 28 non-T, non-B ALL) to that of normal peripheral blood lymphocytes (PBL). Random motility was assessed in a closed, double chambered system by determining the percentage of cells crossing a nucleopore membrane filter with a pore size of 8u following a 3 hr. incubation period. Directed motility of leukemic lymphoblasts was examined in response to a casein gradient and was found to be <50% of that of normal PBL. Mean random motility of both T and non-T, non-B ALL cells (15%) was similar to that of normal PBL (18.3%). However, a marked correlation between increased locomotor activity and Fc-IgMR expression was observed for both normal T lymphocytes and leukemic lymphoblasts. A nearly two-fold increase in random motility was observed in Fc-IgMR+ ALL cells. Fc-IgMR expression and increased motility were observed in the lymphoblasts from 8 of the 28 non-T, non-B ALL patients. Furthermore, all 8 of these pts. were < 3 or > 10 years of age and had WBC counts > 10,000/mm3. These data demonstrate that ALL cells exhibit diminished chemotactic ability and suggest possible biological differences in leukemic lymphoblasts from pts. with known adverse prognostic characteristics.

800 THE INCIDENCE AND SIGNIFICANCE OF HEMOGLOBIN BART'S IN CORD BLOOD. Patricia Reilly, Ganesh N.Deshpande. (Spon. by J.R. Humbert). Children's Hospital of Buffalo, Department of Pediatrics, State University of New York at Buffalo, Buffalo, NY.

Previous studies have demonstrated the relation of alpha thalassemia and hemoglobin (Hb) Bart's in cord blood. We quantitated Hb Bart's in 158 (125 white, 33 black) random cord blood samples by microchromatography (Isolab, Akron, Ohio). All babies had measurable quantities of Hb Bart's. Normal babies (defined as having a mean corpuscular volume (MCV) > 105) had a 0.91 ± 0.3% Hb Bart's. There was no significant difference in the mean Hb Bart's level between white/black babies.

The presence of increased Hb Bart's (> 2 SD) along with low MCV (< 105) and negative discriminant function (DF) were used for evaluation of alpha thalassemia.

The following results were obtained:

Hb Bart's > 2 SD	Low MCV	Negative DF
Black (n = 10)	9/10	8/10
White (n = 9)	4/9	3/9

Statistical tests failed to show any correlation between increased Hb Bart's, low MCV, and negative DF.

It is concluded that while the presence of an increased amount of Hb Bart's accompanied by low MCV and negative DF may suggest alpha thalassemia, the presence of measurable amounts of Hb Bart's in cord blood is common to all babies.

801 "The Use of the Positive Pressure Cell Filtration System (PPCFS) in a Study of the Effect of Perfluorocompound (FC-43) on the Rheology of Sickle Erythrocytes

Perfluoro-compounds dissolve large amounts of gases. They have been used as oxygen-carrying blood substitutes to sustain life. Perfluorotributylamine (FC-43), a very stable perfluoro-compound, was used to study its effect on the rheology of sickled erythrocytes Studies done last year by Dickson and Reindorf have shown that FC-43 does reduce the viscosity of sickled erythrocytes. This year the Positive Pressure Cell Filtration System (PPCFS) was used to study the effect of FC-43 on sickled erythrocytes. Deoxygenation of sickle cell anemia blood (HbSS) caused an increase in sickling with increases in the relative resistance (R_r). The study showed that oxygenated FC-43 effectively reduced the relative resistance of deoxygenated HbSS blood by reducing the percentage of sickled cells. The study indicated that there may be future clinical uses for perfluoro-compounds as oxygen carriers. The PPCFS was the first of its kind built at Howard University.

Carl A. Reindorf, MD.
Theopolis Gilliam, Jr.

802 THE USE OF THE POSITIVE PRESSURE CELL FILTRATION SYSTEM (PPCFS) IN A STUDY OF THE EFFECT OF PERFLUORO-COMPOUND, PERFLUOROTRIBUTYLAMINE(FC-43), ON THE RHEOLOGY OF SICKLE ERYTHROCYTES.
Carl A. Reindorf, Theopolis Gilliam,Jr., Joseph Kurantsin-Mills

Perfluoro-compounds dissolve large amounts of gases. They have been used as oxygen-carrying blood substitutes to sustain life. Perfluoro-tributylamine(FC-43), a very stable perfluoro-compound, even in the emulsified state, has been used to study its effect on the rheology of sickled erythrocytes. Following our discovery that FC-43 reduces the viscosity of sickled erythrocytes the Positive Pressure Cell Filtration System(PPCFS) has been used to study the effect of FC-43 on sickled erythrocytes. Deoxygenation of sickle cell anemia blood caused an increase in sickling, with subsequent increase in the relative resistance (R_r). The study further showed that oxygenated FC-43 emulsion effectively reduced R_r of deoxygenated sickle cell anemia blood by reducing the percentage of sickled cells. Future clinical uses of perfluoro-compounds as oxygen-carriers include:-1. Supplying oxygen for the reversal of sickling of erythrocytes entrapped in hypoxic areas of erythrostasis in the microvasculature.2.Delivering oxygen to the tissues which would otherwise be infarcted as a result of erythrostasis and vascular obstruction that could occur in vaso-occlusive crisis. 3.Transfusing stroke patients who need monthly blood transfusion in order to prevent recurrence.4.Saving the life of a sickle cell patient in acute aplastic crisis, or sequestration crisis or acute hemolytic crisis but cannot take blood because of alloimmunization, or religious reasons.

803 Hematologic Indices of Umbilical Cord Blood Specimens from FA and FAS (Normal and Sickle Cell Trait) infants

A study was done to determine the normal range of value for Hct, Hgb, WBC, RBC, MCV and ESR on umbilical cord blood of infants born at Howard University Hospital. Since using blood from the umbilical cord is very non-invassive to the infant, it is very convenient to use in experiments. Knowing the normal range to expect in these infants can possibly be beneficial in detecting a disease process. The purpose of this paper is to describe the normal range of values for Hct, Hgb, WBC, RBC, MCV and ESR on umbilical cord blood. To determine if there is any significant difference of indices between infants of genotype FA and and those with the genotype FAS and determine if there is any difference in indices with birth weight.

Carl A. Reindorf, Gail Nunlee and Jeanie Westry

804 Study of The Mean Corpuscular Hemoglobin (MCH) in Cord Blood from Black Newborn Babies

Erythrocyte indices in cord blood samples from 277 black newborn babies were determined using an electronic cell counter (Model ZBI, Coulter Electronics). The mean red cell volume (MCV) was 109μ3 (± 7.93 SD). The mean corpuscular hemoglobin (MCH), a value that remains constant despite possible time-related changes in red cell volume, had a lower coefficient of variation (6%). The mean MCH was 35.57±2.13μμg with a mode of 36.0μμg. The MCH was unrelated to sex or birth weight. The mean MCH in 20 newborn babies with an FAS blood hemoglobin phenotype (35.38± 2.51μμg) was not significantly different from that of the total population.

The incidince of electrophoretically detectable Bart's Hemoglobin was 3.2%. The mean MCH in these cord blood samples was 32.18±2.5 μμg (N=9), a value that was not significantly lower ($p<0.001$) than that of the total population. However, 35 cord blood samples (12%) had an MCH of 32μμg or less. Among these only 4 had Bart's Hemoglobin. Although 5 of the 9 samples with Hb Bart's had an MCH of 32μμg or higher, none was greater than 35.7μμg.

Therefore, follow-up studies of all newborn babies with low MCH, including globin synthesis studies are necessary for determining whether these children have alphathalassemia despite absence of detectable quantities of Hb Bart's at birth.

Carl A. Reindorf, Jeanie Westry, Gail Nunlee, William P. Winter, Oswaldo Castro and Roland B. Scott

805 STUDIES OF ERYTHROID PROLIFERATION IN CHILDHOOD LEUKEMIA. A.Kim Ritchey and Nancy Abrams. (Spon by D. Komp). Yale University School of Medicine, Department of Pediatrics, New Haven, CT.

To elucidate the interaction of childhood leukemia and erythroid stem cell proliferation we studied bone marrows (BM) from 5 children with ALL (4 newly diagnosed; 1 relapsed - M3) utilizing the plasma clot culture technique. Erythroid colony-forming-units (CFU-E) were absent in the new patients and markedly reduced in the relapsed patient ($4/10^4$ nucleated cells) compared to controls (58±6, SEM). During early complete remission (3 pts), CFU-E proliferation remained subnormal (0,0,17), but increased subsequently in 1 patient studied (34). The relapsed pt. had subnormal colony formation at time of partial (M2) remission (16 CFU-E) and normal numbers with complete remission (55±3). To further study the effect of leukemic cells on erythroid growth conditioned media (CM) from 4 pts. were obtained by incubating leukemic BM or peripheral blood (66% blasts) in RPMI plus 10% fetal calf serum for 4 days. When added to cultures of normal allogeneic BM, 10% CM from 2 pts. inhibited CFU-E production by 40% when compared to normal control BM CM. When added to the patient's own remission marrow, 10% CM caused 25% and 70% inhibition, respectively. CM from the other 2 pts. had either minimal or no effect in either the allogeneic or autologous system. We conclude that the leukemic process in childhood ALL decreases the functional erythroid stem cell pool. Our results suggest that one of the causes of this effect is the production of a soluble factor by leukemic cells which directly inhibits erythroid proliferation.

806 ASSESSMENT OF CELLULAR AND HUMORAL IMMUNITY IN PTS WITH SICKLE CELL ANEMIA. Robert D. Ronnlund, Vipul N. Mankad, Donna D. Phelps and Robert M. Suskind. Univ. of South Ala., Coll. of Med., Dept. of Ped., Mobile, Alabama.

29 patients (18 M, 11 F) with documented SS hemoglobin disease were evaluated for the following cellular and humoral immune parameters: T-cell percentage, percent T-gamma cells, cytotoxicity by K and NK cells, response to the mitogens Con-A, PHA and PWM, and serum levels of IgG, IgM, IgA, IgD, C_3 and C_4. In the functional testing a subject was considered abnormal if his value were below the lowest normal control value. It was found that 21/21 had ↓ T-cell percentage as measured by SRBC rosettes (40.3↓ 10.2* vs 70.1±5.0 $p<.001$). 28/28 had an ↑ percentage of T-gamma cells as measured by rosetting nylon wool non-adherent cells with IgG coated OX-RBC (37.8±8.5 vs 14.9±5.1 $p<.001$). 10/19 had ↓ K cell lysis of IgG coated CRBC (38.7±18.1 vs 66.2±19.3 $p<.01$). 9/15 had ↓ NK lysis of K-562 (32.5±19.9 vs 67.3±21.2 $p<.001$). Mitogenic response to Con-A was depressed in 18/26 (37.7±33.0 vs 101.6±20.1 $p<.001$), to PHA in 19/25 (58.7±47.0 vs 91.0±15.4 $p<.02$) and to PWM in 22/26 (12.0±9.3 vs 38.6±9.7 $p<.001$). Radial immunodiffusion studies showed that compared to established normals, IgG was elevated in 20/28 (1771±519 vs 1222±549 $p<.001$), IgM in 7/28 (163±85 vs 141±64 $p>0.3$), IgA in 3/28 (285±175 vs 194 ±140 $p>0.1$) and IgD in 5/28 (14.3±12.2 vs 13.6±13.5 $p>0.8$). C_3 levels were ↓ in 15/28 (87.5±25.9 vs 100.7±12.1 $p<.05$) while C_4 was elevated in 14/28 (46.5±12.1 vs 35.7±10.1 $p<.01$). The number of abnormalities (out of 13) ranged from 3-11 per patient (average of 7). The etiology and reversibility of these defects are presently being studied.

* M ± SEM

807 EOSINOPHILIA IN PREMATURE NEONATES. Alan D. Rothberg, Ruben Sher and Richard Cohn (Spon by M. Jeffrey Maisels). Witwatersrand University, Johannesburg Hospital, Department of Pediatrics, Johannesburg, South Africa.

Ten premature neonates were studied prospectively to document eosinophilia within the first six weeks of life. Mean birth weight was 1229±314 g, mean gestational age 31.5±1.5 wks. Simultaneous changes in eosinophils (E), total lymphocytes, suppressor and helper cells, neutrophils and IgE were monitored. Infants were designated as responders (R) (E>1000/cu mm for >5 days) and non-responders (NR). In R (n=6), E increased from 353±76 (mean± SEM) at birth to a peak of 2783±430/cu mm at 21-25 days. NR (n= 4) had significantly lower E from birth (75±26/cu mm, $p<.05$) to 21-25 days (332±190/cu mm, $p<.01$). R had significantly lower neutrophils at birth (2499±428 vs 4843±984/cu mm, $p<.05$), and 5 of 6 R increased neutrophils by ≥100% within 10-15 days vs 0 of NR ($p<.03$). Lymphocytes, suppressor and helper cells increased progressively in both groups over the period of study, with no differences between R and NR. Birth weight and gestational age were similar in both groups, and there were no apparent causes for the lower neutrophils in R at birth (e.g., maternal disease, drugs, neonatal sepsis). R and NR had similar exposure to blood transfusions, antibiotics, intravenous nutrition and artificial formula. Bacterial sepsis was not observed in any infant. Eosinophilia was not related to an IgE response. The incidence of eosinophilia is similar to that reported previously, and appears to be a maturational response occurring after an initial neutrophilia in those premature infants born with a lower neutrophil count.

● **808** RECEPTORS FOR PEANUT AGGLUTININ IN THE IMMUNOLOGICAL SUBGROUPING OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL). E.C. Russell, T. Mohanakumar, N. Dunn. N. McWilliams, H.M. Maurer, Medical College of Virginia, Department of Pediatrics and Surgery, Richmond, Virginia 23298

Childhood ALL is composed of subgroups defined by immunologic markers and certain markers are known to have prognostic significance. Null cell ALL is the largest subgroup and additional markers are needed to identify patients at increased risk of early relapse within this non-T, non-B category. We have used a direct immunofluorescence assay to identify the presence of receptors for the lectin peanut agglutin (PNA) on blasts from 26/46 (63%) of our null cell ALL patients and have subsequently noted a high rate of relapse (17/26) in this PNA+ group. Relapse has occurred in only 5/20 patients whose blasts lacked the PNA receptor. The PNA+ and PNA- groups were comparable in clinical features (i.e., age, leukocyte count, follow-up times) and the striking difference in relapse rate was correlated only with the presence of receptors for the lectin ($p<0.01$). PNA receptors are commonly found on fetal thymocytes but not on mature peripheral lymphocytes except after neuraminidase treatment. SDS-PAGE analysis of NaB^3H_4-galactose oxidase labelled solubilized cell membrane extracts revealed a 68,000 dalton glycoprotein found only on PNA+ ALL lymphoblasts. Neither PNA- blasts nor PNA+ normal thymocytes expressed this component. The lectin PNA seems to define a high risk group of null cell ALL patients and to be associated with a specific cell membrane component.
(Supported by NIH CA 27416 and ACS 190B)

809 FEVER IN ACUTE MYELOGENOUS LEUKEMIA (AML). P. David Sadowitz and James A. Stockman III. Dept. Peds., SUNY, Upstate Medical Center, Syracuse, N.Y.

The management of AML differs markedly from that of acute lymphocytic leukemia (ALL). The differences in underlying disease and the types of therapies used might be expected to lead to differing rates of infectious complications in these two forms of leukemia. In an attempt to identify any relationship between fever, granulocytopenia (<1000 polys/ul), infection and disease status, 20 patients with AML were observed over a period of 16.5 patient years and comparisons were made with our previous experience with ALL (Wolk et al, Am J Dis Child 131:157, 1977). In AML an infectious origin for fever was found in 70% of fevers during induction, in 25% in remission, and in 67% in relapse. In ALL, the cause of the fever was identified in 27% of fevers during induction, in 65% in remission, and in 8% in relapse. In AML, the most common infectious causes for fever in induction and relapse were sepsis (33% of fevers) and pneumonia (45% of fevers). In induction and relapse among patients with AML who had pneumonia the most common causative organism recovered from needle aspirations or open lung biopsies was mycoplasma pneumoniae (50% of all pneumonias). This organism was rarely seen during induction or relapse of ALL but accounted for 14.5% of fevers in remission. Persistance of M. pneumonia in the throat for many months was common. These data indicate that most febrile granulocytopenic episodes during induction of remission and relapse of AML are caused by definable organisms unlike the situation in ALL in which the disease apparently may cause fever. In both diseases, M. pneumoniae should be considered as a possible etiology for fever.

810 MEAN CORPUSULAR VOLUMES AND DISCRIMINATE FUNCTION IN LEAD (Pb) POISONING. P.David Sadowitz and James A. Stockman III. Dept. Peds. SUNY, Syracuse, N.Y.

Microcytosis in the pediatric age group is usually due to one of 3 disorders: iron deficiency (Fe def), thalassemia minor, or Pb poisoning. Previously, formulae were devised to utilize the RBC indices provided by electronic counting equipment to distinguish between Fe def and thalassemia minor. The most popular of these are the Discriminate Function (D.F.)=MCV-RBC-(5xHb)-3.4 where ⊕ values suggest Fe def and ⊖ values suggest thalassemia minor and Mentzer's Formula (M.F.)=MCV/RBC, where values >14 suggest Fe def and <12 suggest thalassemia minor (Lancet 1:882, 1973). Children who were Pb poisoned and had microcytosis without evidence of Fe def were studied to determine what the characteristics of the M. F. and D.F. are with respect to Pb poisoning alone. From a Pb clinic population, 50 children with ↑ free erythrocyte protoporphyrin and blood Pb levels were further examined. The FEP levels ranged from 81 to 315 µg/dl and the blood Pb ranged from 35-54 µg/dl. Microcytosis (> 2SD below mean normal MCV for age) was noted in 35 subjects. Of these, 25 had evidence of Fe def (serum ferritin <12 µg/l) while only 10 appeared to have isolated Pb poisoning. In the latter group, the M.F. yielded values of >14 in 7/10 subjects (the remainder were 13.4, 13.5, 13.9) while the D.F. gave ⊕ results in 9/10 subjects. These data suggest that the changes in RBC indices in Pb poisoning more closely resemble the pattern seen in Fe def rather than thalassemia and indicate some degree of ineffective erythropoiesis which causes the RBC count to decline relatively more than the MCV.

811 TERMINAL CARE OF CHILDREN WITH CANCER: A SIX CENTER STUDY. Olle Jane Z. Sahler, U of Roch, Strong Mem Hosp Dept of Ped. Rochester, NY. Spon by RA Hoekelman

Home-based care of dying children has become an increasingly popular option for families. However, because little is known about families that choose such care or about their special needs during this time, 6 university affiliated oncology centers in NY State (Babies' Hosp, Buffalo Children's, LI Jewish, Roswell Park, Upstate Med Ctr-Syracuse & the U of Rochester)gathered data on 63 children who relapsed or died between 10/1/80 and 12/1/81.

Half of the study families provided some home care (range: 1 day to 3-1/2 mos.) for their terminally-ill child. Two-thirds of these children died at home. Readmission to the hospital occurred within 48 hours of death for many of the others.

Special equipment or parental training was seldom needed, and most families did not seek help from home care agencies. Rather, ongoing contact with the oncology staff was their most frequently cited need. Whereas home visits by hospital staff were rarely required, telephone or direct contact ranged from weekly contacts during quiescent periods to several times daily during crises.

In almost every instance, the patient preferred to be at home in familiar surroundings, free from painful procedures. The major parental concerns were adequacy of pain control and handling of the event of death itself. Information and reassurance, as well as the option of readmission if necessary, almost always resulted in acceptance of home care by the family. On follow-up, families generally felt very positive about their experience.

Thus, home-based terminal care appears to be a satisfactory and functional option for many families.

● **812** LONG-TERM PULMONARY SEQUELAE OF DIFFUSE INTERSTITIAL PNEUMONITIS IN CHILDREN WITH CANCER. Shyamal K. Sanyal, Alvin Culp, Paul W. Mackert, Rhomes J. Aur. Cardiopulmonary Disease Service, St. Jude Children's Research Hospital, Memphis (TN) 38101.

Specific ventilatory functions were assessed in 33 children with cancer 1-20 yrs (mean 7.2 ± 6.2) after recovery from P. carinii pneumonitis (23 pts) or varicella pneumonitis (10 pts). The results were derived from clinical spirometry, expiratory flow-volume curves, pulmonary gas-transfer factor, arterial blood gases, specific airway conductance and volume of isoflow, and expiratory flow at 50% of FVC ($Vmax_{50}$) after patients had breathed an 80% helium – 20% oxygen mixture. Methotrexate had been administered to 32 patients, cyclophosphamide to 27 and mediastinal irradiation to 1. Residual pulmonary function abnormalities were present in 21 patients (64%). An increased volume of isoflow in 14 patients (> 21.8% of FVC), indicating small airway disease, was the most common abnormality; 7 of these also had a reduced $Vmax_{50}$. Five patients had restrictive lung disease (as determined from decreases in total lung capacity, FVC and inspiratory capacity below 2 SD of the predicted mean for age- and sex-matched normal controls); 4 had decreased pulmonary gas-transfer factor; 6 had arterial hypoxemia at rest; and 5 had an increase in specific airway conductance. Eleven patients had more than one abnormality. Clinical variables significantly related to dysfunction were: need for ventilatory support, higher oxygen concentration, and total dose of methotrexate ($P < 0.05$ each). On repeat measurements in 7 patients after bronchodilation, volume of isoflow had decreased and $Vmax_{50}$ had increased in each. The data indicate (i) a high prevalence of residual pulmonary dysfunction after "apparent" recovery from diffuse pneumonitis in children with cancer (not previously reported) and (ii) possible reversibility of small airway dysfunction.

813 GROWTH IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA H.K. Schedewie, D.H. Berry, W. Crist, V. Land, V. Lui, C. Sexauer, L. Dickinson, M.J. Elders, Pediatric Dept. University of Arkansas for Medical Sciences, Little Rock, AR.

Increasing numbers of children surviving after treatment of acute lymphoblastic leukemia (ALL) have drawn attention to questions of long-term morbidity, including disease- or treatment-related growth retardation. Southwest Oncology Group project #7581 was initiated in 12/1975 to evaluate the effect of ALL as well as chemotherapy and irradiation on body growth, serum growth hormone (GH) and somatomedin (Sm) concentrations. The study included 127 children from 5 participating institutions, 83 males and 44 females, with a mean age at ALL diagnosis of 6.6 years. Height, weight, and hormonal concentrations were determined at the time of initial diagnosis and at regular intervals for up to 5 years of follow-up. 84% of children were observed for longer than 12 months. Boys <4 years showed significant growth retardation ($P<.01$) at diagnosis. Growth retardation persisted through ALL therapy so that 83% of these patients were growing below the 50th percentile by the end of observation ($P<.01$). Linear regression analysis of growth rates in children with ALL versus normal standards confirmed differences in growth patterns. Serum GH and Sm concentrations were similar to controls. However, hormone levels at initial diagnosis were significantly higher than during remission ($P<.001$). In conclusion, our data suggest that a significant number of children with ALL are shorter than their peers prior to onset of therapy. GH and Sm levels appear to be elevated at the time of disease onset and to decrease with therapy.

814 HOSPITALIZATIONS OF CHILDREN WITH ACUTE LYMPHOCYTIC LEUKEMIA (ALL). W. Frederick Schwenk, II, Peter C. O'Brien, and Gerald S. Gilchrist, Mayo Clinic, Department of Pediatrics, Rochester, Minnesota.

Recent advances in the treatment of childhood ALL have dramatically increased the duration of disease-free survival and the potential for cure. There is, however, no published information on how long or how often these new treatment programs necessitate hospitalization. In order to evaluate hospitalization patterns for children with ALL, we reviewed the records of all children diagnosed at the Mayo Clinic between 1972 and 1979. There were 87 patients who had a total of 331 hospitalizations covering 270 patient-years. Our patient population was similar to other reported groups of children with ALL with respect to age and sex distribution; white blood counts, hemoglobin values, and platelet counts at diagnosis; and percentages and survival in various risk categories.

The median length of the initial hospitalization was 4 days (range 0 to 51 days); the median length of subsequent hospitalizations was 3 days (51.1% primarily for the administration of chemotherapy, 19.2% because of suspected or proven infection, and 5.6% for transfusions). The median number of hospitalizations per patient per year of observation was 1.4. During the 10 year observation period, children with ALL spent a median of only 5.7 days per year in the hospital.

This analysis provides information which can provide a basis for analyzing cost-effectiveness of care delivery in childhood ALL and a standard against which the cost of newly developed treatment programs can be compared.

815 FETAL AND MATERNAL MORBIDITY/MORTALITY IN SICKLE CELL DISEASE.

This study comprises 51 pregnancies in 47 mothers with sickle cell disease. The phenotypes of mothers were: HbSS 31, HbSC 14 and two HbS-Thalassemia. The fetal outcome of the pregnancies are shown in table 1.

Table 1

Genotype	Term Birth	Premature Birth	Spontaneous Abortion	Induced Abortion	Death In Utero
SS	8	11	9	2	1
SC	4	6	2	2	1
S-Thal.	1	1			

Only 13 pregnancies (25.5%) resulted in full term births. There were 18 premature births (58.1% of total live births). Total fetal wastage (abortions and death in utero) occurred in 17 instances (33% of total pregnancies). The mean birth weight of the 13 full term infants was 3336. Gm. with a range of 2758-4508 Gm. Cesarean section was performed in 11 mothers. The average hemoglobin levels in the patients was 9.4 grams (SD± 2.1) and the average hematocrit was 28% (SD ± 5.8%). In 8 (17%) of the subjects, the diastolic blood pressure was greater than 140 mmHg. Urinary tract infections occurred in 34.1% of the mothers. Other maternal complications were edema 3 (6%), pelvic inflammatory disease 2 (4.5%), chest syndrome 2 (4.5%) and one case of jaundice (2.2%). There were seven episodes of crises, preeclampsia/eclampsia occurred in 6 (85.7%) mothers and a variety of post partum complications with 3 cases (33%) of retained placental fragments. Eleven of the pregnant women received blood transfusions. This study demonstrated significant maternal morbidity and fetal mortality as complications of sickle cell disease.

● **816** A RAPID AND ACCURATE METHOD FOR DETERMINING SUSCEPTIBILITY TO CHICKENPOX. Ziad Shehab and Philip A. Brunell. The Dept of Pediatrics, Univ of Texas Health Science Center, San Antonio, Texas.

A method which can be used to determine susceptibility to chickenpox rapidly, accurately and which can be performed routinely is sorely needed. This is particularly important in the management of children who are at high risk of complications should they develop chickenpox. Determination of varicella-zoster (V-Z) antibody by ELISA, using antigen coated plates that can be stored at 4°C for at least two months, has correctly predicted the outcome of exposed individuals following household exposure. There has been a 97% correlation (140/144) with the fluorescent antibody against membrane antigen - FAMA assay. Results have been reproducible with different lots of antigen and conjugate. In testing children in our oncology program, 2 of 27 who were said to have had varicella were found to be susceptible; 10 of 30 with a negative history were seropositive. Of the 10, three had recently received ZIG and 2 others blood transfusions. On retesting of sera obtained subsequently from these 5 children, all were found to be susceptible. Testing of children who are at a high risk of complications of chickenpox for immunity by ELISA should replace reliance on past history. Testing should become a routine part of their care to provide guidance as to the risk of exposure to chickenpox and the need for passive immunization. The technique is also useful for rapid identification of susceptibles, should a patient develop chickenpox on an inpatient service.

817 TRANSIENT ERYTHROBLASTOPENIA AND CHRONIC ANEMIA AS A MANIFESTATION OF SYSTEMIC CARNITINE DEFICIENCY. Susan B. Shurin, Douglas Kerr & Charles L. Hoppel. Case Western Reserve Medical School, Rainbow Babies & Childrens Hospital and V/ Medical Center, Departments of Pediatrics, Medicine & Pharmacology, Cleveland, OH.

Carnitine, an essential cofactor for transport of long-chain fatty acids into mitochondria for oxidation, is normally synthesized in liver and kidney. Dietary carnitine is not sufficient to prevent lethal disease in patients with congenital defects in carnitine biosynthesis (carnitine deficiency). Twin girls presented with Hgb 4 to 5 gm/dl and absent bone marrow erythroid precursors at 3-1/2 mos, while receiving a soy formula, which contains no carnitine. Erythroblastopenia resolved spontaneously when diets were liberalized. Both children developed fatty infiltration of liver, heart and muscle and recurrent hypoglycemia with fasting. Systemic carnitine deficiency was documented in both, with deficient butyrobetaine hydroxylase activity in liver. One child died. The other is doing well on oral L-carnitine, but mild anemia (hgb 10 gm) and reticulocytosis (2-3%) persist. Red cells are normocytic without i antigen. Hgb F is 1-2%. Marrow erythroid precursors are not vacuolated. Five other patients with carnitine deficiency have been reported to be anemic.

Supplementation with carnitine at levels which improved liver, muscle and cardiac function has not completely prevented anemia, suggesting that accumulated metabolites such as butyrobetaine may be toxic to marrow erythroid precursors. However, small amounts of dietary carnitine appeared to reverse the severe erythroid hypoplasia with which these patients presented, whose mechanism is unknown.

818 PATHOPHYSIOLOGY OF THE ANEMIA OF HAEMOPHILUS INFLUENZAE MENINGITIS (HIM). Richard H. Sills, Mary T. Caserta, Stephen A. Landaw. (Spon. by J.R. Humbert). State Univ. of NY, Children's Hospital, Dept. of Peds, Buffalo NY; and Dept. of Med. VA Hospital, Syracuse NY.

The pathophysiology of the anemia associated with HIM is poorly understood. We examined red cell deformability by measuring the filtration time (FT) of washed red blood cells through polycarbonate filters. Nineteen children with HIM, 11 with aseptic meningitis and 30 normal subjects were studied. The hemoglobin levels of the HIM patients ($\bar{x}\pm$S.D. = 10.8 $\pm$1.1 gm/dl) were significantly lower than the aseptic meningitis patients (12.7$\pm$1.6, $p < 0.001$) and the 30 normal children (12.6$\pm$0.8, $p < 0.001$). The FTs of the HIM patients were prolonged (76.8$\pm$83.3 secs) compared to those with aseptic meningitis (24.4$\pm$5.8, $p < 0.05$) and the normals (24.1$\pm$5.3, $p < 0.01$). Carboxyhemoglobin (HbCO%), an excellent index of red cell destruction, was measured to determine if the anemia was hemolytic in nature. The HbCO% levels in patients with HIM were 1.03$\pm$.63% with 64% of patients exhibiting elevated values (>.78%). There was a significant positive correlation between the HIM FTs and the CO ($r=0.77$, $p < 0.01$). There was also a positive correlation between the FTs and the absolute band and granulocyte counts. No patients had evidence of disseminated intravascular coagulation.

The elevated HbCO% in patients with HIM supports the hemolytic nature of the anemia associated with this disorder. The correlation of the HbCO% and the FT suggests that the diminished red cell deformability in HIM results in a decreased red cell survival and anemia.

819 DERANGEMENT OF CYCLIC NUCLEOTIDE SYSTEMS OF MONONUCLEAR BONE MARROW CELLS IN ACUTE LYMPHOBLASTIC LEUKEMIA (ALL). Josef P. Skala, Paul C.J. Rogers & Ian A. MacLaren. University of British Columbia, Department of Paediatrics, Vancouver, B.C., Canada V5Z 1L7.

Concentrations of both adenosine 3':5' monophosphate (cAMP) and guanosine 3':5' monophosphate (cGMP) were determined during incubations of mononuclear cells isolated from marrows of ALL patients at diagnosis and at subsequent remission periods. Incubations for 1-20 min. in the presence of 1-methyl-3-isobutylxanthine resulted in equal increases of both nucleotides whereas addition of sodium nitroprusside resulted in large elevations of cGMP only. Both isoproterenol and epinephrine increased markedly concentrations of cAMP in cells (>70% lymphocytes) isolated from patients undergoing remission of ALL. Carbamylcholine addition resulted in slight increases of the cGMP concentration, whereas serotonin exhibited pronounced stimulatory effect upon guanylate cyclase activity. Cells isolated from ALL patients at diagnosis (>90% blasts) exhibited diminished responsiveness of both cyclic nucleotides to hormonal stimuli, the catecholamine activation of adenylate cyclase being almost absent. The sensitivity had reappeared already by 2 weeks after the initiation chemotherapy. Attempts are made to correlate the characteristics of the cAMP and cGMP systems with the growth behavior of the cells in long-term cultures. The techniques may eventually be used to determine the effectiveness of particular therapeutical interventions in individual patients.

(Supported by the British Columbia Health Care Foundation and the Vancouver Foundation).

● **820** A NEW PROGNOSTIC INDICATOR IN CHILDHOOD NON-HODGKIN'S LYMPHOMA (NHL): IN VITRO LYMPHOMA COLONY CULTURE. Stephen D. Smith, Steven E. Kisker, LaTina M. Bush, Robert C. Trueworthy, University of Kansas College of Health Sciences and Hospital (KUMC), Department of Pediatrics, Kansas City, Kansas.

The objective of this study was to evaluate the sensitivities of two methodologies for determining bone marrow (BM) involvement in NHL. These methodologies were histologic examination of the BM aspirates and clot sections vs. growth of lymphoma colonies in vitro. 14 children with NHL without BM involvement were diagnosed at KUMC between 6/76 and 6/81. Serial BM aspirates were processed for culture on soft agar and histologic review. 7 BM aspirates demonstrated lymphoma (histology +) and 6 grew lymphoma colonies (agar +). 35 BM aspirates were normal (histology -) and 29 failed to grow lymphoma colonies (agar -). However, 6 histology - BM aspirates were agar +. Both the Fisher's exact test and κ statistic were significant ($p < 0.002$) indicating not only an association between histology and soft agar results, but also a close agreement. At this time, there is no statistical difference between duration of survival and 1) clinical stage at presentation (I, II vs. III), and 2) BM involvement with lymphoma (histology + vs. -). However, the duration of survival of children who were agar + was 6.8 months and agar - was 22.7 months ($p < 0.02$). Children whose BM aspirate grew lymphoma colonies on soft agar have all died. In this patient population, in vitro growth of lymphoma colonies was predictive of a very poor prognosis and their short survival was independent of both clinical stage and histologic evidence of BM involvement with lymphoma.

821 ADVERSE EFFECT OF INCREASED BLOOD VISCOSITY IN AN IRON DEFICIENT ADOLESCENT WITH CYANOTIC CONGENITAL HEART DISEASE (CCHD). Clark M. Smith II, Kenneth L. McClain, David P. Tukey, James H. Moller, William Krivit. Univ. of Minnesota Health Sciences Center, Pediatrics, Mpls. MN 55455

Iron deficiency (ID) may lead to cerebrovascular symptoms (CVS) in CCHD by lowering hemoglobin (Hb) and oxygen carrying capacity, by altering tissue iron proteins (neurotransmitter metabolism, mitochondrial respiration), or by increasing red cell rigidity and blood viscosity (η). The contribution of η to the CVS of an adolescent girl with partially corrected transposition of the great vessels and ID was evaluated by measuring oxygen delivery determinants before and after isovolemic exchange transfusion (ET) with iron sufficient blood. ID was due to menorrhea and was diagnosed by microcytosis (69fl), low serum ferritin (16ng/ml), low serum iron/total iron binding capacity saturation (37/466;8%) and elevated erythrocyte porphyrin (3.7µg/gHb). CVS were present daily for 2 weeks prior to the ET and included headache, vertigo, paresthesia, and transient loss of vision. A one blood volume ET with CPD blood in fresh frozen plasma lowered η from 17.4±0.9cp to 13.6±0.5cp at shear rate 11.25 sec^{-1}, increased mean cell volume from 69 to 81fl, and stopped all CVS. Cr51 red cell mass and blood volume, Hb, HCT, weight, pulse, blood pressure, and blood gases were not altered by the ET. CVS recurred in two weeks as the Hb and η increased in response to iron therapy, but were less severe. The experience suggests that the increased blood η of iron deficient blood may be important in the CVS of ID and CCHD. Blood η may not be adequately reflected by Hb or HCT, and should be measured in CCHD with CVS.

822 ABNORMALITIES OF GLUTATHIONE METABOLISM IN NEUTROPHILS FROM HUMAN NEONATES. Ronald G. Strauss and Esther L. Snyder. University of Iowa College of Medicine, Department of Pediatrics, Iowa City, Iowa.

Neutrophils (N) with abnormal glutathione (GL) metabolism and decreased concentrations of GL exhibit dysfunctions that have been ascribed to oxidant damage. We measured GL reductase activity, total GL (GSH + GSSG) concentrations and GL depletion during oxidant stress in N from neonates to determine if the previously reported deficiency of GL peroxidase and increased susceptibility of neonates' N to oxidant damage could be related to additional GL abnormalities. GL reductase activity/mg N protein was similar in N of 14 neonates and controls (3.11 ± 0.01 and 3.91 ± 0.43 units, respectively). GL concentrations were significantly less ($p < .04$) in N from 32 neonates than controls (3.1 ± 0.3 and 3.5 ± 0.2 μg/5 x 10^6N, respectively). Moreover, a greater depletion of GL occurred in neonates' N during oxidant stress produced by exposing N to H_2O_2 generated enzymatically by glucose oxidase + glucose. Total GL (GSH + GSSG) fell from basal concentration an average of 84% in neonates' N and 57% in control N exposed to 0.3 units glucose oxidase. Similar values for N exposed to 0.6 units glucose oxidase were 88% (14 neonates) and 75% (controls) ($p < .01$). In conclusion, neonates' N exhibit decreased GL peroxidase, normal GL reductase, decreased basal concentrations of GL and excessive depletion of GL during oxidant stress. Abnormalities of GL in conjunction with the previously reported deficiency of catalase in neonates' N may render these cells prone to oxidant damage with consequent dysfunction.

823 BINDING OF THE CHEMOTACTIC PEPTIDE, FMLP, TO NEUTROPHILS FROM HUMAN NEONATES. Ronald G. Strauss and Esther L. Snyder. University of Iowa College of Medicine, Department of Pediatrics, Iowa City, Iowa.

Diminished chemotaxis has been consistently demonstrated in neutrophils (N) obtained from human neonates. We measured the binding of tritiated formyl-methionyl-leucyl-phenylalanine (FMLP-H^3) to N obtained from 10 human neonates and 10 adult controls to determine whether N assumed to exhibit decreased chemotaxis also have abnormal chemotactic factor binding. N were isolated from venous blood and were incubated at 22°C for 20 min with FMLP-H^3 (40 nM) either in the absence (total binding) or presence (nonspecific binding) of excess (10^{-4}M) nonradioactive (cold) FMLP. N with bound FMLP were separated from free FMLP molecules by rapid centrifugation through silicone oil. N pellets were dissolved in scintillation fluid and radioactivity was measured. Neonates' N bound significantly less FMLP-H^3 than did control N (total cpm bound per 2 x 10^6N were 7,444 ± 677 and 10,435 ± 763, respectively). Likewise, specific binding (total binding - nonspecific binding) was less ($p < .02$) by neonates' N (6,223 ± 614 cpm) than by control N (8,903 ± 722 cpm). Each neonatal N specifically bound 150,582 ± 15,661 FMLP-H^3 molecules; control N bound 219,851 ± 25,298 ($p < .02$). Binding was saturable, presumably via a plasma membrane receptor, because excess cold FMLP decreased uptake of FMLP-H^3 by 83 ± 1.4% in neonates' and 85 ± 1.3% in control N. Since binding of chemotactic factors to membrane receptors is the initial event in chemotaxis, decreased binding may be one of the mechanisms responsible for decreased chemotaxis in neonates' N.

824 MEGAKARYOCYTES METABOLIZE ARACHIDONIC ACID (AA) TO PRODUCE BOTH CYCLOOXYGENASE AND LIPOXYGENASE PRODUCTS. Marie J. Stuart, Jonathan L. Miller and Ronald W. Walenga. Depts. of Pediatrics & Clinical Pathology, SUNY, Upstate Medical Center, Syracuse, New York 13210.

Megakaryocytes (megs) were isolated from adult guinea pigs by the method of Levine et al (J. Cell. Biol., 69:159, 1976) with yields of 1.4 to 5 x 10^5 megs per animal (purity of 75-90%). The metabolism of 1-^{14}C-AA(53-55 or 255 Ci/mole) by these cells and by platelets isolated from the same animals was evaluated using an AA concentration of 5 μM/for 5'. Megs were demonstrated to convert AA to metabolites of both the lipoxygenase (12 HETE) and cycloxygenase pathway (HHT and TXB_2). These products were identified by their mobility in TLC analyses both as free fatty acids and methyl ester derivatives, as well as by their comigration with authentic standards or the AA metabolites of human platelets. As in other cell systems Indomethacin (30 μM, 15' preincubation) was demonstrated to inhibit the formation of the cyclooxygenase metabolites, while enhancing the production of the lipoxygenase product HETE. Results (Mean ± SEM) were as follows:

	TXB_2	HHT	HETE	
Plts (n=5)	11.7±1.9	47.6±9.2	53.0±11	p moles/10^8 cells
Megs (n=8)	5.6±1.1	15.5±3.0	17.7±1.4	p moles/10^5 cells

The enzymes for the metabolism of AA that are present in platelets (cyclooxygenase, thromboxane synthetase, and lipoxygenase), are also active in their precursor cells the megakaryocytes.

825 SERUM LDH VALUES IN CHILDHOOD ACUTE LEUKEMIAS AND NON-HODGKIN'S LYMPHOMA (NHL). Carlos R. Suarez (Spon. by Lewis E. Gibson). Memorial Sloan-Kettering Cancer Center, New York, NY, and Loyola Medical Center, Chicago.

Serum lactic dehydrogenase (LDH) activity is elevated in a broad spectrum of malignant diseases. This elevation has been used as a marker of tumor activity, also prognostic significance has been attributed to LDH levels in adults with NHL, particularly those with histiocytic type. LDH serum levels (Normal 98-230 U/L) were measured in 116 untreated children with NHL, 66 untreated cases with acute lymphoblastic leukemia (ALL) and 26 cases of acute non-lymphocytic leukemia (ANLL). LDH levels were not significantly different in ALL and ANLL (970 vs. 817 U/L, $p=.329$) but the difference between ALL and NHL was highly significant with $p<.001$ (970 vs. 551 U/L). Among the ALL cases 95% had elevated LDH, for the ANLL group was 96% and 77% in NHL. Only 13% of NHL cases had marked elevations (>1000 U) whereas 32% and 23% of ALL and ANLL respectively did. LDH correlated directly with WBC counts and was significantly higher ($p=.007$) in patients with high counts compared to those with low counts. Patients with diploid stemlines as determined by computerized flow cytometry had significantly higher LDH levels than those with aneuploidy ($p=.001$). LDH levels did not correlate with sex or French-American-British classification though there was a trend to higher levels in females ($p=.08$) and L1 morphology ($p=.06$). In NHL the histiocytic type had lower mean LDH than the lymphocytic poorly differentiated (416 vs. 573 IU/L). In summary contrary to other reports LDH levels do not distinguish between ALL and ANLL, LDH is significantly higher in ALL than in NHL, LDH in histiocytic NHL is not higher.

826 COMPUTERIZED FLOW CYTOMETRY CELL KINETIC DETERMINATION IN CHILDHOOD ACUTE LEUKEMIA, BONE MARROW ASPIRATES (ASP) AND BIOPSIES (BX) COMPARISON. Carlos R. Suarez, Denis R. Miller and Michael Andreeff (Spon. by Lewis E. Gibson). Depts. of Pediatrics Memorial Sloan-Kettering Cancer Center, New York, and Loyola Medical Center, Chicago.

We investigated the adequacy and reliability of Asp. for cell kinetic analysis in comparison to Bx. in 74 paired simultaneously taken samples from 40 pediatric patients and the cell cycle distribution for patients with acute lymphocytic (ALL) and non lymphocytic (ANLL) leukemia. Nononuclear cells from Asp. and Bx. were separated by Ficoll-Hypaque gradient and stained with Acridine Orange (Andreeff et al Blood 55, 1980). DNA stemline, cell cycle distribution and RNA Index (RI) were determined. Paired samples were taken before therapy and during therapy. The Bx. shows significantly higher proportion of cells in the proliferation phases (S=10%, S+G2+M=14%) than the Asp. (S=6%, S+G2+M=85%) with $p<.001$. As expected the difference in proliferation became more pronounced during chemotherapy ($p=.006$ before therapy, $p<.001$ during therapy). The cell cycle distribution was essentially the same for cases of ALL (G0/1=90.4%, S=7%, S+G2+M=9.6%) and those with ANLL (G0/1=91%, S=G.1%, S+G2+M=9%). We conclude that bone marrow biopsies more accurately reflect the proliferative status of the bone marrow; the difference is exaggerated in patients receiving chemotherapy due to dilutional effect of peripheral blood; adequate and reproducible cell kinetic studies should be based on biopsies and not aspirates; there is no significant difference in cell cycle distribution or cell proliferation in ALL and ANLL.

● **827** FURTHER CHARACTERIZATION OF PYRIMIDINE 5'-NUCLEOTIDASE DEFICIENT RED CELLS. Mark S. Swanson, Carol R. Angle, Sidney J. Stohs, Jimmy M. Salhany, Shao Wu. University of Nebraska Medical Center, Departments of Pediatrics and Biomedicinal Chemistry, Omaha, NE 68105

Nonspherocytic hemolytic anemia associated with congenital red cell pyrimidine 5'-nucleotidase deficiency (PND) is characterized by abnormal elevation of red cell pyrimidine nucleotides and basophilic stippling. Studies have also demonstrated elevated erythrocyte GSH content, decreased PRPP synthetase activity and evidence of impaired glucose utilization associated with this disorder. However, at present the etiology of hemolysis in subjects with PND remains obscure. This study was performed on erythrocytes obtained from a young male confirmed as homozygous for deficiency of the enzyme via enzymatic and chromatographic techniques. Dilute suspensions of PND patient red cells were less filterable than normal cells using 3 micron pore-size filters. Anion exchange HPLC revealed an abnormally low ATP concentration accompanied by elevated CTP and UTP as well as other pyrimidine nucleotides in PND patient red cells. These cells were found to have a decrease in intracellular pH, as determined by ^{31}p-NMR spectroscopy. Although the intracellular magnesium was increased, Mg-ATP, the biologically functional form of ATP, was calculated to be approximately one-half normal. Red cell calcium was normal. These studies have further characterized both physical and metabolic defects associated with this disorder. (Supported in part by USPHS Grant 1RO1ES01857).

828 STUDY OF FOLINIC ACID RESCUE IN VINCRISTINE OVERDOSE IN MICE. William J. Thomas, Sam W. Lew, William M. Barnett, Alton L. Lightsey, Tawfik Bailoney, Naval Regional Medical Center, San Diego, California.

Reports of accidental overdosage of vincristine (VCR) describe severe morbidity and mortality resulting from the neurotoxic and hematotoxic effects of large doses of VCR. Several authors have recommended the use of folinic acid (FA) in the management of patients with VCR overdose. This was based on experimental evidence in which mice given FA were protected from the lethal effects of VCR. Since the biochemical basis of FA rescue in VCR overdosage is unclear, we elected to repeat the animal experiments. Groups of 20 $C_3b_6F_1$, hybrid mice received either a) a single intravenous LD_{50} dose of VCR alone or the same dose of VCR followed by b) 10 daily intraperitoneal (IP) injections of FA (140 mg/kg) or c) 10 daily IP injections of normal saline (NS). The observed pattern of neuromuscular toxicity, i.e. hind leg incoordination and weakness (days 4-10) was similar in all three groups. However, 14/20 mice in group (a) died compared to 5/20 and 3/20 mice in groups (b) and (c) respectively ($p<.001$). In each group death occurred between days 6-11 and recovery of neuromuscular function in survivors was noted between days 12-16 following VCR. We conclude that an equal volume (0.3 cc) of daily IP NS is as effective as FA in preventing the lethal effects of VCR in mice. Survival may be related to improved hydration since survivors were noted to maintain a urine output during the observable period of toxicity (days 4-11), whereas mice who subsequently died did not. FA does not appear to be a specific antidote for VCR poisoning in mice.

829 GROWTH PARAMETERS IN PATIENTS WITH MAJOR HEMOGLOBINOPATHIES.

In the past, children with sickle cell anemia have frequently been described as having the "Sickle Cell Habitus". The majority of our patients do not have the body habitus so often described. Using height and weight as growth parameters, we compared the growth patterns of 178 patients with major sickle hemoglobinopathies (SS, SC and S-Thal) for 5 years.

No. of Patients	No. of Observations	
	Weight	Height
SS - 133	277	259
SC - 35	65	63
S-Thal - 10	20	20

We observed that the majority of children with Hgb SS disease had a normal growth pattern up to age 10. Definite retardation was seen at about 10 years of age and the patients were generally below the 50 percentile for height and below the 5th percentile for weight from this age on. Patients with Hgb SC disease and sickle thalassemia generally followed the normal growth pattern.

830 UNIQUE SENSITIVITY OF HB ZÜRICH TO OXIDATIVE INJURY BY PHENAZOPYRIDINE: REVERSAL OF THE EFFECT BY ELEVATING CARBOXYHEMOGLOBIN LEVELS IN VIVO AND IN VITRO. David M. Virshup, Wm. H. Zinkham, Ronald L. Sirota and Winslow S. Caughey. Johns Hopkins Univ. Sch. of Med., Johns Hopkins Hosp., Dept. Peds., and Dept. Path., Greater Balto. Med. Ctr., Baltimore, Md., and Dept. Biochem., Colorado State Univ., Fort Collins, Colo.

Severe Heinz body (HB) hemolytic anemia in association with therapeutic doses of phenazopyridine (PAP) in a subject with Hb Zürich (HbZ) and normal renal and hepatic functions led to a study of the susceptibility of HbZ red cells (RBC) to oxidative injury by PAP. Incubation of whole blood from three asymptomatic HbZ subjects with PAP at a molar ratio of PAP/Hb of 1.3:1 produced a marked increase in methemoglobin (MHb) and HB formation and moderately decreased levels of reduced glutathione (GSH) in RBC from two of the subjects who were non-smokers with in vivo carboxyhemoglobin (HbCO) values of 4-6%. RBC from the third HbZ subject, a smoker with HbCO%'s of 15-18, exhibited minimal formation of HB, a moderate increase in MHb formation and a slight decrease in GSH levels. Rates of MHb formation were proportional to the concentrations of PAP. Increasing levels of HbCO from 8.2 to 14.3% by the in vitro addition of carbon monoxide (CO) caused a marked reduction in the rate of HB formation and a moderate decrease in MHb formation. Normal rates of MHb formation occurred at HbCO of 89.2 and 99.2%. Red cells containing HbZ are extremely sensitive to oxidative injury by PAP, either in vivo or in vitro. The degree of oxidative injury diminishes as the HbCO level increases, a phenomenon that is enhanced by preferential binding of CO to the abnormal ß subunit of HbZ.

831 HEINZ BODY HEMOLYTIC ANEMIA IN NEWBORNS AND FAILURE TO IMPLICATE A PHENOLIC DISINFECTANT IN THE LABORATORY. Steven A. Vitkun, Roger P. Smith, E. Elizabeth French, William H. Edwards, and Nancy Watkins. (Spon. by Robert Klein). Dartmouth Med. School, Depts. of Pharmacology and Toxicology, Pathology, and Maternal & Child Health, Hanover, N. H.

Phenolic disinfectant detergents have been implicated in epidemics of neonatal hyperbilirubinemia. A hepatic mechanism involving inhibition of glucuronyl transferase activity has been proposed. Two premature female infants in our intensive care nursery simultaneously developed features characteristic of Heinz body hemolytic anemia (HBHA): decreased hemoglobin and hematocrit, red cell inclusion bodies (Heinz bodies), anisocytosis, fragmented cells, hyperbilirubinemia and reticulocytosis. Laboratory investigation failed to reveal an etiology. Epidemiologic studies indicated a possible association between the reaction and the improper use of an inappropriately high concentration of a phenolic disinfectant* to clean the inside of the two infants' incubators. The hemolytic anemia resolved spontaneously in both infants. Extensive experimental efforts failed to produce Heinz bodies or HBHA. In vitro tests included incubation of the phenolic detergent with human adult blood and gestational age matched human cord blood. Animal experiments included administration of various concentrations of the phenolic detergent by multiple routes (intravenous, dermal, subcutaneous and inhalation). Studies were made in cats, mice, and both intact and splenectomized rats. While we failed to prove a hemolytic reaction to phenolics, it should be considered in future epidemics of neonatal hyperbilirubinemia.
*Ves-Phene, Vestal Laboratories, St. Louis, Mo.

832 EXPRESSION OF RECEPTORS FOR EPSTEIN-BARR VIRUS (EBV) ON LYMPHOID LEUKEMIC CELLS. Larry B. Vogler, Gilbert M. Lenoir, George Flandrin, Paul Gerber. (Spon. by Alexander R. Lawton) Laboratories of Immunochem. & Immunopath. & Cytology, Hôpital St. Louis, Paris, France; International Agency for Res. on Cancer, Lyon, France; Div. of Virology, F.D.A., U.S.A.

EBV has an unique affinity for human B lymphocytes. It is associated with infectious mononucleosis, African (endemic) Burkitt's lymphoma, nasopharyngeal carcinoma, and an x-linked lymphoproliferative (Duncan's) disease. To better understand the nature of EBV receptors on B cells, we examined receptor expression on lymphoid leukemic cells representative of discrete stages of lymphocyte differentiation, using an immunofluorescent method. Cells were incubated with EBV, then FITC-$F(ab')_2$ fragments of human IgG anti-EBV membrane antigen. The proportions of each leukemic type with cells bearing EBV receptors were:

T-ALL	0/4	B-CLL	5/5
"null"-ALL	2/36	plasma cells (normal, mitogen-stimulated)	0/2
pre-B and transitional pre-B/B-ALL	5/9	non-endemic Burkitt's cell lines	1/5
non-endemic Burkitt's ALL	0/4		

We conclude that EBV receptors appear very early, at the pre-B stage, in B cell development and that they are lost at or shortly before terminal differentiation to plasma cells. Non-endemic Burkitt's cells lacked receptors for EBV, suggesting an origin of this malignancy from an unique set or developmental stage of B lymphocytes.

833 VALUE OF SERIAL COAGULATION TESTING IN BIRTH ASPHYXIATED INFANTS. Tom F. Hard, Philip A. Gordon (Spon. by Ernest E. McCoy). University of Alberta, Department of Pediatrics, Edmonton, Alberta.

A study of coagulation status in birth-asphyxiated newborn infants was carried out to determine whether detailed serial testing would allow earlier detection of coagulation abnormalities. 16 infants with an Apgar score of 5 or less at one minute and less than 7 at 5 minutes were studied. 14 infants had estimated gestational ages between 37 and 43 weeks. Coagulation tests were performed on admission day 1, and on days 3 and 5. Blood was collected for PT, APTT, platelet count, fibrinogen, P and P test (prothrombin-proconvertin), factors V and VII assay, F.D.P.'s and peripheral smear was examined for red cell fragmentation. The majority of hypoxic full-term infants did not show significant coagulation abnormalities and serial testing did not reveal evolving abnormalities. One full-term infant did show features compatible with intravascular coagulation with prolongation of PT, and APTT, elevated F.D.P.'s and reduction of platelet count. The study suggests the overall incidence of coagulation abnormalities in birth asphyxia is low. It also suggests that the use of PT, APTT, and platelet count would provide adequate coagulation screening in birth-asphyxiated newborns and identify those infants in whom further coagulation testing should be carried out.

834 TREATMENT OF ACUTE MYELOGENOUS LEUKEMIA (AML) IN CHILDREN. Howard J. Weinstein, Felice S. Coral, Bruce M. Camitta, Richard D. Gelber, and Emil Frei III. (Spon. by Stephen E. Sallan). Harvard Medical School, Children's Hospital and Sidney Farber Cancer Institute, Boston.

Although complete remission (CR) can be achieved in greater than 70% of children with AML, the median duration of remission rarely exceeds 12 to 18 months (mos). We previously reported a protocol which was designed to address the problem of relapse in AML (NEJM 1980:303; 473-8). Patients (pts) received 14 mos of treatment in remission which included early intensification with adriamycin (Adr) and high-dose continuous infusion cytosine arabinoside (ara-c), followed by sequential combinations of Adr/azacytidine and prednisone/mercaptopurine/methotrexate/vincristine, and late intensification with ara-c. Central nervous system (CNS) prophylaxis was not included but surveillance lumbar punctures were performed. This report updates our results for the pediatric pts. Sixty-one previously untreated children with AML were entered on protocol from February 1976 to May 1980. Pts ranged in age from 3 mos to 17 years (median, 9.5 yrs). 45/61 (74%) achieved CR. There have been 18 relapses (9 marrow, 8 CNS, and 1 myeloblastoma). By Kaplan-Meier analysis, the probabilities of continuous CR +/- 95% confidence intervals are 55 +/- 16% at 24 mos and 55 +/- 23% at 36 mos. Twenty-six pts have completed treatment and 22 remain in remission with a median follow-up off therapy of 12 mos. The monocytic subtype of AML was associated with a significantly shorter duration of CR. Our follow-up data continues to indicate that intensive sequential chemotherapy is effective in prolonging remission duration in children with AML.

835 SEQUESTRATION CRISIS IN CHILDREN WITH SICKLE CELL DISEASE. Doris L. Wethers, Ranjeet Grover St. Lukes-Roosevelt Hospital, New York City, New York

Seven patients with SS disease have been treated over the past 5 years with one year of transfusion therapy in lieu of surgery after they had sustained their 2nd sequestration crisis. The ages of the children range from 8 1/2 mos. to 5 1/2 years. The diagnosis was made on the basis of sudden drop in Hg greater than 30% of baseline, rise in reticulocyte count, and massive splenomogaly. No child experienced a solitary sequestration crisis over this period. Packed R.B.C. were given with the objective of keeping Hb>10 gms and %S between 30-35%, and were administered as partial exchange or simple transfusion at intervals of 4-6 weeks. Three children completed the year of treatment. A splenectomy was performed on one of these children after she developed a third sequestration crisis one month after completion of transfusion therapy. The other two children have had no recurrence in 2 1/2 and 3 1/2 years post treatment. In our experience, recurrence of sequestration crisis is high, and consequently with conventional management would result in surgery for a significant number of young children. Treatment with transfusion therapy at the most will prevent surgery, and at the least will allow the young child to retain a functioning spleen for a longer period during his vulnerable years.

836 WISKOTT-ALDRICH SYNDROME (WAS): AN INTRINSIC OR EXTRINSIC PLATELET DISORDER? James G. White, David D. Mundschenk, Alexandra H. Filapovitch, University of Minnesota Hospitals, Department of Pediatrics, Minneapolis, Mn.

Patients with WAS are thrombocytopenic (Tp). Their platelets (Pl) are half normal size and reported to be deficient in granules (G), dense bodies (DB) and mitochondria (M), poor in metabolic ATP and reduced in storage pool adenine nucleotides (AN). WAS Pl respond poorly to aggregating agents and have a shortened life span in patients and normal recipients. Splenectomy, however, has restored normal Pl count and volume in many WAS patients (N Eng J Med 302:892,1980). We have evaluated megakaryocytes (Mk) and Pl from 5 children with WAS. One patient was studied 6 times following splenectomy 3 years ago. His Pl count and volume became normal and have remained so, except during periods of infection. G, DB, M, levels of AN, capacity to form thromboxanes, ^{125}I-labelled surface membrane glycoproteins, and responses to all aggregating agents were identical to controls. Ultrastructural features of Pl from Tp WAS patients were also normal, despite reduced size. Electron microscopy of Mk from Tp WAS patients and the non-Tp child were identical to controls. Our findings suggest that WAS Pl are intrinsically normal. Prolonged maturation in the bone marrow causing excessive development of Mk demarcation membranes may result in small Pl size and Tp. Due to delayed maturation, small WAS Pl would be 1 to 2 days older than normal on delivery to the circulation, explaining the shortened half-life and relative metabolic incompetence. Abnormal thrombopoiesis caused by cells or factors concentrated in the spleen may be responsible, rather than intrinsic faults in progenitor cells.

● **837** METHOTREXATE METABOLISM BY BONE MARROW CELLS FROM CHILDREN WITH LEUKEMIA. V. Michael Whitehead, David S. Rosenblatt, Mary-Jane Vuchich and Denise Beaulieu, McGill University-Montreal Children's Hospital Research Institute, Montreal, Canada.

Methotrexate (MTX, 4-NH_2-10-CH_3 PteGlu) is metabolized to MTX polyglutamates by lymphoblasts(ALL) myeloblasts(AML) and bone marrow cells from children with leukemia (Dev.Pharmacol.Ther.1: 40,1980). After 24h incubation in 1.0μM (^{3}H)MTX,levels of non-exchangeable MTX, 4-NH_2-10-CH_3-PteGlu$_2$ and 4-NH_2-10-CH_3-PteGlu$_n$ in remission marrow were 152±80, 57±22 and 99±46 (mean±S.D;n=16); in ALL at diagnosis were 73±55, 37±20 and 271±282 (n=13); in ALL at relapse were 143±102, 71±27 and 484±185 (n=6); and in AML were 103±52, 127±123 and 344±165 (n=4) pmoles/10^9 cells respectively. Higher levels of total cell MTX and of 4-NH_2-10-CH_3 PteGlu$_n$ were present in ALL at relapse and in AML, where leukemic cells are more likely to be resistant to MTX, than in ALL at diagnosis. Decreased uptake of MTX and synthesis of increased levels of dihydrofolate reductase are two mechanisms of resistance to MTX. Our data do not support the former as the mechanism of presumed resistance to MTX in our patients. Co-incubation of leukemic cells with both MTX and folinic acid (d,L,-5-CHO-H4PteGlu) resulted in a marked decrease in accumulation and polyglutamylation of MTX. This finding is similar to that described in fibroblasts. (Mol. Pharmacol.19:87,1981). Folinic acid also preserved DNA synthesis and cell growth in fibroblasts when co-incubated with MTX.These results provide evidence that folinic acid may "rescue" leukemic cells as well as host cells from MTX toxicity.

● **838** CORD SERUM ERYTHROPOIETIN VALUES AND DISAPPEARANCE RATES AFTER BIRTH IN POLYCYTHEMIC NEWBORNS. John A. Widness, Joseph A. Garcia, William Oh and Robert Schwartz. Dept. of Pediatrics, Brown Univ., Providence, RI; Lawrence Berkeley Labs, Univ. of California (Berkeley).

Since erythropoietin (Ep) responds to fetal hypoxemia, fetal oxygenation prior to delivery was assessed indirectly in 22 randomly selected newborns with polycythemia (P) (venous Hct ≥65%) in the first 3 days. Cord Ep was determined by a sensitive, specific double antibody RIA. A control group of 30 term infants from uncomplicated pregnancies had Ep cord values of 23.7±12.8 mU/ml (M±SD). In contrast, 15 of the 22 P infants (68%) of comparable gest. age had elevated Ep levels (>2 SD). No differences were found between the P groups for Apgar scores (1' and 5'), meconium staining, C-section, or maternal smoking. P infants with elevated Ep were more likely to be SGA. Ep levels from 5 newborns in the elevated Ep group were studied with sequential venous plasma Ep levels in the first 24 hrs of life. None had respiratory distress requiring O_2 therapy. First order log disappearance curves were parallel with a mean half-life of 2.7 hrs (range: 2.3-3.0). It is speculated that an elevated cord Ep level indicates fetal hypoxemia at birth and is a frequent antecedent factor in neonatal P. The postnatal fall in Ep reflects normoxemia after birth. A serial fall in Ep after birth may be useful in differentiating ante- from postnatal hypoxemia.

P Groups:	Normal Ep	Elevated Ep
Ep*:	23.3 (12-42)	1361 (56-16,006)
AGA	6	8
LGA	1	1
SGA	0	6

*mean (range) mU/ml $\chi^2 = 6.50$ $p < 0.05$

● **839** POLYMORPHONUCLEAR LEUKOCYTE (PMN) CYTOSKELETAL ABNORMALITIES IN SHWACHMAN SYNDROME (SS). David A. Williams, Robert J. Rothbaum, Cynthia C. Daugherty, James L. Lessard and Richard E. Harris, (Spon. by William K. Schubert). Children's Hospital Medical Center, Cincinnati, Ohio.

To assess PMN structure and function in SS, we studied PMN movement, degranulation, concanavalin A (Con A) surface distribution and microtubule numbers in 3 SS patients. Directed movement under agarose was defective in all 3 compared to controls(mean:95 units vs 153; range: 45-120 vs 70-300). Random movement was near normal in all 3 (mean: 50 vs 58; range:20-80 vs 20-140). The % of total β-glucuronidase degranulated during exposure to zymosan was normal (73.5 ± 12.4% vs 79.0 ± 15%, mean ± SD). Distribution of fluorescein-conjugated Con A was distinctly abnormal showing a unique patched distribution in 27.5 ± 7.4% Shwachman PMN vs 3.4 ± 1.6% in controls. Patching was also associated with a significant increase in fluorescence photometric intensity (p<.01):

Patient	Con A Distribution	Intensity(mean±SD)	n
I	Diffuse/Patched	94.5±57.0/534.2±353.6	32/32
II	Diffuse/Patched	107.6±53.9/326.5±75.3	13/13
III	Diffuse/Patched	509.3±178/2870.1±1204	27/27

Colchicine had no effect on the % of patched cells nor on fluorescence intensity. EM centriole-associated microtubule (MT) counts were normal (5.3/14μm^2-patients vs 5.7 controls). The MT counts in SS PMN did not increase with Con A stimulation. A distinct population of PMN in SS have abnormal distribution of Con A and increased fluorescence intensity. In conjunction with diminished PMN movement these findings suggest a PMN cytoskeletal defect may contribute to infectious complications in SS.

840 NEUROMETRIC FINDINGS AND LEARNING DISORDERS IN CHILDREN TREATED FOR ACUTE LYMPHOCYTIC LEUKEMIA (ALL) R.S.WIMMER, W.B.HILL, L.S. PRICHEP, H.W.BAIRD (ST. CHRISTOPHER'S HOSPITAL FOR CHILDREN, TEMPLE UNIVERSITY SCHOOL OF MEDICINE, PSYCHOLOGY OF READING DEPT., TEMPLE UNIVERSITY,BRAIN RESEARCH LABORATORY,NEW YORK UNIVERSITY SCHOOL OF MEDICINE. Children treated for ALL who survive have been found to have significant learning disorders. Nine of 10 children chosen at random from those treated at St. Christopher's Hospital for Children were found to be functioning two grades below their expected levels by performance tests. Only one had been recognized previously in school. Neurometric testing, using EEG and evoked potential data, showed severity scores to be 1 to 3 standard deviations from normal. Of special interest is the lack of response in the parietal areas 50-90 milliseconds after light stimuli, a finding which would correlate well with perceptual motor impairment. In contrast,responses to auditory stimuli in the same areas were not affected. Whether or not these findings can be attributed to ALL therapy which includes cranial irradiation and intrathecal methotrexate is not clear.
The averages of the tests results are as follows: Follow-up, 99 months; Expected grade, 7.6; Word Preception grade, 6.0; Math reading comp.,5.2; Attention, 4.6; Concentration 4.3; Index of EEG reported in Std. deviation, 1.80.

841 DECREASED ASSOCIATION OF PROTEIN 4.1 WITH HEREDITARY SPHEROCYTOSIS (HS) SPECTRIN IN SOME FAMILIES WITH HS. LC Wolfe, KM John, J Falcone, and SE Lux. Children's Hospital Medical Center and Harvard Medical School, Boston, MA.

The shape and stability of the red cell (RBC) membrane is largely determined by a "membrane skeleton" composed of spectrin, actin and protein 4.1. To test whether defects in this structure might be responsible for HS we tested all of the known membrane skeletal protein interactions with particular attention on the previously unexplored spectrin-actin-4.1 association. HS ^{125}I-spectrin dimer (S_D) bound actin (A) normally in the absence of 4.1, but in 2/7 families the enhancement in S_D to A binding normally produced by 4.1 was muted, suggesting a defect in the S_D to 4.1 association. We examined this interaction directly in one HS kindred by precipitating the complex of HS S_D and ^{125}I-labeled normal 4.1 with antispectrin antibody and protein A. At saturation, S_D from 4/4 HS patients bound 39% less 4.1 than normal. This deficiency was not related to splenectomy or RBC age and was equally expressed in HS spectrin from fetal and adult RBCs. Scatchard analysis indicated a 40% deficit of 4.1 binding sites on HS S_D, but normal affinity. When chromatographed on a column of immobilized normal 4.1 all normal S_D was detained but 41% of HS S_D was not. This material did not interact with 4.1. In contrast, after elution the retained HS S_D (59%) bound 4.1 normally. All other testable HS S_D functions were normal. We conclude that HS is a genetically heterogeneous disorder. In some kindreds two populations of S_D are present, one of which is unable to bind 4.1 and binds to actin poorly. It is likely that this is the product of the dominant gene responsible for the HS phenotype.

842 A CONTROLLED STUDY OF HYPNOSIS FOR PAIN AND ANXIETY DURING BONE MARROW ASPIRATIONS AND LUMBAR PUNCTURES IN CHILDREN WITH CANCER. Lonnie Zeltzer and Samuel LeBaron. (spon. by Charles Grose). The Univ. of Tex. Health Sci. Ctr., Dept. of Pediatrics, San Antonio, Texas.

Hypnosis (H) was compared to nonhypnotic behavioral techniques (NH) for efficacy in reduction of pain and anxiety during bone marrow aspirations (BMA's) and lumbar punctures (LP's) in children with cancer. Fifty-two patients (pts.), 7-17 years, rated their pain and anxiety during BMA's and LP's. Twelve pts. (23%) reported minimal distress. The remaining pts. were prospectively randomized to an H or NH group and they and observers rated their pain and anxiety during 1-3 baseline and 1-3 intervention procedures. The inter-rater reliability (Pearson r) between pts. and observers during 202 procedures was 0.51 for pain and 0.58 for anxiety, and between 2 independent observers during 22 procedures was 0.90 for pain and 0.91 for anxiety (all $p<.001$). Baseline ratings of pain and anxiety did not differ between the H and NH groups, but baseline BMA's were rated higher than LP's for pain ($p<.001$) and anxiety ($p<.01$). Both types of behavioral intervention resulted in pain reduction for the 21 pts. who received intervention for BMA's ($p<.03$). However, the H group demonstrated greater pain reduction than did the NH group ($p<.0001$). Anxiety reduction during BMA's followed a similar pattern. For 17 pts. who received intervention during LP's, H and NH were equally effective in reducing pain ($p<.01$) and anxiety ($p<.02$). We conclude that H may be more effective than NH for reducing pain and anxiety during very stressful and painful procedures, but both H and NH may be equally effective during less difficult procedures.

IMMUNOLOGY

● **843** ABNORMAL MOBILITY OF NEONATAL (N) PMNs: RELATIONSHIP TO IMPAIRED ORIENTATION & POLYMERIZATION OF MICROTUBULES (MT). D.C. Anderson, B.R. Brinkley, G. Perry, C.W. Smith, Dept Peds & Cell Biol, Baylor Coll Med, Houston, 77030, & Dept Anatomy, Michigan State Univ, E. Lansing, MI 48824.

The basis for the impaired chemotaxis of N PMNs was studied by evaluating their capacity to orient in chemotactic gradients. Assessments of 27 healthy N PMN suspensions demonstrated that both the proportion of responding cells & their accuracy of orientation were diminished compared to adult (A) PMNs. Only 13±7% (fMLP) & 14±6% (C5a) of N PMNs were observed to orient compared to adult PMN values of 37±6% & 33±15%, respectively ($p<.001$). Of responding N cells, 73±11% (fMLP) 74±8% (C5a) oriented accurately as compared to 92±4% & 88±7% ($p<.001$), respectively, for A PMNs. Preincubation of N PMNs with antioxidants (Vit E or dihydroxybenzoic acid) enhanced orientation into fMLP gradients ($p<.01$). To evaluate a possible cytoskeletal basis for these abnormalities, immunofluorescent techniques employing sheep antitubulin & anticentriole sera were developed. Results were evaluated in "double-blind" experiments by two observers. Oriented into gradients of fMLP, N PMNs demonstrated 26±6 MTs/cell compared to 33±7 for A PMNs. The average MT length was also diminished in N (8.1μm) as compared to A (10.5μm) PMNs. As shown by flow microfluorimetry, the mean intensity/cell of antitubulin fluorescence of N PMNs (242±50) was significantly ($p<.001$) diminished compared to A PMNs (440±85). Diminished chemotaxis & orientation of N PMNs into CF gradients may be functionally determined by diminished polymerization of and/or peroxidation of cytoplasmic MTs in response to CF stimuli.

● **844** IMPAIRED C5a GENERATION IN NEONATAL SERA BY TYPE III GROUP B STREPTOCOCCUS (GBS). Donald C. Anderson, Bonnie J. Hughes, Morven S. Edwards, Gregory J. Buffone, & Carol J. Baker. Baylor Coll Med, Depts Peds & Path, Houston.

The role of neutrophil (PMN) mobilization in the pathogenesis of III GBS neonatal infection was evaluated with a chemotaxigenesis (CTG) assay employing adult or neonatal sera, III GBS cells, & adult PMNs. Generation of C5a by 13 adult sera with moderate-high (3-40 μg/ml) or low (≤2 μg/ml) levels of specific antibody (Ab) was confirmed by PMN aggregometry, neutralization of CTG by anti-C5, & C5 depletion. CTG was significantly greater in high vs low specific Ab-containing sera ($p<.001$); stepwise increases in CTG occurred when specific IgG was added to hypo γ sera. Immunospecificity of CTG was shown by a failure of type III GBS to generate C5a in sera with high levels of Ia GBS Ab. Mean CTG in 3 high & 16 low Ab-containing sera from healthy term neonates were 24% & 62% of high ($p<.001$) & low ($p<.01$) Ab adult sera, respectively. For all low Ab neonatal sera, CTG was diminished compared to all adult sera ($p<.01$). Addition of both complement (C) & specific IgG to neonatal sera was required to restore CTG to high Ab adult values. The relative rank order of CTG, opsonic & aggregating activities were similar among each test group. Three high Ab & 4 low Ab maternal-cord serum pairs were studied with adult & neonatal PMNs. CTG with neonatal PMNs was ≈ half of that observed with adult PMNs for all serum pairs, & CTG by neonatal sera-neonatal PMN mixtures was only 20% (high Ab) & 9% (low Ab) of values for paired maternal sera when adult PMNs were used ($p<.001$). These findings indicate that CTG in neonatal sera by III GBS is impaired & that low levels of specific Ab, immature C function, & motile properties of neonatal PMNs contribute to impaired host defense.

845 EFFECTS OF PROSTAGLANDIN E_1 (PGE_1) ON PMN LEUKOCYTE FUNCTION IN INFANTS WITH CYANOTIC CONGENITAL HEART DISEASE (CHD). D.C. Anderson, M.R. Nihill, Z. Friedman. Dept. of Pediatrics, Baylor Coll of Med, Houston, TX, 77030.

Previous in vitro studies have demonstrated inhibitory effects of PGE_1 on selected PMN functions, & some clinical observations suggest that CHD infants may be at increased risk for the development of systemic infections as a result of PGE_1 treatment. Therefore, assessments of the pharmacokinetics of PGE_1 & determinations of PMN chemotaxis (CTX), adherence, phagocytosis & bactericidal activity were performed in 24 infants prior to, during &/or following PGE_1 infusions. Following a PGE_1 regimen of 0.1 μg/min for ≈1.5 hrs, mean ± S.D. plasma concentrations of PGE_1 = 530±203 pg/ml, values > that which modulate PMN functions in vitro. No accumulation of PGE_1 concentrations in plasma were demonstrated following 24 hrs of administration. Random PMN mobility & CTX (C5a/bacterial chemotactic factor) values for infants on PGE_1 were 79±9 & 88±16/95±20% values observed prior to PGE_1 treatment ($p>.05$). During PGE_1 infusions, mean baseline PMN adherence values were 89±16% of pretreatment controls ($p>.05$). Phagocytosis-chemiluminescence values were 94±18% of pre- or post-treatment values ($p>.05$). Intracellular bactericidal activity (S. aureus) of PMNs obtained during PGE_1 infusions was comparable to pretreatment bactericidal activity. No inhibitory effects of PGE_1 containing plasma obtained from the same infants were observed when reacted with healthy adult PMNs. No significant correlations between PGE_1 concentrations & any PMN function tested were observed. These findings fail to demonstrate inhibitory effects of PGE_1 on PMN functions when administered therapeutically to CHD infants.

846 NATURAL KILLER CELL ABNORMALITIES RELATED TO PREGNANCY. J.E.Baley and B.Schacter. (Spon. by A.A. Fanaroff) CWRU, RB&C Hosp., D.Peds.& Path., Cleve.,OH

Natural killer(NK) activity, implicated in tumor surveillance and the response to some viral infections, may be important in the regulation of the immune response. Resistance of spontaneous NK activity to 3000 rads γ irradiation is under x-linked control in adults. Since pregnant women and newborns have many immunological abnormalities, we have examined NK activity and radioresistance in infants and mothers immediately after birth. NK activity assayed with ^{51}Chromium release from the target cell K562 was lower in 15 mothers (22.4±14.6%) than adult controls (30.0± 7.8%, p<.01). 24 neonates (26-42 wks gestation) had NK activity (11.5±7.8%) significantly lower than both controls and their mothers (p<.01). No relationship was noted with gestational age, birth weight percentile, sex of the infant or gravidity of the mother. Using the single cell assay, lymphocytes from 12 newborns were found to form slightly fewer conjugates (9.88±1.33%) with the K562 than the controls did (11.98±1.8%, p<.01), while conjugates formed by the mothers (11.9±2.35%) were not significantly different. Lymphocytes from 7 newborns caused significantly less killing of K562 in conjugates (12.9±7.3%) than their mothers (24.3±5.4%, p<.01) or controls (26.2±4.4%, p<.01).

The radioresistance of NK activity in the newborns and mothers did not conform to the previously described pattern of x-linked inheritance, consistent with the hypothesis that NK activity in the mothers and infants is a property of a cell different from the conventional NK cell, one less efficient at killing and more resistant to radiation.

● **847** IgG AND IgM PNEUMOCOCCAL POLYSACCHARIDE ANTIBODY RESPONSES IN INFANTS. Douglas J. Barrett, Elia M. Ayoub, and Arthur J. Ammann, Departments of Pediatrics, University of Florida, College of Medicine, Gainesville and University of California, San Francisco.

Studies were performed to determine if the age-dependent variation in antibody (Ab) level following immunization with pneumococcal polysaccharide (PnPs) antigens also varied with the serotype of PnPs and immunoglobulin class of Ab. IgG and IgM Ab to PnPs types 3,6,18,19, and 23 were measured by enzyme-linked immunosorbent assay before and after PnPs immunization in 31 normal children aged 2-18 months and 13 normal adults. Prior to immunization, IgG Ab but no IgM Ab was found to all five serotypes in 2-6 month olds. Post-immunization IgG titers were significantly depressed for type 23 only. In contrast, post-immunization IgM Ab levels at this age were similar to the adult levels for all but type 3. By 12-18 months of age, pre-immunization IgG levels had fallen for all but type 3; again, IgM Ab was rarely detected prior to immunization. While IgG Ab levels following immunization were lower than adults for types 3,6,18 and 23, the rise in Ab titer for these serotypes was not significantly different than adults.

Certain serotypes gave consistently better responses than others. IgG and IgM responses to type 3 could be found as early as 2 months of age, while types 6 and 18 were poorly immunogenic for either IgG or IgM Ab even at 18 months of age. Types 19 and 23 stimulated greater fold-increases in IgM Ab than IgG Ab. These results emphasize the complex ontogeny of the antibody response to PnPs antigens. Responses are age-dependent and serotype-dependent, for both the level and class of Ab produced.

848 THE EFFECT OF MULTILAMELLAR VESICLE LIPOSOMES ON POLYMORPHONUCLEAR LEUKOCYTE (PMNL) FUNCTION. T.G. Cleary, R.L. Juliano, L.K. Pickering. Univ. of Texas Medical School, Program in Infectious Diseases and Clinical Microbiology, Depts. of Pharmacology and Pediatrics, Houston, Texas.

Previous work with colostral lipid and Intralipid has suggested that lipid particles depress neutrophil function by exhausting metabolic substrates and decreasing availability of Fc receptors. In the current study, we examined the effect of multilamellar vesicle (MLV) liposomes made of phosphatidyl choline, cholesterol, and phosphatidyl serine (10:5:1 ratio) on PMNL function. Small MLVs (<1u in diameter) and large MLVs up to 10u in diameter (concentrations range from 0 to 35 mg/ml) were exposed to PMNL for 2 hours prior to and immediately before assay. Zymosan stimulated hexose monophosphate shunt activity in CPM/10^6PMNL (1152 ± 51 control versus 989 ± 50 for small MLVs and 1058 ± 103 for large MLVs) was not significantly depressed in cells exposed to MLV when compared to unexposed cells. Fc receptors 88 ± 1% for control versus 86 ± 2% for small MLVs and 84 ± 4% for large MLVs were likewise not significantly decreased. Uptake, internalization, and killing of ^{3}H thymidine labeled S aureus 502A was unaffected by low concentrations of small or large MLVs. Low concentrations of liposomes do not induce defects in neutrophil function of the type seen when PMNL are exposed to colostral lipid or Intralipid.

Supported by NIH grant HD13021.

849 REQUIREMENT FOR LYMPHOCYTES IN C2 PRODUCTION BY CULTURED HUMAN MONOCYTES. Larry Consenstein, Thomas R. Welch and Roger E. Spitzer. SUNY, Upstate Medical Center, Department of Pediatrics, Syracuse.

Several investigators have demonstrated that long-term cultures of human mononuclear cells produce functionally active C2. Human mononuclear cells were isolated by ficoll-hypaque sedimentation and cultured in RPMI or M199 supplemented with 15% heated fetal calf serum. C2 was measured at intervals by standard hemolytic assay. Cultures could be maintained for over 5-8 weeks with good viability of cells and C2 production. If the mononuclear cells were washed vigorously after two hours of initial incubation, the remaining adherent cells (all monocytes by nonspecific esterase staining) produced minimal C2 despite long-term cultures. If the vigorous washing was omitted, however, C2 was detected within the first two weeks and reached maximum levels at 4-5 weeks (2-10 x 10^8 effective molecules/culture). In a second series of experiments, non-adherent cells (lymphocytes by nonspecific esterase staining) were added to cultures of monocytes which had been thoroughly washed. Returning lymphocytes to the cultured monocytes restored their ability to synthesize C2. The time of appearance of C2 and its maximum level was related to the number of lymphocytes added to the cultures. Cultured lymphocytes alone, however, did not produce C2. These data suggest a requirement for lymphocytes in order for cultured monocytes to synthesize C2. Whether this requirement is for a soluble lymphocyte-produced factor or for actual contact between the cells is not clear from these studies. Nevertheless, the lymphocyte appears to be a potent modulator of C2 synthesis.

850 EXCESS SUPPRESSOR FUNCTION ASSOCIATED WITH EXCESS SUPPRESSOR (OKT8+) LYMPHOCYTE POPULATIONS IN AN INBRED PEDIGREE WITH OMENN'S SYNDROME, A VARIANT OF SCID. J.B. Cooper, J. Eng, R.A. Karol, D.K. Dennison, M.A. Sawyer, E.C. Lawrence, D.M. Marcus, and W.T. Shearer, Baylor College of Medicine, Depts. of Pediatrics and Medicine, Houston.

We report 2 new cases of Omenn's syndrome, a variant of SCID, with characteristic rash, eosinophilia and histiocytic proliferation. At age 4 months patient 1 had 4,216 lymphocytes (lcytes)/mm^3 of blood with 79% E-rosette+(T lcytes) and 3% surface Ig+(B lcytes). Serum IgG was low (49 mg/dl) while IgE was increased (500 IU/ml). Lcyte responses to mitogens were low, but MLC reactivity was normal. Monoclonal antibody studies using an Ortho Cytofluorograf revealed a helper/suppressor (OKT4+/OKT8+) lcyte ratio of 0.64 (nl. 1.8-3.0) and was due to an absolute increase in OKT8+ lcytes. Patient 2, at 1, 3 and 4 months of age had OKT4+/OKT8+ of 6.5, 2.5 and 2.3, and the fluorescence intensity of the OKT8+ population became identical to patient 1 at 4 months. Ia+ cells fell from 50% at 1 month to 5% at 4 months. There were 17.6% OKT6+ lcytes present at 4 months, indicating circulating stage II thymocytes. In 90 healthy members of this highly inbred family, 22 had OKT4+/OKT8+ < 1.6. Suppressor lcyte function assessed by reverse hemolytic plaque assay revealed 70 to 80% functional suppression of normal lcytes by patient 2 but no suppression by a relative with OKT4+/OKT8+ of 1.1. Thus, Omenn's syndrome is associated with disturbed T lcyte subpopulations as tested with phenotypic markers and a functional suppressor assay; moreover, phenotypic expression of the lcyte defect was found in an extraordinary number of family members.

851 DEFICIENT LYMPHOCYTE-MEDIATED COMPLEMENT SYNTHESIS IN THE NEWBORN. Larry Consenstein, Thomas R. Welch, Roger E. Spitzer and Ann E. Stitzel. SUNY, Upstate Medical Center, Department of Pediatrics, Syracuse.

It has been shown that stimulated T lymphocytes enhance monocyte (Mn) production of C2 in adults; in the newborn, however, the T cell population appears to be balanced towards suppression of lymphocyte (Ly) function. Since the neonate is characteristically hypocomplementemic, the role of Ly in Mn C2 production in the newborn was, therefore, investigated. Mn were harvested from adult (Ad) or umbilical cord (Co) blood by ficoll-hypaque sedimentation followed by adherence onto plastic dishes. Ad and Co Mn were cultured with or without the addition of 10^6 Ad or Co Ly. C2 was measured hemolytically in supernates at regular intervals. Six experiments with 4 Co and 5 Ad bloods were done. Results of representative experiments reveal: Ad Mn produce minimal C2 without added Ly (peak=0.9 x 10^8 effective molecules/ml culture). With Ad Ly, 4x more C2 was produced, but with Co Ly only 1.5x more C2 was generated. Co Mn, like Ad Mn, produce minimal C2 without added Ly (peak=0.3 x 10^8 EM/ml). When mixed with Ad Ly, 26x more C2 was produced; with Co Ly, however, only 7x more C2 was produced. Ly mixed with Mn cultures also allowed for earlier production of C2. Ad Mn alone first produce measurable C2 on d 11. C2 production began 4 d earlier with Ad Ly, but only 1 d earlier with Co Ly. Co Mn alone first made C2 on d 17. With Ad Ly, C2 was produced 8 d earlier, but only 3 d earlier with Co Ly. These data indicate that the lymphocyte is essential for efficient production of C2 in man. The newborn lymphocyte is deficient in this function, perhaps resulting in the hypocomplementemia seen in the newborn.

● **852** OXIDATIVE METABOLISM OF BREAST MILK MACROPHAGES. Nancy P. Cummings, Marianne R. Neifert, Richard B. Johnston, Jr. National Jewish Hospital and Research Center and University of Colorado School of Medicine, Denver.

Little is known about the physiology of human tissue macrophages (Mϕ) or the process of Mϕ activation in the human. We have shown previously that mouse Mϕ can be primed by exposure in vitro to the bacterial products lipopolysaccharide (LPS) and muramyl dipeptide (MDP), or by injection of MDP, so that they produce more of the bactericidal agent superoxide anion (O_2^-) when stimulated by phagocytosis or contact with phorbol myristate acetate (PMA). We have studied release of O_2^- by breast Mϕ obtained from 30 normal mothers and have examined the capacity of these cells to undergo priming for greater O_2^- release, a characteristic of activated Mϕ in animals. Mϕ were isolated by dextran, Ficoll-Hypaque, and adherence and were > 99% phagocytic. In 16 paired samples, PMA-stimulated O_2^- release was similar with Mϕ from colostrum (0-3 days) or transitional milk (5-8 days) (585±48 and 484±45 nmol/mg protein, respectively, $\bar{x}$±SEM). Release of O_2^- by milk Mϕ was almost identical to that by the mothers' blood monocytes. Incubation of milk Mϕ overnight with LPS, 10 ng/ml, "activated" the Mϕ for greater PMA-stimulated O_2^- release (837±38 nmol/mg, vs. 382±27 for controls, n=6). Incubation with MDP, 1-100 µg/ml, did not activate; but incubation with the 6-0-steroyl derivative of MDP activated the Mϕ for greater O_2^- release (672±109, vs. 362±74 for controls, n=3). We conclude that breast Mϕ released into both colostrum and milk undergo a vigorous oxidative metabolic response that is equivalent to that of blood monocytes. Our data also suggest that human Mϕ have the capacity to be activated rapidly by exposure to certain bacterial products; this activation could enhance their capacity to resist infection.

853 TREATMENT OF VASCULITIS WITH PROSTAGLANDIN E_1. Karen D. Dunn, Michael J. Welch, E.R. Stiehm, UCLA Medical Center, Dept. of Pediatrics, Los Angeles, CA.

We report the apparently successful reversal of vasculitis and penile necrosis with intravenous prostaglandin (PG) E_1 in an 8 year old Black male with a repaired tetralogy of Fallot, hereditary spherocytosis and a 2 year history of recurrent necrotizing vasculitis. Previous episodes of vasculitis were localized to the extremities and resulted in loss of several digits. Laboratory investigation revealed only elevated levels of circulating immune complexes (CIC) with each episode. Treatment, including aspirin, dipyridamole, dextran, intra-arterial reserpine, nitroprusside, high-dose steroids and plasmaphoresis did not prevent progression of vasculitis and tissue loss. The last episode began with pain and swelling in the penis rapidly progressing to purpuric discoloration of the entire penis and base of the scrotum. Within 12 hours of the onset of symptoms, a 72 hour infusion of PGE_1 was begun. The dose was increased slowly over 5 hours to a final concentration of 0.021 ug/kg/min and maintained at that level for the remainder of the trial. The patient also received steroids. Over the next 4 days, the swelling and discoloration entirely resolved. CIC were found to be elevated (730 ug/ml) at the onset but were only minimally elevated (350 ug/ml) 5 days later. Skin flushing was noted 1 hour after the infusion was begun along with enhanced palpation of the popliteal, dorsalis pedis and posterior tibial arteries bilaterally. No other side effects were noted. We conclude that this therapeutic success was due in part to the vasodilating and antiplatelet effect of PGE_1 in preventing further vascular and tissue damage.

854 ABNORMALITIES OF LYMPHOKINE GENERATION IN CHILDREN WITH JUVENILE RHEUMATOID ARTHRITIS. Janet E. Ellsworth, Leonard D. Stein, Paulette J. Thebert, Carol G. Ragsdale, Donita B. Sullivan, and James T. Cassidy, University of Michigan Medical School, Rackham Arthritis Research Unit, Departments of Pediatrics and Medicine, Ann Arbor.

Cell-mediated immunity was assessed in 74 children with Juvenile Rheumatoid Arthritis (JRA) using 2 in-vitro assays: (1)generation of Leucocyte Inhibition Factor (LIF) by concanavalin A (ConA) stimulated lymphocytes and (2)Lymphocyte Transformation (LT) using 4 dilutions of phytohemagglutinin and optimal doses of ConA and pokeweed mitogen. Results were analyzed by onset types of JRA and compared to results from 42 normal adults and 30 hospitalized children. In LT, abnormalities were infrequent and occurred most often when autologous rather than AB+ serum was used in the cultures. Sera from some children depressed LT in normal cells. In LIF, abnormal responses were seen in all onset types and in hospitalized children in spite of normal LT to ConA. While inflammatory disease activity contributed to this finding in the polyarticular and systemic onset groups, it did not for the children with pauciarticular disease who were relatively well, but expressed other notable immunologic abnormalities such as antinuclear antibodies and uveitis. We concluded that there was a basic difference in immune reactivity as measured by lymphokine generation in children with pauciarticular JRA compared with healthy adults.

	Control Values	Pauci-articular	Poly-articular	Systemic onset	Hospitalized children
ConA LT	25-87(x10³)	3/44	1/20	1/10	0/30
ConA LIF	0.88	18/44	7/20	5/10	9/30

855 DECREASED SUPPRESSOR CELL ACTIVITY IN DiGEORGE SYNDROME. Etzioni, A., DiGeorge, A.M. and Lischner, H.W. St. Christopher's Hosp. for Child., Philadelphia, PA.

In DiGeorge syndrome a wide spectrum of immunological abnormalities from complete deficiency to almost normal cellular immune response can occur. In 4 patients with partial DiGeorge syndrome we have noted exaggerated delayed hypersensitivity skin test responses by comparison with most normal children of the same age. For this reason we studied concanavalin A (Con A)-inducible suppressor activity in the peripheral blood lymphocytes of 3 children (6 mos, 15 and 17 yrs) with partial DiGeorge syndrome but without evident infection. The percentages and absolute numbers of T cells were, respectively: 20-39%, 1200-1800/mm^3; 40-60%, 1200-2200/mm^3; and 50-60%, 900-1100/mm^3. Peripheral blood mononuclear cells which were preincubated with or without con A for 48 hr were incubated with equal numbers ($5x10^4$/microtiter well) of unstimulated cells in the presence of 1/2, 1/6 and 1/18 of the concentration of con A causing optimal proliferative response as measured by ^{3}H-thymidine uptake. No cultures containing the patients' con A-pretreated cells showed greater than 20% suppression, whereas control con A-treated cells caused 30-90% (usually 55-80%) depression of ^{3}H-thymidine uptake by the same responder cells. This relative excessive depression of suppressor activity may be secondary or may indicate selective exhaustion of T suppressor cells. It is possible, however, that fewer suppressor cells are produced either because maturation of the latter is more sensitive to deficiency of epithelial thymus or because of absence of a portion of the thymus which is more important for maturation of the suppressor cells. (Supported in part by USPHS NIH grant RR75).

856 IMMUNE DEFICIENCY WITH INCREASED T-SUPPRESSOR AND DECREASED T-HELPER CELLS IN SARCOID SYNDROME. Roger Friedman, George Mallory, Frank T. Weng and Philip Fireman. University of Pittsburgh School of Medicine, Dept. of Pediatrics, Pittsburgh, PA.

At 4 years of age, a female developed thrombocytopenia, anemia, lymphopenia and hepatosplenomegaly which improved following splenectomy. Liver and spleen histopathology showed typical sarcoid granulomas. From age 4 to 12 she did well except for cough and dyspnea which improved with Prednisone therapy. At age 12 following 3 recent episodes of H. influenzae sepsis, immunologic studies revealed hypogammaglobulinemia (IgG:164 mg%, IgM:48 mg%, IgA:9 mg%, IgE:5 IU) with deficient functional antibodies but normal B-cells, 14%. Cellular immune studies showed absent delayed skin tests with normal PHA, MLC and LIF to Candida. Studies using monoclonal antibodies showed total T-cells 20% (nl 68±20%), T-helper cells 13% (nl 50±10%), T-suppressor cells 34% (nl 20±10%). C4 was decreased, 9.9 mg% (nl 17-50), but other complement components were normal. She had elevated angiotension converting enzyme, 157 (nl 80±20) despite high dose Prednisone therapy. Pulmonary function showed decreased flow rates, DLCO 75% of predicted with normal lung capacities. Gamma globulin therapy was instituted with marked clinical improvement. An immunoregulatory defect is suggested as the pathogenesis of this immunodeficiency syndrome with multi-system sarcoid granuloma, hypersplenism, pulmonary disease and hypogammaglobulinemia.

857 SINUSITIS COMPLICATING IMMUNOLOGIC DISEASES. Roger Friedman, Ellen Wald, Michael Ackerman, Gilbert Friday, Gregory Milmoe and Philip Fireman. Univ. of Pgh. School of Medicine, Dept. of Pediatrics, Pittsburgh, PA.

Radiographic abnormalities of paranasal sinuses are frequent in children with asthma or immunodeficiency syndromes. Whether bacterial infection or other inflammatory mechanisms produce sinus x-ray abnormalities has not been determined.

Six children, ages 2 to 15, with exacerbation of asthma, purulent rhinorrhea and sinusitis on x-ray had maxillary sinus aspirates. Cultures were positive in 4: B. catarrhalis (2), S. pneumoniae (1) and non-typeable H. influenzae (1). Nose and throat cultures did not correlate with sinus cultures. Following antibiotic therapy, 5 showed clinical and x-ray improvement including the 4 with positive cultures. Pulmonary functions improved in 4 of 5 studied.

Two antibody deficient children with cough, purulent rhinorrhea and sinusitis by x-ray underwent sinus aspiration. One child's culture grew H. influenzae, type d, resistant to Ampicillin and Cefaclor. Following TMP-SMX therapy, cough decreased, weight gain occurred and pulmonary function improved. Sinus x-rays improved slightly. The other child's aspirate culture grew S. pneumoniae. After antibiotic therapy cough and rhinorrhea improved but sinus x-rays remained abnormal.

Bacterial sinusitis was documented in 6 of these 8 children with asthma or immunodeficiency and its treatment led to clinical improvement.

858 ATAXIA-TELANGIECTASIA: A MULTIPARAMETER ANALYSIS. Richard A Gatti, Michael A. Medici, Miriam Bick, Chick Tam, Kathleen Hall, Vivianne Oxelius, Allan L. Goldstein and Elena Boder. UCLA School of Medicine, Department of Pathology and Cedars-Sinai Medical Center, Department of Pediatrics, Los Angeles, CA; University of Lund, Department of Pediatrics, Lund, Sweden; and George Washington University, Department of Biochemistry, Washington, D.C.

Eight families, including twelve patients with AT, were investigated for parameters which tested the current models of pathogenesis for this autosomal recessive disorder. We found: T cells decreased, B cells elevated, PHA responses decreased, variable T suppressor activity, serum IgA and IgG_2 decreased. Serum alpha fetoprotein and liver enzymes were elevated. Increased Con A capping of lymphocytes and increased cyclic nucleotides of T-lymphocytes correlated in individual patients. Chemotactic responses of neutrophils were decreased in most patients. Thymosin-α-1 levels of patients and family members did not differ from age-matched controls. Excision repair of gamma-induced DNA damage was decreased in some patients and parents. Translocation of chromosome 14q was not noted in any of our patients. Taken together, these data are not easily reconciled with any of the current hypotheses but suggest that a primary or secondary cytoskeletal disorder may underlie the pathogenesis of AT. Heterozygotes could not be reliably identified, even by multiparameter analyses.

● **859** FAMILIAL RETICULOENDOTHELIOSIS - A PRIMARY OR SECONDARY DISEASE? Erwin W. Gelfand, C. Pandu Rao, Debby McCurdy, Nolan H. Sigal and Amos Cohen. Division of Immunology, Hospital for Sick Children, Toronto, Canada.

Patients with familial reticuloendotheliosis and eosinophilia (Omenn's syndrome) are reported to have variable degrees of impairment of humoral or cell-mediated immunity. We have studied three children with this syndrome; all presented in the first year of life with hepatomegaly, lymphadenopathy, a generalized exfoliative dermatitis, frequent infections and failure to thrive. Common to all were markedly elevated levels of serum IgE (>4000 ng/ml). Despite the presence of relatively normal numbers of T lymphocytes, normal T-lymphocyte subset distribution and proliferative responses to lectins and allogeneic cells in two of the patients, thymic biopsies revealed marked lymphocyte depletion and the absence of Hassall's bodies. B and T lymphocytes from all three patients were totally deficient in ecto-5'-nucleotidase activity while other cells (bone marrow, fibroblasts, granulocytes) had normal 5'-nucleotidase activity. On the other hand, lymphocyte endo-5'-nucleotidase activities and sensitivity to the addition of deoxyadenosine or deoxyguanosine were entirely normal. The failure to express ecto-5'-nucleotidase activity may reflect abnormalities in lymphocyte differentiation which accompany this syndrome or alternatively, represent the consequences of an, as yet undefined, extrinsic process. The presentation of this syndrome in one patient with a lymphoproliferative disease, another with severe combined immunodeficiency and a third with cartilage-hair hypoplasia may suggest a common pathogenetic event being expressed in susceptible individuals.

● **860** ISLET CELL ANTIBODIES AND IMMUNE COMPLEXES IN JUVENILE DIABETICS. Mohammad A. Ghalambor, Stanley A. Schwartz, Sumer Pek and Dale L. Oxender. The University of Michigan School of Medicine, Departments of Biological Chemistry, Pediatrics and Medicine, Ann Arbor, 48109.

Previous studies have indicated the presence of islet cell antibodies (IC-Ab) and immune complexes (IC) in insulin-dependent diabetics sera (IDD-S). Present studies describe the isolation and characterization of IC-Ab and IC. Rat pancreas islets were dispersed by Dispase, the cells cultured and tested for insulin secretion. The results obtained showed the presence of 2 types of Ab in IDD-S. Islet cell surface Ab identified by a) immunofluorescence, b) reactivity with ^{125}I-labeled sera and immunoglobulins derived therefrom (IG) and c) reactivity with ^{3}H-labeled cell membranes. Assays were done by measurement of ^{125}I-IG bound to unlabeled cells, ^{3}H-labeled cells bound to cold IG and protein concentration in the supernate. The reaction of IDD-S or IG with cells or membranes was 2-5 fold higher than those of normals. Using the soluble fraction of islet cells (SF) as Ag, the reactivity of IDD-S was linear with SF concentration, whereas the normals had no detectable activity. The Ab found in IDD-S was differentiated from anti-insulin by inhibition studies. The IC was precipitated by polyethyleneglycol using ^{125}I-labeled sera and IG. The amount of ppt. from IDD samples was higher than normals. IC was identified by m.w., >300k, C_1q test and dissociation into Ag and Ab. Further evidence for presence of IC-Ab in IDD-S was obtained by inhibition studies. Addition of mouse-antirat islet cell Ab to ^{125}I-labeled IDD-S incubated with islet cells gave inhibition, with no detectable change in the reactivity of normal sera. (Supported by NIH grant #AM 26315.)

861 SPECIFICITY OF HUMAN BACTERICIDAL (BC) ANTIBODY FOR OUTER MEMBRANE PROTEIN (OMP) OF NON-TYPABLE H. INFLUENZAE (NTHI). Hanspeter E. Gnehm, Stephen I. Pelton, Sunita Gulati, and Peter A. Rice (spon. by J.O. Klein). Boston Univ. Sch. of Med., The Maxwell Finland Laboratory for Infectious Diseases, Boston City Hospital, Depts. of Pediatrics and Medicine, Boston.

Infection due to H. influenzae results in the production of antibodies directed against multiple antigens including outer membrane (OM) antigens such as lipopolysaccharide (LPS) and OMP. We studied immune antibody specificity in a patient with respiratory infection due to NTHI, using ELISA. When compared to normal human sera, the convalescent serum contained 10-fold higher specific antibodies of both IgG and IgM classes against LPS and OMP derived from the infecting strain.

Since complement-fixing BC antibody may be important in protection against respiratory infection due to NTHI in children, we examined BC activity of antibodies specific for selected OM antigens. We have reported (Pediat Res 15:611, 1981) that OMP inhibited human BC activity in direct absorption experiments. We employed purified OMP, affixed to solid-phase, as immunoadsorbents for human sera to define the antigenic specificity of OMP for BC antibody and to examine anti-LPS antibody for potential BC activity. The convalescent serum depleted of >80% of OMP specific activity (IgG and IgM) lost comparable BC activity. Two normal sera depleted of >60% of OMP antibody also lost comparable BC activity, while maintaining 97% of IgM and 80% of IgG anti-LPS activity. OMP may be an important OM target both for natural and immune BC antibody.

● **862** EFFECTS OF THE DURATION OF PREGNANCY ON THE IMMUNOLOGIC SYSTEM IN HUMAN MILK. Armond S. Goldman, Cutberto Garza, E. O'Brian Smith, and Randall M. Goldblum. The University of Texas Medical Branch in Galveston and Baylor College of Medicine, Department of Pediatrics.

The study included 14 women who delivered after and 13 women who delivered before 36 weeks of gestation. Milk was obtained between 2-12 weeks of lactation. Mean concentrations of lysozyme, lactoferrin, total IgA, and secretory IgA (SIgA) were greater in preterm milk at each phase of lactation (p values 0.07, 0.003, 0.05, and 0.05, respectively). Whereas SIgA levels in term milk were stable between 6-12 weeks (0.6-0.7 mg/ml), mean levels in preterm milk rose from 1.3 mg/ml at 6 weeks to 2.9 mg/ml at 12 weeks (p 0.05). SIgA antibodies to E.coli somatic antigens increased 4 fold or more in several individuals in both groups. In addition, antibody titers were significantly higher (p. 0.05) in milk from a subgroup whose preterm infants were appropriate size for gestational age. Lymphocytes and macrophages-neutrophils in term milk which were initially 2.4 and 6.5 x 10^4/ml, respectively, fell to 0.6 and 0.8 x 10^4/ml, respectively by 8 weeks. In contrast, mean lymphocyte counts in preterm milk which were initially 0.3 x 10^4/ml rose progressively (3.3 x 10^4/ml at 12 weeks; p 0.07) and the number of macrophages-neutrophils remained relatively unchanged (1.5 x 10^4/ml at 2 weeks; 3 x 10^4/ml at 12 weeks).

Thus, the duration of pregnancy significantly affects the development of the immunologic system in human milk during the first 3 months of lactation. In addition, this study raises the question whether these alterations may be beneficial for premature infants whose immunologic systems are not fully developed.

863 IMMUNOLOGIC FACTORS IN HUMAN MILK DURING WEANING. Armond S. Goldman, Cutberto Garza, E. O'Brian Smith, and Randall M. Goldblum. The University of Texas Medical Branch in Galveston and Baylor College of Medicine, Departments of Pediatrics.

Although dramatic changes in the levels of immunologic proteins in human milk have been reported during abrupt weaning, there are no reports concerning the effects of gradual weaning upon the immunologic system in human milk. Seven women age 20-35 years began weaning at 6 months of lactation by reducing the frequency of breast feeding by 10-15% weekly for 12 weeks. The mean volume of milk collected from the subjects decreased to 67% of the initial volume at 4 weeks, 40% at 8 weeks, and 20% at 12 weeks. No leukocytes were detected in the milk specimens from these subjects during the study. The concentrations of lactoferrin and lysozyme remained unchanged in most of the subjects. The principal type of IgA in these milk specimens was secretory IgA (SIgA). In contrast to the other immunologic proteins, the concentrations of total and secretory IgA steadily increased during weaning (total IgA, 0.6 ± 0.3 mg/ml before weaning and 1.1 ± 0.6 mg/ml at 12 weeks)($p<0.05$). In addition, significant rises in antibody titers to E.coli somatic antigens in four of these individuals could not be explained by increases in total SIgA in the milk. This finding indicated that the enteromammary gland pathway of SIgA antibody production was operational during weaning. Thus, this study suggests that the effects of gradual and abrupt weaning are distinct and that the concentrations of certain protective factors in human milk are maintained or increased during the period of gradual weaning.

● **864** EVALUATION OF THE PROLIFERATIVE AND DIFFERENTIATION POTENTIALS OF B CELLS FROM HYPOGAMMAGLOBULINEMIA PATIENTS. Patricia Haber, Taro Kuritani, Joachim Ledwoch, John Kearney and Max Cooper. Cellular Immunobiology Unit, Departments of Pediatrics and Microbiology, University of Alabama in Birmingham, Alabama.

Individuals with common varied immunodeficiency (VID), or late onset forms of panhypogammaglobulinemia, usually have normal numbers of B lymphocytes but few plasma cells. We have examined their B cells for responsiveness to T cell factors, polyclonal mitogens and stimulation via surface immunoglobulins. When B cell fractions of blood mononuclear cells from individuals with VID were cultured with $F(ab')_2$ fragments of rabbit anti-human μ chains, cells from 9 of 13 patients proliferated at least as well as controls (mean stimulation indices of 10.8 ± 4.2 versus 6.3 ± 2.9). In addition, 9 out of 9 had normal proliferative responses to culture supernatants of MLR stimulated T cells. Plasma cell responses to pokeweed mitogen were greatly reduced, but B cells from 10/10 patients showed an ability to differentiate into IgM producing plasmablasts in response to Epstein-Barr virus. After two weeks in culture, 22 ± 12 % of the patient's cells contained IgM as compared with 30 ± 15% of the cells from normal controls. B cells from five patients were fused with a nonproducer variant of the mouse myeloma line Ag8653. In each instance heterohybridomas secreting human IgM were formed. The results suggest that B cells from these hypogammaglobulinemic individuals (i) can proliferate normally in response to T cell factors and to cross-linkage of their immunoglobulin receptors, and (ii) have the capacity for differentiation into plasma cells. We conclude that their B lymphocyte arrest may reflect defective reception of differentiation signals.

865 CELLULAR AND HUMORAL IMMUNE STATUS OF BREAST VS. FORMULA FED INFANTS DURING THE FIRST SIX MONTHS OF LIFE Robert T. Hall, Robert J. Dockhorn, William J. Braun, Carolyn G. Kurth, Sandra K. Bowen and Melinda Brewer. University of MO, KC School of Medicine, Children's Mercy Hospital, KC MO

There are reported to be fewer gastrointestinal and respiratory infections in breast fed compared with formula fed infants. This has been attributed to cellular and humoral immune factors in breast milk, however there have been no comprehensive serial studies of the immune status of breast vs. formula fed infants. The present study compares the development of the immune system of 27 breast fed with 12 formula fed infants over the first six months of life.

Age	Birth		4 wks		6 wks		4 mo		6 mo	
	Br.	Fo.	Br.	Fo.	Br.	Fo.	Br.	Fo.	Br.	Fo.
IgG	1016	1425	599	548	477	433	312	352	373	417
IgA	2	1	5	5	7	12	14	17	17	22
IgM	27	25	54	47	55	46	82	63	81	82
IgE	3	4	3	7	5	7	6	23	6	30
C_3	95	104	99	73	87	91	102	102	114	138
Total C	74	81	76	72	72	70	79	98	94	108
T cells	35	36	39	43	37	45	29	33	33	44

None of the differences was significant. Determinations after elimination of breast fed infants receiving supplemental feedings less than six wks of age or those who received supplemental feedings or discontinued breast feeding after six wks were not different than the means of the total or exclusively breast fed group.

These data indicate that the influence on the immunologic status of breast feeding during the first six months of life is not reflected by cellular or humoral differences measured in infants in this study.

866 ENHANCED BACTERIAL PHAGOCYTOSIS BY NEUTROPHILS FROM HEALTHY AND "STRESSED" NEWBORN INFANTS. M.C. Harris, J. Stroobant, C. Cody, S.D. Douglas, and R.A. Polin. Univ. of Pa. Sch. of Med., and Dept. of Peds., Children's Hospital of Philadelphia, Philadelphia, PA.

Developmental deficiencies of the immune system are major determinants of host susceptibility to infection. The purpose of this study was to investigate the effect of severe stress on neonatal neutrophil (PMN) phagocytosis, and to compare the ability of neonatal and adult PMNs to ingest ^{3}H-labelled group B streptococcus (GBS). Three patient populations were studied: healthy infants (n=15, B.W. 3160.7 ± 648.3 g, (m ± SD) G.A. 38.0 ± 2.4 wk), "stressed" infants (n=33, B.W. 2019.3 ± 990.4 g, G.A. 33.5 ± 4.9 wk), and healthy adults (n=22). 32 of 33 "stressed" infants had acute respiratory illnesses requiring mechanical ventilation. Radiolabelled type Ic GBS was opsonized with 5% adult serum, and incubated with PMN monolayers adherent to coverslips. Bacterial uptake was determined at 0, 40, 60, and 80 minutes and expressed as cpm/10^6 PMNs. For all study groups, there was a significant increase in uptake with time ($p < .05$). PMNs from "stressed" infants demonstrated enhanced bacterial uptake when compared to adults: (40 min., "stressed" 7670.1 ± 6187.1 (m ± SD), adult 4972.8 ± 4005.7, $p < .05$; 60 min., "stressed" 10522.2 ± 6634.5, adult 6368.5 ± 3855.4, $p < .01$, 80 min., "stressed" 13408.4 ± 8046.5, adult 8750.6 ± 7522.7, $p < .025$. Phagocytosis was significantly greater in healthy infants vs. adults (40 min., healthy 5667.9 ± 4089.1, $p < .05$, 60 min., 9614.7 ± 7644.7, $p < .01$, and 80 min., 12955.5 ± 8518.6, $p < .01$). There were no significant differences in bacterial uptake between "stressed" and healthy infants or between infants > or < 1500 grams. In conclusion, PMN phagocytosis of GBS is enhanced during the neonatal period and not adversely affected by severe stress or prematurity.

867 A NEW DIAGNOSTIC TEST FOR CEREBRAL CYSTICERCOSIS. Douglas C. Heiner, Bruce Miller, Mark A. Goldberg and Aileen Myers. Harbor-UCLA Medical Center, UCLA School of Medicine, Depts. of Pediatrics and Neurology, Torrance, CA

Cerebral cysticercosis is the commonest cause of epilepsy in some African countries. It is also common in Mexico and in areas of the United States which have large numbers of Mexican and other immigrants. It may involve children as well as adults and may be associated with hydrocephalus, aseptic meningitis, and cerebral calcifications of typical size and configuration.

Cysticercus cellulosa antigen was bound to CNBr-activated cellulose discs. Five μl of serum or 20 μl of CSF were incubated overnight with an antigen coated disc and buffer to make 55 μl. After thorough washing, the disc was incubated with radiolabelled staphylococcal protein A for 3 hours. After 3 more washings the counts bound reflected IgG antibodies to C. cellulosa in the serum or CSF. An initial study involved the serum and CSF of 64 patients. All 15 patients with known cysticercosis had elevated serum IgG antibodies and most had antibodies in the CSF. Many had a selective increase in specific antibodies in the CSF, indicating specific production, or extraction, by the CNS. IgE, IgG4 and IgD antibodies were produced by most patients and were also present in the CSF, but not so consistently as total IgG antibodies. Nine of 17 patients with suspected cysticercosis and 0/32 with unrelated neurological diseases had antibodies in either serum or CSF. Cerebral cysticercosis is a virtual certainty when CSF antibodies are high. It should be suspected when serum antibodies are high and there are CNS signs. If neither fluid has antibodies the diagnosis is highly unlikely.

868 INDUCTION OF EOSINOPHIL HISTAMINASE IN ACTIVE ASTHMA. J.J. Herman, B.B. Holson, R.S. Schneiderman. Northwestern University Medical School, Children's Memorial Hospital, Allergy Div. Chicago. (Spon. by S.T. Shulman)

Mast cell mediators are released during hypersensitivity episodes, associated with release or increased granulocyte, especially Eosinophil (Eos), inhibitory activity. In status asthmaticus in humans, Eos histaminase (Hx) and monocyte histamine methyl transferase activity along with plasma and urinary histamine metabolites increase.

The increased Eos Hx (205±32 to 741±68 Units) correlated to the level of pulmonary obstruction (≤20 to 65% decrease FEV_1). Asthmatic Eos Hx content increased (210±28 to 614±56 Units) by incubation with the histamine analog NαMethyl histamine (10^{-10}-10^{-9}M); this analog did not affect control Eos Hx (192±21 to 232±25 Units) nor the Hx assay at these concentrations. The increase Eos Hx increase was temp. (max. 40°C) time (max. 15 min.) and pH (max 7.2) dependent as well as inhibited by metabolic inhibitors. A trypsin sensitive protein component of asthmatic serum increased Eos Hx activity in a dose dependent manner 0.1-1.0 mcg/10^7 Eos; the maximum increase in asthmatic Eos (+286 Units) was two-fold--the increase in control Eos (120 Units). Upon Sephadex G-200 separation this activity was found in glycoproteins of two fractions (160,000 MW and 40,000 MW); DTT reduction diminished the Hx inducing activity in both; control serum had no activity. Eos Hx activity was increased in an additive manner by NαMe histamine and the serum components. Thus, exogenous histamine and inflammatory proteins contribute to the increased Eos Hx.

● **869** CHARACTERIZATION OF A FACTOR THAT PROMOTES T-LYMPHOCYTE COLONY FORMATION BY CORD BLOOD MONONUCLEAR CELLS. Henry G. Herrod and William R. Valenski (Spon. by Fred F. Barrett), University of Tennessee Center for the Health Sciences, Department of Pediatrics, Memphis, Tennessee.

We previously demonstrated impaired T-lymphocyte colony formation (TLCF) by cord blood mononuclear cells when compared to the TLC forming capacity of adult mononuclear cells (AMC). Co-cultures of irradiated AMC with CBMC results in enhanced TLCF by CBMC (284+72 colonies/plate vs. 752+78 $p < 0.001$). A similar degree of enhancement of TLCF is seen when a colony promoting factor (CPF) produced by PHA stimulated AMC is added to cultures of CBMC (361+98 vs. 766+138, $p < 0.005$). CBMC do not produce CPF. CPF is not produced when AMC are treated with the monoclonal antibody OKT4 plus complement (C') prior to stimulation. Treatment of AMC with OKT8 and C' does not affect the production of CPF.

CBMC Alone	Supernatants From CBMC + OKT4 Depleted AMC	Supernatants From CBMC + OKT8 Depleted Cells
243+82	253+77	917+88

When CBMC are cultured with CPF for 1-3 hrs prior to culture and then washed, the enhanced TLCF is still evident. Based on Sephadex column chromatography CPF has a molecular weight of less than 12,000. It is stable at 56°C for 1 hr. Addition of Interleukin-2 from two sources failed to enhance TLCF by CBMC.

CPF is a soluble substance capable of enhancing the TLC forming capacity of CBMC. Failure of CBMC to produce CPF may account in part for the relative functional immaturity of newborn lymphocytes.

● **870** IDENTIFICATION OF ANTIGEN (Ag)-SPECIFIC CIRCULATING IMMUNE COMPLEXES (CICs) USING THE RAJI-CELL RADIOIMMUNOASSAY (RC-RIA). Stanley C. Jordan, Robert B. Ettenger, Rebecca S. Sakai and Richard N. Fine. Department of Pediatrics, UCLA Center for the Health Sciences, Division of Pediatric Nephrology, Los Angeles, CA. 90024.

The RC-RIA was used to detect CICs in 2 pts. with thyroglobulin (HuTg)-mediated immune complex glomerulonephritis (ICGN) and in an experimental in vitro system of pre-formed bovine serum albumin (BSA-anti-BSA) CICs. Preincubation of (+) CIC samples with the suspected (HuTg) or known Ag (BSA) resulted in a profound inhibition of ^{125}I Protein A binding to RCs. HuTg decreased binding by 25-50% in the 2 pts. with ICGN mediated by HuTg but did not decrease binding of CICs to RCs in pts. (+) for CICs without evidence of anti-Tg Abs. Binding was not decreased by preincubation with related (B-Tg) or unrelated (BSA) Ag. BSA-anti-BSA ICs pre-formed @ (3X) Ag excess were (+) in RC-RIA. Preincubation of BSA-anti-BSA ICs with BSA resulted in a (70%) inhibition of binding in the RC-RIA. Preincubation of the ICs with a related Ag (ovalbumin) resulted in an intermediate inhibition of binding (65.5%) but was not decreased when samples were preincubated with unrelated Ag. Sucrose density gradient studies confirmed the IC nature of materials reactive with the RC-RIA, and also confirmed the mechanism responsible for the inhibitor of RC-RIA activity was an Ag-specific diminution in CIC size and number. This new technique can be used to evaulate the specific Ag content of CICs detected in human sera and may be helpful in differentiating immunopathogenic from non-immunopathogenic CICs.

● **871** CIRCULATING IMMUNE COMPLEXES IN A NEW SYNDROME OF ACQUIRED T-CELL DEFICIENCY. Stanley C. Jordan, Howard Schanker, Eugene Barnett, Andrew Saxon, Michael S. Gottlieb. Divisions of Pediatric Nephrology and Clinical Immunology and Allergy, UCLA School of Med., L.A.,Calif.

We recently described a new syndrome of acquired T-cell imbalance in previously healthy homosexual men which we termed the gay-related immunodeficiency syndrome (GRID). Patients experience multiple opportunistic infections including Pneumocystis carinii pneumonia, mucosal candidiasis and cytomegalovirus (CMV) infection at multiple sites. Profound lymphopenia and virtual elimination of the helper/inducer T cell subset as defined with monoclonal reagents were uniform features of the syndrome. Despite absolute B lymphopenia, these patients had normal levels of IgG and IgM and elevated levels of IgA (mean 2-3 times normal). We believe that this syndrome represents an acquired immunodeficiency resulting from CMV infection which is hyperendemic in the male homosexual population. The majority of patients developed retinal lesions which had the appearance of the cotton-wool spots seen in systemic lupus erythematosus and in other disorders involving the microvasculature. We therefore measured circulating immune complexes in these patients with three assays (Raji-RIA, C1q-SPA & IgG polyethylene glycol precipitation). High levels of immune complexes were uniformly demonstrated. These findings may account for the prominent retinopathy. Immune complexemia may result from intense antigenic stimulation and could be involved in the pathogenesis of the immune deficient state.

872 CONCANAVALIN A INDUCED SUPPRESSOR CELL FUNCTION IN PEDIATRIC AUTOIMMUNE DISEASE. Shelby H. Josephs, and Julee S. Staley. (Spon. by Glenn Rosenquist)

Children's Hospital National Medical Center, Washington, D.C.

Concanavalin A (Con A) activates a subset of peripheral blood lymphocytes to function as suppressor cells in a variety of immunologic assays in vitro. In several autoimmune diseases, depressed suppressor cell function has been documented with this technique. We have studied 11 normal young adults and 14 patients (aged 3-18 years) with autoimmune diseases: 7 with juvenile rheumatoid arthritis (JRA), 4 with dermatomyositis (DM), and 3 with Reiter's Syndrome (RS). Peripheral blood mononuclear cells were incubated for 48 hours either with or without 50 mcg/ml of Con A. These cells were then added to a standard one-way mixed lymphocyte culture on day zero. Suppression of uptake of 3H-thymidine was assessed on day 6 of culture as shown in the table. In these samples, disease activity and drugs did not distinguish recognizable subgroups of patients with regard to suppressor activity.

	Normal	JRA	DM	RS
Number of Experiments	29	7	4	3
% Suppression (mean±SEM)	52±6	49±12	48±14	30±15

Group means for patients did not differ significantly from control (Student's t-test, $p>0.05$). In all groups except RS, Con A treated cells irradiated prior to addition to the MLC were less suppressive than those not irradiated. Our data suggest that pediatric patients with these autoimmune diseases retain activity of that subpopulation of suppressor lymphocytes stimulated by Con A.

873 ABNORMALITY OF T DEPENDENT B CELL DIFFERENTIATION OF CORD BLOOD. L.K.L. Jung, R.A. Good, and S. Pahwa. Memorial Sloan-Kettering Cancer Center, N.Y., N.Y., 10021

The maturational defect of human cord B lymphocytes was investigated using polyclonal B cell activators and antigens as probes for the abilities of cord B lymphocytes to proliferate and differentiate. In the presence of T dependent mitogen, pokeweed mitogen (PWM) the mononuclear cells (MC) from cord blood proliferated equally well as the adult cells. However, the cord cells could not differentiate to become immunoglobulin secreting cells (ISC) in response to PWM as did the adult cells. In contrast, in the presence of T independent mitogen, Epstein Barr virus (EBV), cord cells proliferated and differentiated into ISC in a manner similiar to the adult cells. Antigen specific antibody response of cord cells to sheep red blood cells following in vitro sensitization of MC cultures with antigen was found to be lower than the response of adult cells, although some cord samples were found to have responses comparable to adult samples. With the addition of T cell mitogen Con A to the cell cultures at 48 hours after the initiation of cultures as a means of amplifying T cell help, the antigen specific response of the cord cells was enhanced to levels comparable to normal adult cells unstimulated by Con A, but not to those of adult cell cultures stimulated with Con A 48 hours after culture initiation. With Con A, the percentage of enhancement of the antigen specific response of cord cells was comparable to that observed in cultures of adult cells. These findings suggest that the immaturity of the B cells in cord blood may be due, at least in part, to defect of B cell subpopulation(s) which require(s) T cell help to enter into differentiative stages.

● **874** RESTORATION OF IMMUNOLOGICAL FUNCTION BY A HISTOINCOMPATIBLE, T CELL DEPLETED MARROW TRANSPLANT IN A CHILD WITH SEVERE COMBINED IMMUNODEFICIENCY. Neena Kapoor, Richard J. O'Reilly, Dahlia Kirkpatrick, Marilyn S. Pollack, Bo Dupont, Robert A. Good and Yair Reisner. Memorial Sloan-Kettering Cancer Center, New York, New York 10021

A male with severe combined immunodeficiency (SCID) chimeric with nonfunctional maternal T cells derived from a transplacental infusion who did not develop Graft vs. Host Disease, was administered a transplant of maternal marrow, depleted of T cells by differential agglutination with soybean agglutinin and sedimentation of E rosettes. A dose of 7.8×10^7 marrow cells/kg was administered. Engraftment was first detected in non-T lymphoid populations. Thereafter E rosettes rose from 20% to 66% of an 800-1400 absolute lymphocyte count. Over 4 mos, lymphocyte transformation responses to mitogens(PHA,Con-A,PWM) antigens(C.albicans, E.coli) and allogeneic cells increased to >90% of that detected in normal controls. Immunoglobulins, which were not detected pretransplant, increased to IgG 318mg%, IgA 35mg%, IgM 76mg%. In addition, the patient developed lymph nodes, appropriate isoagglutinins, and delayed type hypersensitivity response to DNCB. Despite incompatibilities for a full HLA,A,B,D haplotype, no GVHD has been observed. The patient, now 7 mos. post transplant, is clinically healthy, living home. Transplants of HLA-haplotype mismatched marrow depleted of T cells by this technique may allow immune reconstitution without Graft vs. Host Disease in SCID patients lacking an HLA matched marrow donor.

● **875** RELEASE OF PHARMACOLOGICAL MEDIATORS FROM HUMAN NEUTROPHILS BY VIRAL IMMUNE COMPLEXES: EFFECTS ON MUCOSAL SMOOTH MUSCLE FUNCTION AND POSSIBLE ROLE IN CLINICAL DISEASE. Tej N. Kaul, Howard S. Faden, Elliott Middleton, Tetsuzo Fugitani, Pearay L. Ogra. State University of New York at Buffalo, Children's Hospital of Buffalo, Department of Pediatrics, Buffalo, N.Y.

Ficol-hypaque separated human neutrophils (PMN) were stimulated with specifically prepared immune complexes of polio, measles, herpes simplex and respiratory syncytial viruses (RSV). The presence and quantity of immune complexes were determined by radioimmunoassay. The functional effects of neutrophil metabolites released after interaction with immune complexes were determined by their ability to induce smooth muscle contraction in an in-vitro system employing guinea pig ileal smooth muscle strips in a grass polygraph. Interaction of RSV immune complexes with neutrophils resulted in a significant ($p<0.001$) degree of smooth muscle contraction compared to RSV or antibody alone. On the other hand the interaction of neutrophils with immune complexes of other viruses resulted in minimal or no smooth muscle contractions ($p<0.001$). Various inhibitors of arachidonic acid metabolism were tested in the system and were observed to decrease the magnitude of smooth muscle contraction. These observations suggest that RSV specific immune complexes may result in the release of soluble products with potential effects on the contractility of smooth muscles in the mucosal surface. Such neutrophil factors may contribute to the pathogenesis of mucosal disease and possibly bronchospasm in RSV infection.

876 FUNCTIONAL ALTERATIONS OF RABBIT PULMONARY ALVEOLAR MACROPHAGE (PAM) FOLLOWING PROLONGED HYPEROXIA. Aditya Kaul, Ramakrishna Velamati, Moti L. Tiku, Douglas Rhone John L. Skosey, Dharmapuri Vidyasagar and George F. Smith, University of Illinois and Illinois Masonic Medical Center, Departments of Pediatrics, Internal Medicine and Pathology, Chicago.

Assisted ventilation with high oxygen (O_2) concentrations is a common event today. We examined the effects of ventilation with 100% O_2 on PAM function. Adult rabbits were anesthetized & ventilated with 100% O_2 for 3 & 6 hours. Washings were then obtained from left lung, cells were counted and viability assessed by trypan blue exclusion. Cells were allowed to adhere onto labtek slides. Adherent PAM were assessed for Fc-receptor activity by enumeration of rosette formation with antibody coated sheep RBC. Phagocytic activity was examined by phagocytosis of latex beads. No differences were observed in yield or viability of cells obtained in control, nonventilated rabbits and 3 & 6 hour ventilated groups. However, ventilation for 6 hours resulted in a profound depression in Fc-rosette and phagocytic activity, as shown below:

	Control	100% O_2x3 hrs	100% O_2x6 hrs	p <
# Rabbits Tested	4	7	5	
% Fc-Rosettes	85.5±5.9	75±8.3	44.8±6.9	<0.001
% Phagocytic Index	87 ±2.0	86±2.6	40 ±5.7	<0.001

Rabbits ventilated with room air for 6 hours showed no significant depression of PAM function. In vivo hyperoxia for 6 hours results in impairment of phagocytosis and Fc-receptor activity of rabbit PAM. This functional impairment may translate into impairment of local defense mechanisms in the lung. Similar depression in PAM function may occur in newborn and adult humans exposed to prolonged hyperoxia.

877 LOCAL MAMMARY PRODUCTION OF SPECIFIC IgG_4 ANTIBODY IN HUMAN COLOSTRUM (HC). Margaret A. Keller, Douglas C. Heiner, Rose M. Kidd, Aileen S. Myers, UCLA School of Med., Harbor-UCLA Med. Center, Dept. of Pediatrics, Torrance, CA.

Published studies of HC have suggested local mammary production of IgA and IgM, not IgG. We examined HC and plasma samples from 27 postpartum women to determine if IgG_4 may be locally produced or selectively transferred into HC. IgG_4 was measured using RIA, and IgG was measured using radial immunodiffusion. The geometric mean concentrations of IgG_4 were 9.4 µg/ml [0.9-160] for HC and 149.7 µg/ml [21-920] for plasma, and for total IgG were 39.8 µg/ml [12-92] for HC and 7658.9 µg/ml [3250-16000] for plasma. The mean IgG_4 HC/plasma ratio [0.117±0.029] was 20 fold greater than the IgG HC/plasma ratio [0.006±0.001]. In 16 patients, the HC/plasma ratio for IgG_4 was greater than 10 times the HC/plasma ratio for total IgG, suggesting preferential local production or concentration of IgG_4.

We also examined the specimens using RIA for specific IgG_4 antibodies to β-lactoglobulin (BLG), bovine serum albumin (BSA), Bermuda grass (BG), and α-gliadin. Four patients had detectable IgG_4 anti-BLG in HC but not in plasma. Two others had an anti-BLG HC/plasma ratio 10 fold greater than the total IgG_4 HC/plasma ratio, indicating specific antibody production in the breast. Two other women had similar ratio evidence of local antibody production to BSA, three women to BG, and three to α-gliadin. One woman had a higher concentration of anti-BG in HC than plasma, and another woman had a higher concentration of anti-α-gliadin in HC than plasma. IgG_4 antibodies appear to participate in the enteromammary and common mucosal system of immune responses.

878 REGULATION OF THE FLUID PHASE OF THE ALTERNATIVE PATHWAY: ROLE OF FACTORS H AND I. Melanie S. Kim, Roger E. Spitzer and Ann E. Stitzel. SUNY, Upstate Medical Center, Department of Pediatrics, Syracuse.

Under normal conditions, C3 and factors B and D continuously react in the fluid phase resulting in low-grade formation of C3b and subsequent generation of the alternative pathway C3 convertase, C3bBb. Nonproductive utilization of all of the circulating C3 does not occur, however, because of two plasma inhibitors, factors H and I. The present study has examined the control of C3 activity in the fluid phase to determine the relative roles of factors H and I. If purified C3 and factors B and D are mixed so as to maintain "physiologic ratios" of all 3 components, 80% of the C3 is utilized within 10 minutes at 37° C indicating that the utilization of C3 occurs readily in the absence of control proteins. Addition of factor H at even 25% of this "physiologic" concentration, however, completely aborts C3 utilization. By contrast, factor I at 10 times the experimental concentration failed to control C3 turnover. These data indicate that factor H is the primary endogenous control protein for C3 utilization in the fluid phase and presumably acts by accelerating the decay dissociation of C3bBb with loss of factor B activity and concommitant loss of C3 reactivity. The role of factor I, therefore, would then be to control the serum level of factor B by inactivating C3b and preventing further utilization of factor B. Thus, regulation of the fluid phase of the alternative pathway may involve either factor H or I and defective regulation involving these factors may play a major role in a variety of disorders.

879 SUCCESSFUL REVERSAL OF MATERNO-FETAL GRAFT vs. HOST DISEASE IN A PATIENT WITH SEVERE COMBINED IMMUNODEFICIENCY BY IMMUNOSUPPRESSION, AND TRANSPLANTATION OF HLA-D COMPATIBLE PATERNAL MARROW. Dahlia Kirkpatrick, Neena Kapoor, Ricardo Bernalis, Marilyn S. Pollack, Bo Dupont, Richard J. O'Reilly Memorial Sloan-Kettering Cancer Center, New York, N.Y. 10021

An 11 month old female with severe combined immunodeficiency (SCID) developed scaling erythroderma, hepatitis, enteritis and nodal enlargement suggestive of materno-fetal GvHD. Differential HLA typing of T cells, B cells and monocytes demonstrated selective engraftment of maternal-type T cells. Initial mixed lymphocyte cultures indicated that cells from the father were unresponsive to the patient's cells despite HLA-A,B,C and Dr incompatibility. Studies using primed lymphocyte typing techniques confirmed that the father's unshared HLA-D determinant was identical to the patient's maternal HLA-D. To eliminate the maternal graft, the patient was immunosuppressed with anti-thymocyte globulin 30mg/kgx7 days and cyclophosphamide 50mg/kgx3 days. Thereafter, the patient received an infusion of paternal marrow. During early engraftment, manifestations of GvHD were exacerbated, but controlled with prednisone. Engraftment of both hematopoietic and lymphoid elements was followed by full hematologic recovery and immune reconstitution. Over 18 months post transplant, the patient is clinically well, with mild chronic GvHD controlled with low dose prednisone. Thus, lethal GvHD can be reversed by immunoablative therapy and a secondary infusion of histocompatible marrow. This case also provides another rare example of discrepancies between HLA-D and HLA-Dr, and suggests that HLA-D matching can be used to define suitably histocompatible related marrow donors.

880 SERUM POLYMERIC IgA: A SOURCE OF POLYMERIC IgA IN TEARS. Ronald Kleinman, Paul Harmatz, Daniel McClenathan, Bruce Bunnell, Kurt Bloch and W. Allan Walker, Harvard Medical School, Massachusetts General Hospital, Depts. of Pediatrics and Medicine, Boston, MA. 02114

Although polymeric IgA (pIgA) has been identified in tears, it has not been determined whether this antibody derives from local synthesis or by transfer from serum. This study investigates whether circulating serum pIgA is transferred to tears. pIgA anti-dinitrophenyl (DNP) antibody was prepared from the ascitic fluid of mice bearing the MOPC-315 plasmacytoma. The antibody was injected intravenously into lactating (day 1) and non-pregnant, non-lactating adult female Sprague-Dawley rats. Lacrimal secretions were collected 1 hour after injection. pIgA was detected by immunoprecipitation with rabbit anti-mouse IgA antiserum coated polyacrylamide beads and ^{125}I-DNP_{10}-bovine serum albumin. pIgA was detected in tears from lactating but not in tears from non-lactating, non-pregnant animals. These qualitative studies establish that pIgA can be transported from serum to tears during lactation. The observation that the MOPC-315 pIgA appears in the tears of lactating animals suggests that hormonal changes of lactation enhance the transport of pIgA into external secretions.

881 THE ONTOGENY OF HUMAN ANTIVIRAL CYTOTOXICITY. Steve Kohl, Susan E. Denson. Univ. of Texas Medical School, Houston, Tx.

The ability of leukocytes to destroy herpes simplex virus (HSV) infected cells in the presence of antibody (antibody-dependent cellular-cytotoxicity, ADCC) and the absence of antibody (natural killer cytotoxicity, NKC) has been correlated with the outcome of HSV infection. Anti-HSV ADCC has been reported as low or normal in cord blood, and dependent on the route of delivery. Using a 51 Cr release microcytotoxicity assay we studied the cytotoxicity to HSV-infected cells of peripheral blood lymphocytes of term babies during the first 3 months of life. Using an effector to target cell ratio of 30:1, ADCC of babies age 0-60 days (32.2±3.5, mean ± SEM, n= 21) was lower ($p<.001$) than matched adults (59.4±3.7). There was no difference between ADCC of older babies (52.2±12.8, n= 5) and adults (68.3±8.3). NKC of babies age 0-60 days (14.9±2.5) was lower ($p<.001$) than adults (38.8±3.3). NKC was not significantly different in older babies (32.8±15.9) and adults (49.6±12.2). Cytotoxicity of babies' lymphocytes was lower than adults' at all times using lower effector cell ratios. Babies' polymorphonuclear leukocyte cytotoxicity was low at all times tested. Post partum cytotoxicity did not vary with route of delivery. These data demonstrate a gradual normalization in antiviral cytotoxicity, correlating with the age at which humans become resistant to severe HSV infection. Reconstitution of these defects in the human neonate, as demonstrated in mice, may prevent severe HSV-infection.

Supported by NIH Grant 1HD 13021.

● **882** PROTECTION OF NEWBORN MICE FROM LETHAL HERPES SIMPLEX VIRUS (HSV) INFECTION BY HUMAN MONONUCLEAR CELLS (MC) AND HUMAN ALPHA INTERFERON (IFN), Steve Kohl, Lian S. Loo, and Stephen B. Greenberg, Univ. of Texas Medical School and Baylor College of Medicine, Houston, Texas.

Newborn mice and humans have low antiviral natural killer cytotoxicity and are unusually susceptible to severe HSV infection. Newborn C57Bl/6 mice were protected by a combination of IFN and MC (32% survival, $p<.001$) but neither alone when given i.p. one day prior to a 100% lethal i.p. HSV infection. The effective dose of IFN (100-10 units), MC number ($5x10^6$ to $5x10^5$) and active MC (lymphocyte or monocyte but not polymorphonuclear leukocyte) was determined. Protection did not depend on the anti- HSV immune status of the MC donor. Treatment of mice with IFN and MC after infection did not affect the outcome. WISH cells are human fibroblasts that secrete an IFN induced antiviral protein in vitro. Protection by WISH cells and IFN (55% survival, $p<.001$) suggested IFN induced cross species antiviral protein production in vivo.

Mice receiving IFN, MC and subneutralizing doses of anti-HSV antibody were nearly completely protected (95.2% survival), and protected significantly better ($p<.001$) than with either MC plus IFN or MC plus antibody. Protection was not due to viral neutralization. While MC from adult humans mediated this protection, those of neonates did not ($p<.001$). This is the first evidence for defective in vivo IFN stimulated natural killer cytotoxicity or antiviral protein production of neonatal MC. Understanding this defect may facilitate rational immunostimulation or replacement therapy for neonatal HSV infection.

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● **883** IMPAIRED CHEMOTAXIS AND NEUTROPHIL (PMN) FUNCTION IN GLYCOGENOSIS (GSD) Ib. N.L. Koven, M.M. Clark, C.S. Cody, C.A. Stanley, L. Baker and S.D. Douglas, Univ. of Pennsylvania School of Medicine, Children's Hospital of Philadelphia, Department of Pediatrics, Philadelphia, PA.

PMN function was investigated in 2 patients with GSD Ib and neutropenia. GSD Ib was documented by liver biopsy and a normal amount of latent glucose-6-phosphatase activity. Patient A, age 4, had stomatitis, skin infections and septicemia; patient B, 16, had minor infections and periodontitis. Absolute neutrophil counts (ANC) ranged from 160 to 1200/mm^3. Diminished and delayed migration of PMNs into a skin "window" occurred in B; ANC increased from 490 to 1260/mm^3 after epinephrine stimulation. Random and directed PMN migration under agarose toward f-Met-Leu-Phe (FMLP), pepstatin, and zymosan-activated sera were severely diminished in both patients. At 10^{-7} FMLP, mean random and directed migration were 52% and 10% (A, n=3) and 48% and 8% (B, n=4) of controls. These results were independent of incubation time and chemoattractant concentration. Parents' PMN showed normal migration. No cell-directed inhibitors were present in patients' sera, and zymosan activation effected normal control PMN migration. Patients' PMN had diminished quantitative NBT reduction compared to controls. B had a significant defect in PMN bactericidal activity with E. coli with <0.2 log killing at 2 hr. These results further characterize the defect in PMN migration reported by Beaudet et al., J. Pediatr. 97:906, 1980. The finding of other abnormalities of PMN function suggests a membrane "activation" defect in PMN which may be related to the microsomal membrane defect in hepatocytes in GSD Ib.

884 THE EFFECTS OF HYPOCOMPLEMENTEMIA ON RAT LATE-PHASE REACTIONS. ROBERT F. LEMANSKE, M.D., KEITH JOINER, M.D., AND MICHAEL KALINER, M.D., NIH, Bethesda, MD

Immediate hypersensitivity reactions both in the lung and the skin may be followed by delayed-in-time responses termed late-phase allergic reactions (LPR). Human cutaneous LPR are characterized histologically by mixed cellular infiltrates; immunofluorescent analyses suggest that immunoglobulin and complement deposition do not play a significant role in either initiating or propagating these reactions. To better establish the role complement plays in the genesis of LPR, Sprague-Dawley rats (200-250 g), known to produce LPR following skin testing with either rabbit anti-rat IgE or isolated mast cell granules (MCG), were depleted of serum complement. Cobra venom factor (CVF) (200 units/kg, n = 5) or saline (n = 4) was injected IV; CH_{50} and hemolytic C_3 titers, WBC counts and differentials were assessed at 0, 6, and 30 hrs following injection. Compared to controls, CVF-treated rats demonstrated a rise in total WBC counts ($p < .01$) and absolute neutrophil counts ($p < .01$) at both 6 and 24 hrs following treatment. CH_{50} titers in CVF-treated rats decreased from 220 ± 20 units/ml at baseline to < 1 unit /ml at 6 and 30 hrs. C_3 titers in CVF-treated rats were < 10 units/ml compared to 50,575 ± 1,070 units/ml in controls. LPR were induced with either anti-IgE (1:10) or MCG (25 µg) and analyzed 8 and 24 hrs later. Despite the alterations in peripheral leukocyte counts and CH_{50} and C_3 titers, both the histologic characteristics and the intensity of LPR induced in CVF-treated rats were similar to controls. Thus, complement depletion does not affect the normal expression of rodent LPR.

● **885** DEFICIENCY OF NATURAL KILLER (NK) CELLS IN CYSTIC FIBROSIS (CF) - DISSOCIATION OF NK FROM KILLER (K) CELL ACTIVITY. Lischner, H.W., Neville, M.E., Huang, N.N., Palmer, J. and Sun, G.X. St. Christopher's Hospital for Children and Temple University School of Med., Philadelphia, PA.

We are testing the hypothesis that the immune complexes which are frequently present in CF inhibit antibody-dependent cellular cytotoxicity (ADCC) or deplete the K cells which mediate ADCC by binding to their receptors for the Fc portion of IgG (FcR). It was expected that the function of other FcR-bearing cells such as NK cells would be less affected, but preliminary results reveal greater suppression of NK cells. The activity and numbers of functioning NK and K cells among peripheral blood mononuclear cells (MC) were assayed in 12 CF patients and simultaneously in normal adults and non-CF pulmonary patients. Release of ^{51}Cr from labeled K562 human leukemia cells or antibody-coated P815 mouse mastocytoma cells was measured at lymphocyte-to-target ratios of 5:1 to 40:1. Cytotoxic lymphocytes were counted as those conjugated with trypan blue-staining target cells after a 1:1 mixture of MC and the same target cells was incubated in soft agarose. NK activity and/or % of NK cells were markedly depressed in 10/12 patients. Six of those with depressed NK cells had normal K cells. Other data suggest that the pulmonary infection in CF is responsible for the observed deficiency in NK cells, and it is postulated that the latter contributes to the intensity of CF exacerbations due to viral infections. The dissociation of NK and K cell activity in some of these patients is confirmatory of our other data indicating that NK cells are distinct from K cells.

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● **886** MATERNAL-NEONATAL INTERACTION AND BREAST FEEDING: ROLE OF HUMAN MILK IN TRANSFER OF ADOPTIVE IMMUNITY AND TRANSMISSION OF MATERNAL INFECTIONS TO THE NEONATE. Genevieve A. Losonsky, Mark Fishaut, and Pearay L. Ogra. Dept. of Pediatrics, State University of New York, Buffalo, New York.

Groups of breast feeding and non-breast feeding rubella seronegative post-partum women were immunized intranasally or subcutaneously with HPV-77 DE5 or RA27/3 live attenuated rubella virus vaccine. The mother-infant pairs were sequentially tested for the appearance of rubella virus, and specific antibody and cell-mediated immune (CMI) responses in the milk, nasopharynx and peripheral blood employing the techniques of tissue culture infectivity, immunofluorescence and lymphoproliferation. Rubella specific IgA and CMI response was regularly observed in the milk of all subjects studied. Significant shedding of rubella virus was observed in nasopharynx in 30-50%, and in milk in 70-75% of immunized women. Of particular importance is the finding that rubella virus was recovered from the nasopharynx in 56% of breast feeding infants. Of these, 44% developed a modest antibody and CMI response in blood and nasopharynx, which disappeared by 4-5 months. The remaining breast fed infants with nasopharyngeal virus shedding, did not manifest any rubella specific immune response. Virus shedding or development of seroconversion for rubella was notably absent in the non-breast feeding infants. These observations suggest frequent transmission of maternal rubella virus infection to the neonate through breast feeding. The implications of such transmission, associated with the paucity of specific immune response in the neonate must be considered in other natural or vaccine induced maternal infections during lactation.

887 ANTIDIPTHERIA AND ANTITETANUS TITERS IN NORMAL ADULTS AND CHILDREN. Naomi L. Luban, Shelby Josephs, Barbara Taylor, Roger L. Beeckx, (Spon. by Glenn Rosenquist). George Washington University School of Medicine, Children's Hospital National Medical Center, Department of Pediatrics, Clinical Laboratories and Immunology, Washington, D.C.

In the initial work up of children with suspected or known immunodeficiency, antibody titers to diptheria (AD) and tetanus (AT) are frequently measured to assess humoral immunity. This can be done in the previously immunized child or following an active challenge immunization. To define a reference range for AD and AT, we have used a passive tanned cell hemagglutination assay and have obtained values in 86 healthy children from 0 to 17 years of age and 52 healthy adults. Washed, tanned type O red cells are coated with either diptheria toxoid or tetanus toxoid. Utilizing microtiter plates, serially diluted patient sera and antigen coated red blood cell suspension are incubated. Agglutination of the red cells is used to define titer. 95% of all adults had AD of 1:2187 or higher while 96% had AT of 1:19,683 or higher. However, titers were lower in 3 foreign born adults. Age dependent increases are seen for both titers with 78% of the children reaching adult values for AD by one year of age. Similarly, 79% of all children had adult AT by one year of age. Measurement of AD and AT are easily performed in any immunology laboratory. By one year of age AT and AD can be used to accurately reflect immunization status and B cell immune competence.

888 CIRCULATING IMMUNE COMPLEXES IN KAWASAKI SYNDROME: DETECTION BY RAJI CELL AND C1q SOLID PHASE ASSAYS. Wilbert H. Mason, Masato Takahashi, Rebecca Sakai and Stanley C. Jordan. Univ. So. Calif. Sch. Med., Childrens Hospital of Los Angeles and Univ. Calif. Los Angeles Sch. Med., Departments of Pediatrics, Los Angeles.

Epidemiologic and clinical features of Kawasaki syndrome (K.S.) suggest a possible infectious etiology while pathologically K.S. appears to be a vasculitis of medium sized arteries. To determine what role circulating immune complexes (CICs) might play in K.S., the sera of 42 patients with K.S. were tested for CICs by the Raji cell radioimmunoassay (RC-RIA) and C1q solid phase assay (C1q-SPA). Overall 29 patients (69%) were positive by 1 or both assays; 22 (52%) by RC-RIA and 20 (48%) by C1q-SPA. CICs were detected as early as 2 days and as late as 35 days of illness. Clinical data was available for 32 of the patients. An established clinical scoring system was used to estimate severity of disease. No correlation was found between disease severity and incidence or concentration of CICs found. Four patients had coronary artery aneurisms (CAA) detected by 2 dimensional echocardiography and confirmed by angiography. The incidence and concentration of CICs in these patients was not different from 28 patients without CAA. Of 10 patients who had serologic evidence of recent infection with group A, β hemolytic streptococci or a herpes group virus, 8 had CICs. CICs are often found in patients with K.S. and although their incidence and concentration do not correlate with clinical severity, they may play an etiologic role in producing the vasculitis.

889 IMMUNOREGULATORY EFFECT OF RECOMBINANT DNA PRODUCED HUMAN INTERFERON (HuIFNα) ON HUMAN POLYMORPHONUCLEAR LEUKOCYTE (PMNL) FUNCTION. Mercedes Macias, Thomas G. Cleary, Randall Reves, Steve Kohl, Larry K. Pickering. Univ. of Texas Medical School, Program in Infectious Diseases and Clinical Microbiology and Department of Pediatrics, Houston, Texas.

Two recombinant DNA produced HuIFNα preparations (A and D) were evaluated to detect their immunoregulatory effect on oxidative metabolism and functional activities of PMNL. Ficoll-Hypaque separated PMNL from blood of healthy volunteers were incubated with five concentrations of HuIFNα ranging from 125 to 5000 IU/ml. Utilization of 1-^{14}C glucose by resting PMNL was significantly ($p<0.05$) greater after incubation with 500 IU/ml of HuIFN when compared to control cells or PMNL incubated with 125, 250, 1000, or 5000 IU/ml. There was no significant difference in 1-^{14}C glucose oxidation or in oxygen consumption by zymosan stimulated PMNL exposed to the various concentrations of both HuINFα preparations when compared to control cells. No significant difference in uptake, internalization or killing of ^{3}H methyl thymidine labeled S. aureus by PMNL incubated with interferon at 250, 500, or 1000 IU/ml was detected when compared to control PMNL. IFN-A had no effect on non antibody-mediated killing of Herpes simplex virus infected target cells in a ^{51}Cr release cytotoxicity assay. These data suggest that the two HuIFNα preparations tested had little effect on the oxidative metabolism, antiviral natural killer cytotoxicity, or uptake and killing of radiolabeled S. aureus by human PMNL.
Supported by NIH grant HD13021

● **890** NEUTROPHIL SPECIFIC MATERNAL ISOANTIBODIES CAUSING TRANSIENT IMMUNE NEUTROPENIA IN NEONATES. Prema R. Madyastha, David H. Levine, Armand B. Glassman, K. Ramananda Madyastha, Theodosia Wade, Abner H. Levkoff and Hugh H. Fudenberg. Medical University of South Carolina, Departments of Laboratory Medicine, Pediatrics and Basic, Clinical Immunology and Microbiology,Charleston,South Carolina (spon:Milton Westphal)

Few neutrophil specific antigens (NA), (NA1,NA2, NB1, NC1) of paternal origin have been shown to be responsible for the stimulation of maternal antibodies (Ab), which crossed the placenta and destroyed the neutrophils (PMN) causing neonatal neutropenia (NN). In order to evaluate the nature of NN and to understand the involvement of various NA we systematically investigated several cases of NN with and without infection. EDTA-microagglutination and indirect immunofluorescent assays were used to detect Ab. We identified 4 Ab that specifically agglutinated PMN from the father. No maternal auto-agglutinins were detected. We were successful in obtaining blood samples from one of the 4 neonates and identified Ab in the serum. PMN from this patient also was agglutinated by the maternal Ab. These Ab also agglutinated PMN from normal donors of known NA phenotype ranging from 5-40%. But no correlation was found with the pattern of reactivity with the already known NA apparently identifying new antigenic specificities. The NN persisted from 2-5 wks. In follow-up studies we found that in one of the 4 mothers, the Ab dissappeared at 3 mos. In the other 3 cases, the Ab persisted even after 5-9 mos. of delivery. Thus, investigations of the immune destruction of PMN in NN not only is useful in evaluating the causes of neutropenia but also to identify and characterize the polymorphic NA.

● **891** A COMPARISON OF FLOW CYTOMETRIC ANALYSIS AND ^{3}H-THYMIDINE UPTAKE FOR MEASURING LYMPHOCYTE STIMULATION. Daniel J. Marmer,Russell W. Steele, Jerry L. Hudson Dept. of Pediatrics, University of Arkansas for Medical Sciences and National Center for Toxicological Research, Little Rock and Jefferson, Arkansas.

Lymphocyte stimulation is commonly used for measuring cell-mediated immunity in suspect immunodeficiency and for examining the effects of serum factors or potentially toxic drugs on lymphocyte function. The assays most commonly used employ the uptake of ^{3}H-thymidine(UT) to quantitate mitogen or antigen induced stimulation. This method, however, does not allow analysis of mechanisms for suppression. We compared UT to flow cytometric analysis(FCA) using a Coulter TPS-1 Cell Sorter. Parametric, and non-parametric analysis of DNA fluorescence histograms provided the data base. Antiviral agents previously shown to suppress CMI were examined as well as serum inhibitors such as free fatty acids (FFA). FCA was a more rapid and reproducible method as compared to UT. In addition, FCA revealed blocks at various stages of cell cycling for antiviral agents. Some purine and pyrimidine analogues produced enzymatic blocks at the late synthetic(S) or G_2 and M phase or interfered with late replication resulting in a buildup in the S phase. The antiviral thymidine analogue BVDU at low concentrations suppressed UT which was not the case with FCA; at higher concentrations, a block in G_2 or M resulted. Ara C, FFA, and serum from leukemic children produced lysis of lymphocytes during early cycling. Flow cytometry appears to be a sensitive and useful method for delineating mechanisms of immunotoxicity.

● **892** RESISTANCE OF BOVINE ANTI-CHOLERA TOXIN IgG_1 (ANTI-CT) TO IN VITRO AND IN VIVO PROTEOLYSIS. Richard McClead, Susan Gregory (Spon. by Grant Morrow),Ohio State University, The Children's Hospital, Dept. of Pediatrics, Columbus.

In this report, we provide evidence that specific bovine immunoglobulins resist in vivo and in vitro proteolysis.

Methods: (1) Anti-CT were isolated from the colostrum of immunized cows and characterized by immunochemical analysis. Biologic activity was assessed in the rabbit ileal loop (RIL) assay. (2) In vitro pepsin and trypsin digests of anti-CT were similarly characterized. (3) After in vivo digestion, stool proteins from young rabbits fed anti-CT and non-immune colostral IgG were isolated and characterized by immunochemical, RIL, and radioimmunoassay (RIA) techniques.

Results: (1) The anti-CT activity of immune colostrum determined by quantitative precipitation was ≈ 2.65 mg/ml (3.1 mg/100 mg IgG_1). These are predominantly IgG_1 antibodies with traces of IgM and IgA. Dilutions of BCI, 1:1000, provided 100% inhibition of 100 ng of cholera toxin in the RIL assay. (2) In vitro digestion of anti-CT with trypsin resulted in a 50% reduction of antibody activity in the RIL assay. The anti-CT activity of pepsin digestion were not altered. Trypsin and pepsin digestion of anti-CT at more physiologic enzyme:protein ratios and pH optimums did not alter antibody activity. (3) Immunodiffusion, RIL, and RIA of cecal contents from anti-CT-fed rabbits identified the presence of functionally active anti-CT antibody.

Conclusion: Bovine colostral IgG are resistant to in vivo and in vitro proteolysis. Specific antibodies may provide passive protection for infants at risk for enteric disease.

893 THE EFFECT OF ORALLY-FED, SPECIFIC BOVINE COLOSTRAL IMMUNOGLOBULINS (BCI) ON THE TOXICITY OF CHOLERA ENTEROTOXIN (CT) IN THE INFANT RABBIT. Richard McClead, Susan Gregory (Spon. by Grant Morrow), Ohio State University, The Children's Hospital, Dept. of Pediatrics, Columbus, Ohio.

Recent reports indicate that specific bovine colostral, IgG_1 immunoglobulins can resist in vitro and in vivo proteolysis, and may provide passive immunoprotection for infants at risk for enteric disease. In this study, we evaluated the immunoprotective quality of specific anti-CT BCI fed to infant rabbits.

Method: 3-5 day old infant rabbits were fed 9 ml in 24 hr. of anti-CT (immune) BCI (3.1 mg anti-CT/100 mg IgG_1). Control groups were similarly fed non-immune BCI or D5W. After completion of feedings, all animals were anesthetized. The distal ileum of each animal was ligated and inoculated with 100 ng of CT. Some animals were injected with 1 cc of saline as negative controls. 18 hours after injection of CT, mortality rates were noted. The fluid accumulation index (FAI=gm fluid/gm intestine) was calculated on surviving animals.

Results:

	CT- INJECTED			SALINE-INJECTED
	immune BCI	non-immune BCI	D5W	
Mortality	14.3%	66.7%	80.0%	9.1%
FAI (± SEM)	1.09±0.15	2.41±0.06	1.81±0.24	0.85±0.15
n total =	14	12	20	11

Conclusion: The mortality rate of immune BCI-fed rabbits is the same as saline-injected controls, and less than non-immune BCI and D5W-fed controls ($p<0.01$). The FAI of immune-fed animals is less than non-immune and D5W-fed controls ($p<0.01$). This study clearly shows the potential benefit of orally administered specific bovine colostral immunoglobulins in the prevention of enteric disease.

894 THE MOTOR OF NEONATAL NEUTROPHILS. Michael E. Miller, Anthony T.W. Cheung. UCLA School of Medicine, Harbor-UCLA Medical Center, Dept. Pediatrics, Torrance, Ca.

The orientation (chemotaxis) and locomotion (chemokinesis) of human polymorphonuclear leukocytes (PMNs) are controlled by an internal movement mechanism (involving active cytoplasmic movement) and are influenced by external environmental and ionic conditions. We have studied the degree to which the orientation and movement mechanisms of PMNs are self-contained (built-in) within the cell and the degree to which they are under membrane control. Cells were partially demembranated by treatment with the non-ionic detergent octylphenoxyl-polyethoxyethanol (Triton-X-100), thus providing small openings in the membrane through which ATP and necessary ions could achieve unrestricted passage. Upon contact with Triton-X-100, PMNs became spherical and acquired a very compact and rigid morphology. Addition of ATP to the media was followed by activation of the PMNs to motile cells with active cytoplasmic extension and pseudopod formation. Although these PMNs actively locomoted, they did not respond to a chemotactic gradient. Thus, the activation process restored physical movement parameters, but did not re-establish the orientational capacity of live PMNs. Tritonated models of human cord blood PMNs were reactivated and compared with similar studies of adult PMNs. Optimal movement and locomotion attained in the reactivation were identical to that of adult PMNs. Similar to reactivated adult PMNs, cord PMNs did not respond chemotactically or chemokinetically to chemoattractants. The data thus establish that the chemotactic deficiency of cord PMNs is membrane-associated and reflects a developmental functional abnormality of the membrane during ontogeny.

895 DEVELOPMENT OF SAFE, LIVE, GENETICALLY-ATTENUATED BACTERIAL VACCINES. Anne Morris-Hooke, Pedro J.Arroyo, Joseph A. Bellanti, and Max P.Oeschger. International Center for Interdisciplinary Studies of Immunology, Georgetown University, Washington, D.C.

Temperature-sensitive (ts) live bacterial vaccines, in contrast to killed or chemically-extracted cellular preparations, offer several specific advantages - simulation of the initiation of natural infection, stimulation of local antibody formation and, usually, longer-lasting immunity. The presence of significant numbers of virulent revertants (ca. 10^{-7}) in such vaccines has precluded their use in man. We have overcome this problem by constructing a strain of H.influenzae containing 3 attenuating ts mutations of identical phenotype, thus reducing the reversion rate to negligible levels ($<10^{-21}$). The technical difficulties associated with the combination of mutations of identical phenotype have been solved by utilizing linkage of the mutations to selectable chromosomal markers. We have transferred two of the attenuating lesions into an encapsulated type b strain which remains completely viable at 36°C, without replicating, for at least 24 hours. Studies with single ts mutants of P.aeruginosa have demonstrated the efficacy of such strains in inducing protection from challenge with $100LD_{50}$ of the virulent wild-type, for up to 5 weeks after intraperitoneal immunization of mice. The protection induced is specific for the immunotype of the ts strain, and is quantitatively better than that induced by the heat-killed preparations of either the ts or wild-type strains. The results suggest that this approach may be considered for potential use in human beings.

896 IMMUNOMODULATORY EFFECTS OF AMPHOTERICIN-B ON CELLULAR CYTOTOXICITY AND POLYCLONAL B-CELL ACTIVATION OF NORMAL HUMAN LYMPHOCYTES. Madhavan P. N. Nair and Stanley A. Schwartz. The University of Michigan, Departments of Pediatrics and Epidemiology, Ann Arbor, 48109.

Human peripheral blood lymphocytes (PBL) precultured in media demonstrate decreased natural killer (NK) and antibody dependent cellular cytotoxic (ADCC) activities due to the induction of suppressor cells (J. Immunol. 126:2221, 1981.) We report that PBL precultured with amphotericin B (AMB) for 72 h show even greater decreases of cytotoxic activities and in mixing experiments suppress the ADCC activities of fresh autologous PBL. For the NK assay, K562 and CEM cell lines were used as targets; whereas in the ADCC assay, antibody-coated SB cells were used in a 4 h ^{51}Cr release assay. T-cells, G-10 column passed PBL, and NK and ADCC enriched subpopulations from a Percoll gradient precultured with AMB also manifest decreased NK and ADCC activities, and this effect is not reversed by indomethacin. Further, PBL precultured with AMB also show decreased levels of immunoglobulin (IgG) synthesis and secretion in response to polyclonal stimulation of B-cells by pokeweed mitogen. These results suggest that AMB has a significant immunomodulating effect on human lymphocytes which may be of clinical significance. (Supported by NIH grant AI 16216 and the Children's Leukemia Foundation of MI.)

● **897** HELPER CELLS HAVE HISTAMINE H1 RECEPTORS WHILE SUPPRESSOR CELLS HAVE H2 RECEPTORS. Michael Osband and Menachem Shlesinger, Boston U. Med. Ctr., Dept. of Pediatrics, Boston, MA 02118 (Spon. by Joel Alpert)

The previously proven existence of distinct lymphocyte subpopulations bearing either H1 or H2 type histamine receptors raises the question of their role in immunoregulation. Therefore, we studied the effect of histamine and its agonists/antagonists on immunoglobulin (Ig) synthesis by human and mouse lymphocytes. We found that histamine at low concentrations ($<10^{-8}M$) binds predominately to the more affinite H1 receptor and increases Ig synthesis. This effect is blocked by diphenhydramine, an H1 antagonist, but not by cimetidine, an H2 blocker. Histamine at high concentrations ($>10^{-5}M$), binds predominantly to the less affinite but more numerous H2 receptor and suppresses Ig synthesis. This effect is blocked by cimetidine but not by diphenhydramine. The H1 agonists, 2-pyridylethylamine and 2-thiazolylethylamine, increase Ig synthesis, while the H2 agonists, dimaprit and 4-methylhistamine, suppress it. Moreover, when lymphocytes are sorted and subsequently studied for their effect on Ig synthesis of autologous lymphocytes, we found that H1R+ cells (those bearing H1 receptors) are helper cells, while H2R+ cells are suppressor cells (decrease synthesis). These data suggest a dual feedback mechanism by which histamine, released during an immune response, can regulate the immune system. When the released histamine is at low concentration, it activates H1R+ helper cells and amplifies the immune response. This, in turn, causes even greater histamine release which can bind to H2R+ suppressor cells resulting in immunosuppression.

898 POLYAMINE GENERATION IN MIXED LEUKOCYTE CULTURE (MLC). Henry F. Pabst, Joan A. Crawford, Mary Grant, Ken Strynadka, Kyung Bay, Ernest E. McCoy, Department of Pediatrics, University of Alberta, Edmonton, Canada.

Polyamine generation is thought to be an early cellular metabolic event preceding cell replication. Stimulation of lymphocytes by mitogens with resulting blastogenesis correlates well with polyamine generation (Fillingame RH et al, Proc Nat Acad Sci USA, 72: 4042, 1975). We attempted to correlate these two events in 10 consecutive MLC experiments. Mononuclear cells (MC) from identical twins (A+B) and a control (C) were cultured in standard MLC microtitre: $1x10^5$ responders (A,B, or C) plus $1x10^5$ stimulators, in one way, or unirradiated cells in two way MLC were compared with polyamine generation by identical MC mixtures containing $2x10^6$ MC of each cell type. Cadaverine (CD), putrescine (PU), spermidine (SPD) and spermine (SM) was measured by liquid chromatography. Generation of polyamines correlated poorly (R^2, square of multiple correlation) with blastogenesis of allogeneic MLC on day 6:

Culture Day				
3	0.30 (SPD)	0.36 (CD)	0.37 (SM)	0.37 (PU)
4	0.36 (SPD)	0.39 (PU)	0.43 (CD)	0.43 (SM)
5	0.38 (SPD)	0.41 (CD)	0.42 (PU)	0.43 (SM)

On days 2-4, polyamine production in syngeneic MLC was as high as in allogeneic MLC. These findings are in contrast to those from mitogen stimulation and are thought to reflect in MLC the need for polyamine interaction with ribosomal RNA rather than DNA as in mitogen stimulated MC, differentiating these 2 forms of MC activation by basic metabolic events.

899 IMMUNE DYSFUNCTION IN ATAXIA TELANGIECTASIA (AT) S. Pahwa, R. Pahwa, E.M. Smithwick and R.A. Good Memorial Sloan-Kettering Cancer Center, Immunobiology Section, New York, N.Y. 10021

Investigations of in vitro humoral immune responses were done in a pair of identical twins with AT, both IgA deficient. Peripheral blood mononuclear cells (PBM) failed to generate immunoglobulin secreting cells (ISC) as quantitated in a reverse hemolytic plaque assay following stimulation of PBM cultures with pokeweed mitogen (PWM) which is a T-dependent stimulus. In contrast, stimulation with Epstein Barr virus, a T-independent stimulus, resulted in adequate ISC responses, but with secretion of only IgG and IgM and not IgA. In an antigen-specific assay in which anti-SRBC antibody secreting cells are quantitated in a direct hemolytic plaque assay following in vitro sensitization of PBM cultures with SRBC antigen, no responses were elicited even after maneuvers aimed at amplifying T-cell help in the cultures. PWM induced ISC responses of B-cell enriched cultures were only partially reconstituted by providing allogeneic T helper cells. T-enriched populations from the patients did not manifest immunoregulatory abnormalities. The autologous mixed leukocyte reaction (MLR) between patients' own T and non-T cells was grossly defective, but their T and non-T cells functioned adequately as responders and stimulators in allogeneic MLR. The findings in these 2 patients with AT are suggestive of 1) intrinsic B cell dysfunction and 2) defective interaction between T and non-T cell populations. The observed B cell dysfunction might result from the lack of a B-cell subset or an immaturity of the B-cell pool.

900 ABNORMAL B CELL FUNCTION IN CHRONIC MUCOCUTANEOUS CANDIDIASIS (CMC). S. Pahwa, E.M. Smithwick and R.A. Good, Memorial Sloan-Kettering Cancer Center, Immunobiology Section, New York, N.Y. 10021

Six patients with CMC were investigated for antibody production in vitro in polyclonal and antigen-specific assay systems. Cultures of peripheral blood mononuclear cells (PBM) differentiated poorly into immunoglobulin secreting cells as tested in a reverse hemolytic plaque assay using protein A coated sheep erythrocytes, following stimulation of PBM cultures with either pokeweed mitogen, a T-dependent stimulus or with Epstein Barr virus, a T-independent stimulus. Cocultures of isolated T and B cells from patients and normal volunteers revealed the defect to be intrinsic to B cells, although associated abnormalities of increased suppressor cell activity were frequently present. T helper function was adequate in all patients. Antibody responses to sheep red blood cell (SRBC) determinants, tested for by quantitating anti-SRBC plaque forming cells following in vitro sensitization of PBM cultures with antigen, were found to be normal in 2 and decreased in 3 patients. In the latter patients the responses were augmented following delayed addition of the T cell mitogen Con A to the cultures as a means of amplifying T cell help. In one patient with associated hypogammaglobulinemia, no responses were elicited despite these manipulations. These findings indicate that 1) abnormalities of in vitro humoral immune function are frequently present in CMC besides the described defects of cell mediated immunity, and 2) polyclonal and antigen-specific responses might be mediated by different activation mechanisms, possibly involving distinct B cell subsets.

901 PERIODONTITIS, IRITIS, AND PERSISTANT ANTI-ISLETS ANTIBODY IN INSULIN DEPENDENT DIABETES MELLITIS(IDDM). Byung H. Park, Erika Bruck, Robert Genco, and Louis Cianciola. Department of Pediatrics and Oral Biology, SUNY at Buffalo, Children's Hospital, Buffalo, NY.

Amoung the many complications in patients with IDDM, iritis and peridontitis are considered to be rather infrequent and appears to have received less attention. We have evaluated 280 patients with IDDM during past 2 years for their dental conditions; severe gingivitis and periodontitis were noted in 20% of 165 patients aged 12-25 years and in only one of 125 patients aged 2-11 years. Iritis was observed in 7 of 236 patients (11 years or older) seen during past 7 years (6 of 109 females and 1 of 127 males). None of 198 patients 10 years or younger had irits. In patients with iritis, the mean age (year) of diabetes onset was 8.71 (5-11), and the mean duration (year) of diabetes at the time of iritis was 8.43 (5-11). One female patient with iritis had anti-islets cell auto-antibody with titer of more 1:16 7 years after the onset of diabetes. Periodontitis and iritis may be an hitherto unrecognized important complication in certain groups of patients with IDDM. The association of persistant auto-antibody against islets cell and iritis in a patient indicate that the autoimmune mechanism may play a role in the pathogenesis of iritis.

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902 EXPRESSION OF SURFACE IgM (sIgM) By sIg NEGATIVE HUMAN BONE MARROW CELLS IN VITRO. Elliott R. Pearl (Spon. by T. Kelly) Univ. of Virginia Medical Center, Univ. Virginia Hospital, Dept. Pediatrics, Charlottesville, 22908

To explore conditions required for generation of of human B lymphocytes in vitro, I cultured marrow following depletion of sIg+ cells on anti-Ig-coated dishes. I used immunofluorescence methods to enumerate sIgM+ B cells and pre-B cells (cytoplasmic IgM+, sIgM-) before and at various times after culture under a variety of conditions. Spontaneous appearance of sIgM+ cells occurred in only 1 of 19 experiments. In 5 of 5 studies, sIgM+ cells appeared 2-6 days after a 2 hour pulse with supernatant containing Epstein-Barr virus (EBV). Results are expressed as number of viable cells x 10^{-3} before and after culture. The number of pre-B cells always declined and there appeared to be a positive correlation between the increase in B cells and decrease in pre-B cells. Small lymphocytes that stained for both sIgM and cIgM were observed in some experiments. Studies with marrow cells not depleted of B lymphocytes suggest that the observed increase in sIgM+ cells is not a result of proliferation of residual B lymphocytes. These results suggest (i) that some sIg- marrow cells, perhaps pre-B cells, can be induced to express sIgM in vitro and (ii) precursors of B cells may bear EBV receptors.

	sIgM+ B cells		Pre- B cells	
	Before	After	Before	After
Exp.1	<1	32.5	60.0	2.0
2	<1	63.0	210.0	105.0
3	1	17.5	102.0	87.4
4	<1	9.4	79.0	72.4
5	<1	15.3	94.0	78.1
Geom. X	1	22.0	99.1	40.1

903 PHENOTYPIC AND FUNCTIONAL ANALYSIS OF LYMPHOCYTES IN PATIENTS WITH THE TURNER SYNDROME. Elliott R. Pearl (Spon. by T. Kelly) Univ. of Virginia Medical Center, Univ. Virginia Hospital, Dept. Pediatrics, Charlottesville, 22908

Patients with the Turner syndrome are at increased risk to develop thyroid autoimmunity. To seek a cellular basis for this predisposition, I examined mononuclear cells (MNC) from 9 patients, 6 of whom had anti-thyroid antibodies, and 25 controls. All patients had a normal total lymphocyte count. B cells were enumerated by direct immunofluorescence (IF) and total T cells by rosette formation with sheep erythrocytes. I enumerated T cell subsets by indirect IF using OKT4 and OKT8 monoclonal antibodies. Responses to mitogens were estimated by incorporation of ^{3}H-thymidine. The suppression of normal MNC responses to Con-A was examined by co-culturing fresh normal cells with patient and control cells that were preincubated with Con-A for 48 hours. Results are mean±SEM. There were no differences between patients and controls, either male or female. The results indicate that an abnormality of lymphocyte number or function does not underly the tendency to develop autoimmune disease in patients with the Turner syndrome. In particular, the number and functional activity of T suppressor cells is normal in these individuals.

	PATIENTS	CONTROLS
IgM+ B cells (%)	10.7±1.4	10.2±0.6
E rosettes	76.6±2.4	76.1±1.6
T4 helpers	44.6±2.7	45.7±1.5
T8 suppressors	21.0±0.9	22.4±0.9
T4/T8 ratio	2.1±0.1	2.2±0.1
PHA (Stim. Index)	157±37	105±23
Con-A	73±19	58±15
Pokeweed Mitogen	28± 6	26± 6
% suppression	74± 6	47±13

904 T-LYMPHOCYTE CHEMILUMINESCENCE. Allen G. Peerless, E. Richard Stiehm. U. of California, Los Angeles, Dept. of Pediatrics, Los Angeles, California.

Human T-lymphocytes (TL) generate chemiluminescence (CL) in the presence of luminol. We investigated this phenomenon in terms of age dependency, nature of oxidants produced and relationship to cellular immune competence. Sixteen adult and 8 cord rosette purified TL preparations (≈90% purity) were tested for spontaneous and concanavalin A (Con-A) stimulated CL. The chemiluminescence index (CI) is an expression of peak photon emission, adjusted for luminol drift and the spontaneous emission of a dark adapted blank. Mean spontaneous CI was 88 ± 23 in adults and 19 ± 9 in cords, $p<0.1$. Con A stimulated mean CI was 113 ± 30 in adults and 23 ± 10 in cord TL preparations, $p\leq.05$. Mean specific CI, an expression of the difference between mitogen and spontaneous peak emission was 25 ± 8.0 in adults and 3.6 ± 1.4 in cords, $p<0.1$. No difference in time to peak response or CI at the initial measurement point (2.8 ± 0.4 in adults vs. 3.5 ± 0.6 in cords $p<0.4$), was noted. Treatment of adult TL preparations with superoxide dismutase augmented CL a mean 120% over non-treated controls. This effect was dose restricted, peaking at 7.5 ug. Catalase treatment at all doses tested resulted in a mean diminution in total CL of 50%, implicating H_2O_2 as a critical oxidant in this response. CL was tested in a patient with profound cellular immunodeficiency (SCID) a fetal thymus reconstituted chimera and age-matched control. All 3 subjects demonstrated normal granulocyte CL to zymosan opsonization. TL-specific CI was 52 in the control, 7.6 in the chimera and 0.9 in the SCID. This suggests a possible role for CL in the rapid evaluation of TL functional metabolic integrity.

905 IMMUNE COMPLEXES IN THE SERA OF PEDIATRIC PATIENTS WITH RHEUMATIC DISEASE. Donald A. Person, Carolyn M. Leatherwood, Gregory J. Buffone, Edward H. Giannini, Karyl S. Barron, and Earl J. Brewer. (Spon. by Ralph D. Feigin) Baylor College of Medicine and Texas Children's Hospital, Department of Pediatrics and Pathology, Houston.

Three hundred eighty seven sera from 234 individuals were tested for the presence of circulating immune complexes (IC) using a liquid phase C1q binding assay. Binding >8.9% was considered positive. The highest value for each normal and patient was used in the analysis.

CATEGORY	N	POSITIVE/PERCENT	% BINDING X̄, SE	p*
Normal	23	1 (4%)	3.6, 0.5	-
Other	57	9 (16%)	6.6, 1.0	<.003
Rheumatic fever	5	2 (40%)	3.7, 1.6	NS
Dermatomyositis	7	3 (43%)	11.7, 6.5	NS
Pauciarticular JRA	49	1 (2%)	3.3, 0.4	NS
Polyarticular JRA	48	22 (46%)	21.5, 4.0	<.001
Systemic JRA	29	8 (28%)	8.6, 1.7	.0045
SLE	25	13 (52%)	21.7, 5.1	.001

*p based on Student's t test, 1 tailed comparison of means between normals and each group.

Patients grouped under "other" with positive values included 2 Kawasaki's disease, 1 SBE, 1 IC nephritis, 3 SLE-like disease with partial immune deficiency, 1 toxocariasis, and 1 possible JRA. The pauciarticular JRA patients in our large sampling rarely had IC present while active polyarticular and systemic JRA patients, as well as the SLE patients frequently were positive for IC by C1q binding.

906 MATURATIONAL CHANGES IN FETAL B CELL DIFFERENTIATION. W.B.Pittard III, K.Miller, R.U.Sorenson. Dept. Ped., RB&C Hosp., CWRU, Cleveland, Ohio

We have analyzed the effect of gestational age(GA) and intrauterine growth retardation on B cell differentiation. The number of plaque forming cells(PFC)developed/10^6 cord blood mononuclear cells in response to pokeweed mitogen(PWM)alone and PWM plus 10^{-5}M hydrocortisone(HC)was measured in 38 appropriately grown(AGA) and 13 growth retarded(SGA) neonates(gestational age[GA]26-42 wks.).

	PRETERM		TERM	
	AGA	SGA	AGA	SGA
n	23	4	15	9
GA*	31±0.6	29±2.0	40±0.2	40±0.2
B Wt.(kg)*	1.6±0.1	1.0±0.2	3.2±0.1	2.2±0.1
PFC*	12650±3133	35688±10581	3797±1558	6128±2443

*Mean±SEM

The PFC response to PWM and to PWM plus HC(shown in table)was significantly greater($p<.003$) in the SGA preterm than in the SGA term infant and similarly responses were greater($p<.04$)in the AGA preterm than in the AGA term infant. Among the preterm infants the SGA responses were significantly greater($p<.02$)than the AGA but there was no difference between the two groups at term. The increased PFC responses observed in the preterm SGA infants may be due to decreased suppressor T cell function or to the differentiation of B cells in vivo to a more mature state that is responsive to activation in vitro by PWM. The increased perinatal morbidity observed in these infants may be responsible for this B cell maturation.

907 THE IDENTIFICATION OF INTRAUTERINE DERIVED MATERNAL T-CELLS IN FOUR SEVERE COMBINED IMMUNODEFICIENCY PATIENTS BY HLA TYPING. Marilyn S. Pollack, Dahlia Kirkpatrick, Neena Kapoor, Robert Evans, Bo Dupont, and Richard J. O'Reilly. Memorial Sloan-Kettering Cancer Ctr.,NY

During the past three years, four of the fifteen severe combined immunodeficiency patients referred to the Memorial Sloan-Kettering Cancer Center for diagnostic evaluation and possible therapeutic bone marrow transplantation were determined to have intrauterine derived maternal T lymphocytes. The maternal cells in all cases were identified solely by HLA typing techniques since the cells did not have mitotic responses to mitogen stimulation and could not be evaluated by cytogenetic methods. In three of the cases, the maternal cells were homozygous for HLA-A,B and/or DR locus determinants. The engrafted cells were E-rosette and DR positive, sIg, Leu-1, Leu-2, and Leu-3 negative, and weakly positive for the Leu-4 T-cell antigen. The cells were functionally inactive in in vitro tests and, despite the fact that the patients were examined repeatedly between the ages of 6 months and 15 months, 3 of the 4 patients had complete absence of any evidence for clinical graft vs. host disease. These findings suggest that variations in the clinical expression of severe immunodeficiency may reflect variations in clinical effects of maternally derived cells and that the phenomenon of such engraftment apparently occurs with significant frequency. It is also important to note that awareness of this phenomenon allowed identification of an HLA genotypically identical sibling marrow donor for one of the patients who had previously been thought to lack this therapeutic option.

● **908** "SPURIOUS LYMPHOCYTE SYNDROME": SEVERE IMMUNODEFICIENCY WITH PHENOTYPICALLY MATURE T CELLS. Ralph R. Quinones, Steven M. Neudorf, John H. Kersey, and Alexandra H. Filipovich. Univ. of Minnesota (MN), Univ. of MN Hospitals, Pediatric Immunology Division, Minneapolis, MN.

HLA identical daughters of normal (nl) unrelated parents developed intractable diarrhea with failure to thrive, recurrent infection, eczema, developmental delay, and severe autoimmunity in infancy. Both showed hypergammaglobulinemia, multiple autoantibodies, and lymphocytic infiltration of the bowel. Patient (pt) 1 died at 19 months of progressive autoimmunity, viral infection, and transfusion acquired graft-vs-host-disease. At 3 months, pt 2 was asymptomatic, had nl thymic histology and distribution of thymocyte markers in suspension and sections, but severe T cell dysfunction. Both sibs had nl numbers of T and B lymphocytes, mature (OKT3+) immunoregulatory cells (OKT4+ or OKT8+), no proliferation to lectins or antigens, minimal to allogeneic cells, but nl to Ca^{++} ionophore, A23187. Purine pathway enzymes and chromosomes were nl. T cells from pt 2 showed no suppressor or cytotoxic function in vitro. Concanavalin A capping and EM microtubule analysis of lymphocyte membranes were nl, as were natural killer and neutrophil functions. Due to clinical deterioration, pt 2 was treated with a T cell depleted maternal bone marrow transplant. We propose that these pts represent a new autosomal recessive syndrome with intact intracellular metabolism (nl Ca^{++} ionophore response) and nl surface membrane characteristics. Defective intramembrane signal processing may account for severe T cell dysfunction and fatal autoimmune complications.

909 INDUCTION OF MONOCYTE PLASMINOGEN ACTIVATOR (PA) BY ACTIVATED LYMPHOCYTES AND LYMPHOKINES. Carol G. Ragsdale, (Spon. by Stanley A. Schwartz.) University of Michigan Medical School, Department of Pediatrics and Communicable Diseases, Ann Arbor.

Stimulated lymphocytes and lymphokines induce PA secretion by human monocytes. The object of these studies was to determine whether measurement of enzyme induction could be a useful measure of cell-mediated immunity (CMI). Mononuclear leukocytes (MNL) from adults or children were cultured in the presence or absence of phytohemagglutinin, concanavalin A or candida antigen. After 1 to 4 days PA activity of the monocytes in the MNL was determined using a micro fibrin plate assay.

Monocytes in stimulated MNL had more PA activity than monocytes in unstimulated MNL. Maximal differences between stimulated and unstimulated cells were seen after 2 days of culture. Peak enhancement of PA activity was seen using 2µg/ml PHA (241± 89% of control, 2µg/ml ConA (289 ± 150%) and a 1:500 dilution of candida antigen (187 ± 85%). Induction of PA in purified monocytes by supernates from activated MNL also was observed. PA induction with candida stimulation corresponded to skin test results.

Dose-response studies demonstrated that significant PA induction occurred at sub-mitogenic concentrations of mitogen or antigen. Peak induction occurred at suboptimally mitogenic concentrations. Sensitivity of the PA induction assay was equal to or better than the sensitivity of an indirect migration inhibition assay for leukocyte migration inhibitory factor. Measurement of PA induction proved to be a sensitive assay for lymphokines and may be of value in the study of CMI in health and disease.

910 IMMUNE FUNCTION AND GRAFT-VS-HOST REACTION (GVH) AFTER INTRAUTERINE T LYMPHOCYTE ENGRAFTMENT IN SEVERE COMBINED IMMUNODEFICIENCY (SCID). R.J. Rosenstock,* R.M. Goldblum, and J. Sharp.* Department of Pediatrics, University of Texas Medical Branch, Galveston, Texas.

A 1 mo. old male presented with dermatitis, hepatosplenomegaly, lymphadenopathy and skin and lymph node histiology of histiocytosis X. Profound lymphocytosis, eosinophilia and hypogammaglobulinemia were also noted. Despite large numbers of circulating T and B lymphocytes, there was no response to phytohemagglutinin (PHA) and lymphocyte 5' nucleotidase (5' NT) was undetectable. The dermal and hematologic abnormalities resolved rapidly with cytoxic therapy. After developing a persistent parainfluenza URI and stopping prednisone, the original clinical findings recurred at age 6-7 mo. HLA typing of E-rosette separated lymphocytes now demonstrated that the T cells had only maternal antigens. PHA stimulated cells were 46XX (22/30) and 46XY (8/30). Bone marrow cells were all XY and RBS were of host type. Blastogenic responses increased to PHA (SI=208:1) and candida antigen (SI=5:1). Lymphocyte 5'NT did not change. However, nasal excretion of parainfluenza persisted and chronic rotavirus enteritis lead to severe malabsorption. Production of oligoclonal IgM (763 mg/dl) and IgG was noted at 19 mo. The patient developed S. aureus sepsis and succumbed to pneumonia at 20 mo.

Intrauterine lymphoid engraftment in SCID, clinically inapparent in most patients, has caused GVH. Our patient is the first to have developed T lymphocyte function and immunoglobulin production. This potential for reconstitution makes the detection of T cell chimerism important in SCID and in histiocytosis X.

911 SERUM INHIBITOR OF UROPOD FORMATION BY BASOPHILS. Frank C. Schmalstieg, W. Daryl Dickey, and Michael A. Lett-Brown. Department of Pediatrics, University of Texas Medical Branch, Galveston, Texas.

Although it is known that blood basophils may enter areas of inflammation in an immunologically specific manner, knowledge of factors that control this phenomenon is incomplete. Since uropod formation is closely associated with translational movement in some types of cells, control of this feature might be important in cell traffic. Previous work showed that low concentrations of serum stimulated uropod formation in basophils. We have isolated a factor (UIP) from human serum that inhibits uropod formation in guinea pig basophils. In RPMI-1640 alone, uropod bearing basophils were 59±9% (mean ± SD) and 6±4% in the presence of UIP + phosphatidyl choline. Phosphatidyl choline was a necessary cofactor for the action of purified UIP. In addition, this factor inhibits in vitro human basophil chemotaxis to C5a. The association of UIP with the low density lipoproteins (LDL) was utilized in the initial purification of UIP. Further purification of UIP was accomplished by isoelectric focusing. Proteins with uropod inhibitory activity had isoelectric points between 7.9 and 8.2. SDS-PAGE of the proteins prepared by isoelectric focusing demonstrated two bands which correspond to molecular weights of 45,000 and 50,000 daltons. These proteins appear identical to UIP previously described for T lymphocytes. Monospecific antisera to these proteins removes the uropod inhibitory activity for both basophils and lymphocytes. The finding of factors in serum that both stimulate and inhibit uropod formation in basophils suggests that a control system for basophil movement may exist in serum.

● **912** AN INTERFERON-INDUCED SUPPRESSOR CELL PATHWAY IN HUMAN SYSTEMS. H. William Schnaper, Thomas M. Aune, and Carl W. Pierce. (Spon. by Alan M. Robson). Washington Univ. Med. Schl., and Jewish Hosp. of St. Louis, St. Louis, MO.

Murine interferon activates suppressor T cells which produce soluble immune response suppressor (SIRS), a lymphokine which inhibits immune responses by murine lymphoid cells. We investigated whether human leukocyte interferon (IFNα) acts by a similar mechanism. IFNαA(IFLrA-kindly provided by Hoffman-LaRoche, Inc.), at doses >200 units/ml, caused ≈90% suppression of plaque forming cell (PFC) responses by human peripheral blood mononuclear cells (PBMC) stimulated with pokeweed mitogen (PWM). Suppression was not significant before day 6 and peaked at days 7-8, suggesting stimulation of a suppressor cell by IFNαA. Small numbers of PBMC incubated with IFNαA for 24 hrs. suppressed PFC responses by 80% compared to cells incubated with inactive IFNαA when added to fresh autologous PBMC at culture initiation. Concentration of IgM in culture fluids on day 6 and 7 was suppressed >50% by IFNαA at doses >200 units/ml. Suppression of ^{3}H-thymidine incorporation in mixed lymphocyte responses (MLR) was not significant on day 4 and peaked at 50% on day 5. IFNαA and IFNαA-activated cells did not suppress PFC responses in the presence of catalase or 2-mercaptoethanol (2-ME), and MLR was not suppressed in the presence of 2-ME and dithiothreitol (DTT). Delayed onset of suppression, activation of a suppressor cell, and reversal by catalase, 2-ME and DTT suggest that human IFNαA activates a suppressor pathway analogous to that activated by interferon in murine cells and suggest that a SIRS-like mediator may be involved.

● **913** HYBRIDOMA TYPE-SPECIFIC IgM ANTIBODY OFFERS ENHANCED PROTECTION AGAINST SYSTEMIC OR RESPIRATORY GROUP B STREPTOCOCCAL EXPERIMENTAL INFECTION. Ann O. Shigeoka, Seth H. Pincus, Neal S. Rote and Harry R. Hill. Univ. of Utah, Departments of Pediatrics and Pathology, Salt Lake City, Utah

In previous studies, we demonstrated that opsonic antibody (Ab) is effective in altering the course of group B streptococcal infection in humans and in a neonatal animal model. Although high titer human serum or whole blood afforded excellent protection, the available commercial gammaglobulin preparations are less satisfactory. In the present studies, we prepared mouse type-specific hybridoma Ab and examined it for protective efficacy against four strains of type III group B streptococci. Neonatal rats received $5x10^{6}$ organisms by intraperitoneal injection. Type specific hybridoma Ab (0.25 ml/kg) was administered in a separate IP injection. The survival rate of the animals receiving Ab vs controls was: 1) 58% vs 3%; 2) 74% vs 36%; 3) 95% vs 0%; 4) 86% vs 9%. Significant protection was provided when hybridoma Ab was administered as late as 12 hrs postinfection (25% vs 0%; $p<0.0005$), an interval at which gammaglobulin gave no protection. In spite of the fact that the hybridoma Ab was of the IgM class, it also protected against respiratory infection. When inoculation was via the intranasal route, survival of Ab treated animals remained significant (94% vs 0%). The hybridoma type III specific Ab did not protect against type II group B streptococci. These studies indicate that monoclonal antibody preparations could provide a reliable source of large quantities of opsonic Ab for passive immunotherapy of neonatal group B streptococcal disease.

914 PRIMARY IMMUNE DEFECTS IN X-LINKED LYMPHOPROLIFERATIVE SYNDROME (XLP). J.K. Seeley*, S. Harada, T. Bechtold, H. Ochs, M. Ballow and D.T. Purtilo, Univ. of Connecticut Health Science Center, Farmington, CT 06032, Univ. of Washington, Seattle, Washington, WA 98195.

Males with XLP are susceptible to life-threatening Epstein Barr virus (EBV) infections: 67 of 100 affected males have succumbed to infectious mononucleosis and 35 have developed malignant lymphoma. We have reported various immune defects in the surviving XLP patients. Some of these defects are also expressed by certain asymptomatic males at risk, ie., sons of XLP carriers:

Abnormal Immune Function	Normals	XLP	At Risk
Lack of Anti-EB nuclear antigen	0/20	11/11	3/9
Abnormal OKT4/OKT8 Subsets	0/20	8/11	6/15
Anti-ΦX174 defects	0/20	4/4	3/3
EBV T cell memory defect	0/10	6/8	3/3
Hypogammaglobulinemia	0/20	9/11	0/15
Low Natural Killer Activity	0/20	7/9	0/12

The abnormalities shared by affected males and those at risk may reflect (a) primary immune defect(s), while the low levels of serum Ig and low NK in surviving XLP patients may be acquired after EBV infection. This distinction is important for understanding XLP disease process and for designing early treatment protocols. (Supported by NIH CA 30196, BRS6 RR057 12-10 and HD 12050.)

● **915** PARAINFLUENZA (SENDAI) VIRUS DIRECTLY CAUSES RELEASE OF HISTAMINE FROM PERIPHERAL BLOOD LEUKOCYTES. Thomas F. Smith (Spon. by Andre' J. Nahmias), Emory Univ. School of Medicine, Dept. of Pediatrics, Atlanta, Georgia.

The release of histamine from human basophils induced by Sendai virus, a parainfluenza virus which had been adapted to a human (HEp-2) epithelial cell line, was investigated in vitro. Dilutions of a stock suspension of virus were incubated with washed suspensions of human peripheral blood leukocytes (PBL) for 2 min at 37°; either buffer or phosphatidyl serine (PS) at 10 μg/ml was added and the incubation continued for an additional 10 min at 37°C. Controls included buffer and uninfected HEp-2 cells. Histamine released into the supernatants was measured using an enzymatic isotopic assay and was expressed as net percentage released above buffer controls. Results are shown in the Table:

Dilution	With PS (%release ± SEM)	Without PS
Undiluted	20.9 ± 6.0	9.1 ± 7.6
10^{-1}	8.3 ± 3.1	0.6 ± 4.3
10^{-2}	-0.3 ± 1.3	-6.5 ± 4.0
10^{-3}	1.9 ± 3.7	-4.6 ± 2.6
Buffer	-0.3 ± 0.2	0(definition)

There was significant release of histamine from PBL in the presence of virus and PS; there was some release of histamine in the presence of virus without PS. No difference was seen between buffer and HEp-2 cells. It is concluded that Sendai virus can under some circumstances directly induce release of histamine from human basophils in vitro. Direct release of histamine from cells in the airways induced by some respiratory viruses could contribute to symptoms during viral respiratory infections.

916 PULMONARY FUNCTION IN PATIENTS WITH IMMUNODEFICIENCY. Thomas F. Smith, Thomas J. Spira, Jeffery R. Pine, William E. Feldman, and Andre' J. Nahmias, Emory Univ. School of Medicine, Departments of Pediatrics and Medicine, and The Centers for Disease Control, Atlanta, Georgia.

Immunodeficiency patients who have repeated pulmonary infections might be at risk for developing chronic pulmonary disease. To evaluate pulmonary function in patients with various types of immunodeficiency, we performed spirometry and pletheismography. Eight patients had primary or acquired hypogammaglobulinemia, one had dysgammaglobulinemia, and one had hyper-IgE syndrome. Nine had received immunoglobulin replacement therapy since diagnosis. Mean age at testing was 13.7 years (range 7-18 years).

Seven patients with a history of two or more episodes of proven or presumed bacterial pneumonia had abnormal $FEF_{25-75\%}$: five of these had decreased FEV_1 as well. Two patients had increased RV and RV/TLC (hyperinflation): two had decreased TLC (restriction). Of the three patients without repeated pulmonary infections, two had normal spirometry. The other, who had a family history of asthma, showed hyperinflation only. Two of the eight patients with pulmonary function abnormalities showed improvement in response to inhaled bronchodilator; one of these had a family history of asthma.

We conclude that children with immunodeficiency who have repeated pulmonary infections are likely to develop pulmonary function abnormalities. However, immunodeficiency without pulmonary infection does not necessarily predispose to abnormal lung function. Bronchodilator therapy might benefit some of these patients, especially those with a family history of asthma.

917 EARLY LUNG CLEARANCE OF P. AERUGINOSA FOLLOWING LOCAL IMMUNIZATION OF MICE WITH A TEMPERATURE-SENSITIVE (TS) BACTERIAL MUTANT. Daniel O. Sordelli, Maria C. Cerquetti, Anne Morris-Hooke, Barbara J. Zelins and Joseph A. Bellanti. International Center for Interdisciplinary Studies of Immunology, Georgetown University Hospital, Washington, DC.

Different immunoprophylactic regimens have been proposed to overcome or prevent Pseudomonas lung infection in patients with cystic fibrosis (CF). Although current vaccines generate excellent serum antibody responses, they have changed neither the clinical status nor Pseudomonas colonization. In the present studies, lung lavage fluids were studied in mice following Pseudomonas aerosol challenge with either the parental (Immunotype I) or TS mutant strains. The cellular responses were quantitatively and qualitatively similar in both immunized and non-immunized animals. Protection was induced in mice receiving a single aerosol dose of 2-4 x 10^{5} colony forming units of TS mutant of P.aeruginosa. The results suggest that this protection may be a result of the presence of local opsonizing antibodies. Since recent publications have shown impaired opsonizing activity of serum IgG from CF patients, the present results also suggest that local immunization of the respiratory tract might be preferable in these patients.

918 IMMUNODEFICIENCY IN GAUCHER'S DISEASE. Usha Srinivasan, John A. Barranger, Edward I. Ginns, Julie Blatt, Norman W. Barton, R. Michael Blaese, & David G. Poplack. Ped. Onc. Br. & Metab. Br., NCI.; Devel. & Metab. Neurol. Br., NINCDS, NIH, Bethesda, MD 20205

Gaucher's disease is a lipid storage disorder characterized by a deficiency of glucocerebrosidase and the accumulation of its substrate, glucocerebroside in cells believed to belong to the monocyte-macrophage system. In the present study, we evaluated cellular and humoral immunity in 30 patients (pts) with Type 1 Gaucher's disease. 9/30 pts had lymphopenia and/or monocytopenia, although cell surface marker studies revealed normal percentages of peripheral T and B lymphocytes. Skin testing with candida, tetanus and mumps antigens yielded positive responses only in 1/29, 15/20 and 0/13 pts respectively. In addition, in vitro lymphocyte proliferation studies revealed further evidence of a cellular immune defect in that the pts' lymphocytes showed abnormal responses to concanavalin-A (1/2 normal), pokeweed (1/3 normal), streptokinase-streptodornase(1/4 normal) and candida(1/3 normal). In contrast,humoral immunity was intact. Isohemagglutinin titers, quantitative serum immunoglobulins and antibody response to primary immunization with pneumococcal polysaccharide antigen were normal. We also evaluated monocyte-mediated antibody-dependent cytotoxicity and found it normal in 12 pts tested. The apparent cellular immune defects did not correlate with clinical severity of disease, splenectomy, serum triglyceride or alpha globulin levels. In summary,our data indicate that there is a defect in cellular immunity in pts with Gaucher's disease. Further studies are underway to determine its mechanism.

● **919** RADIOSENSITIVITY OF T CELL FUNCTION IN THE REGULATION OF POKEWEED MITOGEN - STIMULATED HUMAN B-CELL DIFFERENTIATION. Leonard D. Stein and Nolan H. Sigal. (Spon. by Erwin W. Gelfand) Division of Immunology, Hospital for Sick Children, Toronto, Ontario.

A number of laboratories have suggested that human T-cell helper function is radioresistant. We have reexamined the radiosensitivity of T-cell helper and suppressor function in the regulation of pokeweed mitogen (PWM) - stimulated human B-cell differentiation in vitro. Increasing numbers of irradiated or nonirradiated T cells (E-rosetting cells) from peripheral blood or tonsil were added to constant numbers of autologous B cells (non-E-rosetting cells), stimulated with PWM, and cultured for 7 days in microtiter plates. Culture supernatants were assayed for anti-dinitrophenyl and anti-phosphorylcholine antibody production, as well as total IgM and IgG secretion by a solid phase radioimmunoassay. We have demonstrated that peripheral blood T helper function can be radiosensitive. More immunoglobulin and antibody is produced by cultures containing unirradiated T cells, than by cultures with irradiated T cells, but only when the T/B ratio is low (i.e., 1/100 to 1/10). At higher T/B ratios (1/1 or greater) irradiated T cells always provide superior helper cell function. The crossover point at which irradiated T cells become more efficient varies from individual to individual and depends on the radiation dose employed. Thus, care must be taken in the in vitro functional evaluation of disease states reported to be caused by regulatory cell imbalance, since information derived from one combination of T and B cells may give a distorted view.

● **920** ACQUIRED CHEMOTACTIC INHIBITORS IN GUINEA PIGS DURING INFECTION WITH GUINEA PIG CYTOMEGALOVIRUS (gpCMV). Raymond Tannous and Martin G. Myers. University of Iowa College of Medicine, Department of Pediatrics, Iowa City, IA.

Anergy and secondary infections during viral illnesses suggest the presence of acquired cellular and/or humoral defects. Weanling strain 2 guinea pigs were inoculated with gpCMV-infected or uninfected control guinea pig fetal tissue culture cells. Four infected (I) and 3 control (C) animals were studied daily (x 10) and results were compared by the t-test. All (I) became viremic and shed virus from the nasopharynx. Concurrent with viremia but not with shedding, there was a 51% reduction in neutrophil directed migration towards C5a (p 0.001), and a 77% reduction in the chemotactic activity of activated plasma (p 0.001). Neutrophil random migration, monocyte random migration and monocyte directed migration were unaffected. Heated plasma from (I), incubated with normal C5a or normal neutrophils, inhibited both C5a chemotactic activity and neutrophil directed migration. Three inhibitory components, designated as gpCMV-Associated-Chemotactic-Inhibitor (MW ∿ 80,000), Helper 1 (MW ∿ 30,000) and Helper 2 (MW ∿ 15,000), were identified by gel column chromatography. The chemotactic activity of C5a was inhibited following its incubation with either Inhibitor+Helper 1 or Inhibitor+Helper 2. The directed migration of neutrophils was inhibited following their incubation with Inhibitor+Helper 2, but not with Inhibitor+Helper 1. No inhibition was seen following their incubation with any of the components alone or with Helper 1+Helper 2. The inhibitors therefore affected both humoral and cellular elements, and may explain the impaired inflammatory response during gpCMV infection.

921 CHANGES IN T CELL SUBSETS IN CHILDHOOD EPSTEIN-BARR VIRUS INFECTIOUS MONONUCLEOSIS. Kristen A. Weigle and Ciro V. Sumaya. Dept of Pediatrics, University of Texas Health Science Center, San Antonio, Texas.

Epstein-Barr Virus (EBV) infectious mononucleosis (IM) is a lymphoproliferative disorder in which infected B cells are transformed and cellular immunity is depressed. To study the changes in cellular immunity during childhood EBV IM we measured helper (T_4) and suppressor (T_8) T cells using monoclonal antibodies during the course of the illness and in normal children. The EBV IM illness was diagnosed by clinical, hematologic and serologic criteria. All the children had VCA-IgM antibodies, but only 2 of 11 had heterophile antibodies.

Week after onset	No.	T4%	T8%	T4/T8
0-3	7	29.9 ±4.7	41.6 ±11.7	.79± .3
4-12	6	41.3 ±6.1	36.9 ± 4.1	1.11± .2
> 12	4	44.5 ±6.8	31.6 ± 2.7	1.42± .3
Normal children	10	46.1 ±7.4	25.7 ± 8.0	2.04±1.0

In acute disease, the percentage of helper T cells was lower ($p < .01$), the percentage of suppressor T cells was higher ($p<.01$) and the ratio of helper to suppressor T cells was lower ($p <.01$) compared to normal children. During the course of the illness these percentages gradually returned to normal levels. In the acute stage the children had less lymphocytosis than an adult group studied, probably reflecting the less marked suppressor T cell response in children, 41%, compared to adults, 64% ($p< .05$). We conclude that the cellular immune response to childhood EBV IM is primarily one of increased suppressor T cells, which may limit the continued proliferation of infected B cells.

922 A POSSIBLE ETIOLOGY FOR THE COLOSTRAL LYMPHOCYTES HYPORESPONSIVENESS TO MITOGENS. Leonard E. Weisman, Joseph Lima and Gerald B. Merenstein (Spon. by Frederick C. Battaglia), Departments of Pediatrics and Clinical Investigation, Fitzsimons Army Medical Center, Aurora, Colorado.

We have previously described that colostral lymphocytes (CL) are hyporesponsive to mitogens when compared to blood lymphocytes (BL).

To determine if a predominant suppressor substance or cell population was present in CL, CL and BL from 12 patients were cocultured and stimulated with PHA. The addition of 25 x 10^3 to 100 x 10^3 CL to BL, added to but did not alter the dose-response curve. Production of a suppressor substance or predominant suppressor cell population was not found. The added response was more than expected for CL.

To substantiate lack of a predominant suppressor cell population, CL and BL of 12 patients were evaluated using monoclonal antibody labeling with fluorescein and alkaline phosphatase.

	CL	BL
OKT3	37%	64%
OKT4	24%	41%
OKT8	13%	23%
ERFC	33%	60%

To substantiate lack of a suppressor product, supernatant from CL in culture with PHA failed to suppress BL in 3 patients.

Conclusion: CL hyporesponsiveness to mitogen is not due to a suppressor product or predominant suppressor cell population. The more than expected lymphoproliferative response of CL cultured with BL suggests a more effective macrophage population in BL.

923 MELKERSSEN-ROSENTHAL SYNDROME ASSOCIATED WITH FAMILIAL DEFICIENCY OF THE FOURTH COMPONENT OF COMPLEMENT. Thomas R. Welch, Roger E. Spitzer and Ann E. Stitzel. SUNY, Upstate Medical Center, Department of Pediatrics, Syracuse

The triad of recurrent facial swelling, facial nerve palsy, and lingua plicata ("Scrotal tongue") characterizes the Melkerssen-Rosenthal syndrome. A twenty-year-old girl with typical features of this syndrome has been followed for five years. Otolaryngologic and oral surgical evaluations showed no cause for her recurrent facial angioedema. She was otherwise healthy, and laboratory studies including anti-DNA titers, rheumatoid factor, and tests for cryoglobulins were negative. The serum level of C4, however, was consistently depressed both functionally and immunochemically, ranging from 16% to 41% of adult normal on 9 determinations. The C4 hemolytic efficiency (ratio of functional to immunochemical C4) averaged .72 (normal for our lab is 1.01 ± .26). All other complement components (C1, C2, C3, C5-9, properdin, factor B, factor H, and factor I) were normal. C1 inhibitor was normal both functionally and immunochemically. No correlation existed between the patient's C4 level and exacerbations of her disease. The patient's father, paternal aunt, paternal grandmother and 3 brothers all have identical complement profiles; none of them, however, have any features of Melkerssen-Rosenthal syndrome or of any collagen vascular disease. These studies document a familial complement deficiency in this patient. The relationship between her complement deficiency and recurrent edema is unclear. The mechanism, however, is different from that found in patients with hereditary angioneurotic edema who may present with a similar phenotypic expression.

● **924** HUMAN PLACENTAL MACROPHAGES (MØ) - DEFICIENCIES OF A FETAL DEFENSE MECHANISM. C.B. Wilson, W.M. Weaver, J.E. Haas. Depts. of Pediatrics & Pathology, Children's Orthop. Hosp. & U of Washington, Seattle, WA.

The placenta is a fetal organ that functions as a barrier to immunologic rejection of fetus by mother and to the spread of infection from mother to fetus. When we digested chorionic villi from 32-42 week gestation placentas with collagenase or trypsin, (MØ) were ∿ 25-50% of the cells recovered. The large number of MØ present suggested a potential role for these cells in fetal reticuloendothelial function and maternal-fetal immunologic interaction. Therefore, we have purified these MØ by sequential density gradient centrifugation and differential adherence. Cell preparations obtained were >80% mature MØ by morphology, phagocytosis of IgG-coated RBC and by light microscopic and ultrastructural cytochemistry; these MØ are >75% fetal in origin by Y chromosome fluorescence. Initial studies of these MØ suggest that deficits in their antimicrobial activity correlate with the neonates' susceptibility to certain pathogens. Placental MØ effectively phagocytosed but did not kill type III Group B streptococci (% surviving = 142±41%). These MØ destroyed only 43 ± 10% of ingested Toxoplasma; surviving Toxoplasma replicated intracellularly (4.2±0.4 Toxoplasma/vacuole). In contrast, placental MØ killed intracellular S. aureus 502A (58±4%, killed) nearly as well as adult monocyte-derived MØ (60±8%, killed). Zymosan and PMA stimulated superoxide anion production by these MØ was less than that by adult MØ ($p<0.001$). Additional study of the effector and the immunoregulatory function of these MØ may provide important information regarding maternal-fetal immunobiology.

925 PHAGOCYTIC AND BACTERICIDAL CAPACITY OF BREAST MILK MACROPHAGES. L.L. Wright, C.S. Cody, M.C. Harris, R.A. Polin, S.D. Douglas. Univ. of Pa. Sch. of Med., and Dept. of Peds., Children's Hospital of Philadelphia, Phila., PA.

Breast milk macrophages (BMM) may have an important role in neonatal host defenses; however, the functional capabilities of the BMM have not been sufficiently evaluated. Previous studies have compared phagocytosis and killing of the neutrophil with the BMM. We analyzed the functional activity of the BMM by comparing its phagocytic and bactericidal capacity for E. coli with that of its presumed progenitor, the peripheral blood monocyte. Fresh BM was obtained from mothers 2-4 days postpartum, refrigerated, centrifuged, and washed in Hanks' balanced salt solution (HBSS). Peripheral blood monocytes (PBM), were prepared from Ficoll-Hypaque interface cells by purification on microexudate-coated flasks. BBM and PBM were adhered to glass coverslips (CS) at $3x10^5$ cells/CS and incubated 1 hr with HBSS/15% FCS (100ul) + $1.5x10^6$ E. coli/CS (100ul) suspended in HBSS/10% human serum (HS) as opsonin. Phagocytosis was evaluated by counting the number of cells which contained at least 1 bacterium and the number of bacteria/phagocytic cell. Fewer BMM (46 ± 5 SEM) than PBM (74 ± 10) ingested E. coli ($p<.05$); however, when ingestion occurred the number of bacteria/cell was similar (BMM = 2.6 ± .31, PBM = 2.1 ± .23). Percent killing, expressed as killed bacteria/total ingested bacteria was significantly greater by PBM (BMM = 60 ± 2, PBM = 81 ± 3, $p<.0001$) with HS as an opsonin. BM (10-100%) was not an effective opsonin with either cell in this system although ingested organsims were killed. Thus, under defined in vitro conditions, the BMM has bactericidal capacity within 20% of the PBM.

● **926** A STUDY OF SPECIFIC IN VITRO ANTIBODY RESPONSES USING HUMAN CORD BLOOD LYMPHOCYTES (CBL). Robert Yarchoan and David L. Nelson. Metabolism Branch, NCI, NIH, Bethesda, Maryland.

Human peripheral blood lymphocytes from over 90% of normal adults produce specific anti-influenza antibody in vitro when stimulated with A/Aichi (H3N2) influenza virus. Cumulative antibody synthesis measured by ELISA using an anti-$F(ab')_2$ antibody is expressed in units (U), 1 U being the amount of antibody in a $1:10^5$ dilution of a pooled reference serum. Antibody production requires the cooperation of B cells, T cells, and monocytes. In the present study, we investigated the ability of CBL to respond to influenza virus in vitro. CBL obtained from each of 6 neonates made no measurable anti-influenza virus antibody in vitro (<0.5 U/ml) when stimulated with A/Aichi influenza virus, whereas 6 normal adults produced 42.8 x/÷ 1.8 U/ml (GM x/÷ SEM). In addition, 1) CBL failed to proliferate to A/Aichi influenza virus (Mean stimulation index 0.7 vs. 13.3 for adult controls), and 2) cord blood B cells produced little or no specific antibody when stimulated either with Epstein-Barr virus or with influenza virus plus irradiated, adult T cells (1200R). These results are consistent with a lack of previous exposure to influenza virus and/or immaturity of the newborn immune system. In each of two cases where it was examined, however, cocultures of irradiated cord blood T cells (1200R) with allogeneic adult B cells produced anti-influenza virus antibody when stimulated with A/Aichi. Thus, in spite of a lack of previous exposure to influenza virus, cord blood T cells are able to mediate a positive allogeneic helper effect for specific in vitro antibody production.

927 NEUTROPHIL RESPONSES AND AGE-DEPENDENT SUSCEPTIBILITY OF THE NEWBORN INFANT TO BACTERIAL INFECTION. B.Zelins, R.Wientzen, J.Walser, D.Armstrong, A.Boner, J.A.Bellanti. Georgetown University School of Medicine, Washington, D.C

The present studies were performed to evaluate the role of the neutrophil (N) in susceptibility of infants to bacterial infection. In the 1st phase, newborn (NB) rats were challenged with Group B streptococci (GBS) following which, sequential responses of peripheral, spleen, and bone marrow N were examined. The results of N responses following challenge with 10^4 GBS/gm body weight, a dosage shown previously to be 100% lethal for NB and 15% lethal for 7 day old rats, revealed that the susceptibility for the NB was associated with the following: 1)smaller baseline numbers of myeloid elements in peripheral blood, spleen, and bone marrow; 2) a failure to maintain these pools during infection; and 3) a lag in initial responses of N to infection. Based upon these findings, studies were initiated in the human infant using cord blood (CB) and heel prick specimens from 1-3 day old infants. Chemotactic responses (CTX) of N from infants was ≤ than 50% of adult values. A striking reduction in the chemotactic capacity of the band form, compared to the mature N, was seen in specimens from CB as well as adults. This may, in part, account for the differences in CTX since 30% of the N in infants were bands vs 9% in adults. These data suggest that both the quantity and quality of N responses may contribute to the known susceptibility of the newborn infant to infection. NIH grant 1P50AI-15321-04.

INFECTIOUS DISEASE

928 FACTORS AFFECTING POLYMORPHONUCLEAR LEUKOCYTE (PMN) DYSFUNCTION INDUCED BY INFLUENZA A VIRUS (IAV). J.S. Abramson, D.S. Lyles, K.A. Heller, D.A. Bass (Spon. by W.B. Lorentz). Bowman Gray School of Medicine, Department of Pediatrics, Winston-Salem, North Carolina.

PMN dysfunction occurs during early stages of IAV infection. We have found that incubation of PMNs with unopsonized IAV causes depressed metabolic responses to particulate and soluble stimuli and decreased bactericidal activity. Additionally, attachment and ingestion of IAV directly stimulated the respiratory burst; this could cause the subsequent PMN dysfunction (e.g., by exhausting the cell or by loss of normal membrane receptor function). These possibilities were studied using 3 infective types of IAV, non-infective IAV and purified IAV glycoprotein incorporated into liposomes. Infective (Texas 77, X-31, X-47) and non-infective X-47 virus, respectively, stimulated varying peak chemiluminescent (CL) responses to 15x, 6x, 3x and 3x that of cells in buffer alone. Incubation of PMNs with each type of virus for 30 min caused similar (∼ 65%) depression of CL responses to receptor dependent and independent stimuli (zymosan, PMA or ionophore A23187). A similar degree of PMN dysfunction was observed when PMNs were incubated with X-47 virus for 0.1, 0.5, 1, 2, 3, 6 and 18 hours. Also, although liposomes stimulated CL (to 10x cells in buffer), incubation with liposomes did not inhibit later CL responsiveness to the above stimuli. The data indicate that the ability of IAV to depress metabolic responses of PMNs is: a) independent of direct metabolic stimulation of the PMNs by IAV (is not due to PMN "exhaustion") and b) independent of alteration of PMN receptors.

929 USE OF URINARY (Ur) MURAMIDASE (MUR) ACTIVITY IN THE LOCALIZATION OF URINARY TRACT INFECTIONS (UTI's). Raymond D. Adelman and Gerald Ling, Univ. of Calif. Davis, Department of Pediatrics and Veterinary Medicine.

Mongrel dogs were infected with pathogenic E.coli by percutaneous nephropyelostomy. Subsequent bladder urine samples were obtained by cystocentesis and pelvis urine samples by percutaneous puncture. Dogs with upper UTI's (bacterial growth in pelvic urine), when compared to dogs with lower UTI's (bacterial growth only in bladder urine) or no UTI's (no bacterial growth), had higher values of Ur MUR* [1.13(0.12) vs 0.17(.06), $p<.001$], NAG* [2.44(.08) vs 2.16(0.07) $p<.02$] and B glucuronidase (BG)* [1.69 (.07) vs 1.35(.05), $p<.001$], higher Ur excretion of white cells [85.8(16.5) vs 8.2(3.0) $p<.01$] and lower Ur specific gravities [1.021(.001) vs 1.030(.001), $p<.001$]. Dogs with upper UTI's when compared only to dogs with lower UTI's had significant differences in Ur MUR and NAG activities but not in Ur BG, specific gravity or white cell excretion (Table). Immunoglobulin coated (IgG and IgA) bacteria were unhelpful in localizing the site of infection.

In summary, Ur MUR activity was helpful in localizing UTI's, the site of which was identified by direct culture in an experimental UTI model.

Site (n)	MUR	NAG	BG	Spec.Grav.	WBC/HPF	+IgG	+MUR
Upper(32)	1.13**	2.44	1.69	1.021	85.8	71%	75%
UTI	(.12)	(.08)	(.07)	(.001)	(16.3)		
Lower(8)	0.11	2.12	1.43	1.026	32.3	50%	0%
UTI	(.11)	(.13)	(.07)	(.002)	(10.8)		
p	.001	.005	NS	NS	NS		

*Log units/mg of urinary creatinine; **mean (SEM)

930 THE EFFECT OF CONTROLLED HYPOTHERMIA ON BACTERIA - POLYMORPHONUCLEAR LEUKOCYTE (PMN) INTERACTIONS. V. Akriotis and W.D. Biggar. Division of Infectious Diseases, Research Institute, The Hospital for Sick Children, University of Toronto, Canada.

In recent years, the use of controlled hypothermia (30°C) in Pediatrics has expanded to include patients with infectious, traumatic and metabolic insults to the central nervous system. Bacterial infections frequently complicate their management. We investigated the effects of hypothermia (30°C) on bacterial growth, and phagocytosis and killing of bacteria by PMN in vitro. Four bacteria were studied; Staphylococcus aureus, Streptococcus faecalis, Pseudomonas aeruginosa and Escherichia coli. The growth of stationary-phase-bacteria was assessed over 6 hrs at 30°C and 37°C. No significant difference in growth was observed. The effect of hypothermia on phagocytosis and killing by PMN varied with the different bacteria studied. Phagocytosis of S. aureus and E. coli was reduced more than killing by hypothermia. In contrast, killing of S. faecalis was reduced more than phagocytosis by hypothermia. Hypothermia had no apparent affect on either phagocytosis or killing of P. aeruginosa by PMN. The kinetics of phagocytosis was measured spectrophotometrically using diisodecyl phthalate-Oil Red O (ORO) droplets. The rate of ORO uptake was reduced at 30°C and the amount ingested after 15 minutes at 30°C was 60±2% of that ingested at 37°C. We conclude that hypothermia of 30°C affected the interaction of bacteria with PMN. This affect varied with the different bacteria examined. Hypothermia may predispose the host to bacterial infections and the spectrum of organisms may differ from the normothermic host.

933 IMMUNOGLOBULIN CLASS-SPECIFIC ANTIBODY TO GROUP B STREPTOCOCCAL (GBS) ANTIGENS IN PREGNANCY. Bascom F. Anthony, Scott A. McGeary, Nelydia F. Concepcion. UCLA School of Medicine, Harbor-UCLA Medical Center, Dept. of Pediatrics, Torrance, CA.

Human type-specific antibody to GBS has been measured in this laboratory by ELISA, using carbohydrate antigens purified from culture supernatants and tyrosylated for binding to microtiter wells and affinity-purified antiglobulins conjugated with alkaline phosphatase. With this immunospecific and quantitative assay, we have confirmed an absence of type-specific IgG antibody in infants with Type III sepsis and have shown that 20-25% of sera from pregnant carriers of types II and III contain measurable IgG (≥0.15 µg/ml) to the homologous antigen at term. By comparison, <5% of noncarriers were antibody-positive.

We have now measured IgM and IgA antibody for Type III in the same maternal population. In contrast with the IgG findings, measurable IgM antibody (≥1 µg/ml) was present in 41/50 of all subjects studied (82%). The prevalence was some what higher in carriers (25/27 or 93%) than in noncarriers (16/23 or 70%)while the mean level was slightly lower (3.7 vs 5.1 µg/ml). As expected, IgM antibody has been undetectable in all infant sera studied. IgA antibody was present in only 2 of 27 carriers (7%) and in no noncarriers at term.

This striking prevalence of type-specific IgM was unexpected and is unexplained. However, if IgM is protective for human GBS disease, it may account in part for the infrequency of invasive infection outside the newborn period.

● **931** INCREASED ANTIBODY RESPONSE TO IMMUNIZATION WITH HAEMOPHILUS INFLUENZAE TYPE B (HIB) AND PNEUMOCOCCAL CAPSULAR POLYSACCHARIDE (PS) VACCINES IN ADULTS WITH THE G2m(n) ALLOTYPE. Donna M. Ambrosino, George R. Siber, Erna van Loghem and Gerald Schiffman (Spon. by Kenneth McIntosh). Harvard Medical School, Sidney Farber Cancer Institute, Department of Clinical Microbiology, Boston, MA.

In order to determine whether the antibody response to bacterial PS antigens is related to immunoglobulin allotypes, we examined Gm (z,a,x,f,n,g,b), A2m (1,2) and Km (1,3) allotypes in 130 healthy adults immunized with Hib polyribophosphate (PRP), meningococcal gp A and C, and pneumococcal vaccines. Post-immunization antibody concentrations were significantly higher in G2m(n)+ than G2m(n)- patients for PRP and 8 of 11 pneumococcal types. Km(1)+ individuals showed a trend for lower post-immunization antibody concentrations to PRP and meningococcus A and C than Km(1)- subjects.

	Geom. Mean post-immunization antibody level (µg/ml)					
	No.	PRP	Men A	Men C	Mean pneumo.	
G2m(n)+	87	34.7	12.3	33.8	1.881	
G2m(n)-	43	21.2	p=.02	11.5	26.7 p=.11	1.217 p=.002
Km(1)+	14	18.9		10.9	21.9	1.501
Km(1)-	116	31.5	p=.13	15.3	32.8 p=.07	1.681 p=.50

We conclude that the G2m(n) allotype, a genetic marker of the IgG-2 subclass, identifies individuals with an enhanced antibody response to several bacterial PS antigens. Conversely G2m(n) negative individuals may be at increased risk of infection by encapsulated organisms.

934 VARICELLA VACCINE: A FOLLOW UP STUDY OF IMMUNIZED HEALTHY CHILDREN. Allan Arbeter, Stuart Starr, Patricia Paciorek, Deborah Miller, Toshiaki Ihara, Hitoshi Kamiya, Stanley Plotkin, University of Pennsylvania School of Medicine, Children's Hospital of Philadelphia, Department of Pediatrics, Philadelphia, PA.

One hundred and seven healthy children who previously received one of the live varicella zoster virus vaccine were followed up 18 to 30 months later. The number of follow up vaccinees restudied per original total number of individuals in each vaccine group were 44/52 OKA-Biken, 27/38 OKA-RIT-SK, 20/25 KMcC p40 and 16/17 KMcC p 50.

Detailed information on varicella/zoster exposures and subsequent illness was obtained. Laboratory studies included detection of antibodies to VZV by FAMA and IAHA assays and for selected sera by ADCC and neutralization assays. In vitro lymphocyte proliferation to VZV antigens was done on peripheral blood of OKA-RIT-SK and KMcC vaccinees.

One case of varicella occurred in a child who seroconverted after receiving KMcC p50. In 21 instances serological boost (≥2-fold) were detected in absence of clinical disease. Five children who had seroconverted (4 OKA-Biken and 1 KMcC p50) became seronegative. Ninety five percent of the vaccinees remained antibody positive. All vaccinees tested for lymphocyte proliferation responded to VZV antigen.

● **932** DETECTION OF EPSTEIN-BARR VIRUS DNA IN LYMPHOID TISSUES BY NUCLEIC ACID SPOT HYBRIDIZATION. W.A. Andiman and G. Miller. Yale University School of Medicine, Department of Pediatrics and Epidemiology and Public Health. New Haven, CT.

A new technique, nucleic acid spot hybridization, permits rapid, sensitive, screening of small numbers of cells for specific DNA sequences. This method detects EBV DNA in cultured cells. We now report preliminary data about its application to diagnosis of EBV infections in clinical samples. We used as DNA probes either whole EB viral genomes or EB viral DNA fragments propagated in plasmids in E.coli. The probes are radiolabelled with ^{32}P, and the content of viral DNA is estimated from radioautograms or by scintillation counting of filters containing samples to which the probe has bound. Statistical analysis, aided by computer, shows that the relationship between genome copy number and the amount of ^{32}Pin the probe bound by the sample, is best described by a log-log plot.

We have studied lymph node, spleen, peripheral blood, bone marrow and tumor tissues from a group of 20 patients with a variety of disorders. Two of nine samples analyzed with an intact viral probe and 2 of 11 samples with probes of cloned fragments contained significant amounts of EBV DNA. Positive reactions, with genome numbers varying from 7-102 copies per cell, were found in patients with nasopharyngeal cancer, B cell lymphosarcoma, nodular sclerosing Hodgkin's disease, and chronic myelogenous leukemia. The spot hybridization technique should be valuable in clarifying the relationship between EB virus and a number of lymphoproliferative diseases. The method can also be adapted for diagnosis of a variety of other diseases.

935 PATHOPHYSIOLOGY OF *HAEMOPHILUS INFLUENZAE* TYPE B (Hib) PNEUMONIA. Jose L. Arredondo, Jose I. Santos and Joseph J. Vitale (Spon. by Jerome O. Klein), Boston University School of Medicine, Boston City Hospital, Departments of Pediatrics and Pathology, Boston, MA.

The pathophysiology of Hib pneumonia is poorly understood and may be related to the host's nutritional status. Using a weanling rat model, pneumonia was produced by intratracheal installation of 10^5 Hib cells into control and iron deficient animals. The kinetics of pulmonary, blood, and splenic clearance were determined by quantitative bacteriology. Capsular antigenemia and antibody response were measured by CIE and an enzyme linked radioimmunoassay, respectively. Bacteremia was detected as early as 12 hours and as late as 12 days after inoculation with peak levels occurring between days 3 and 5 and coincided with gross and histologic evidence of pneumonia. Similarly, lung bacterial counts progressively increased reaching 10^7-10^8 per gram of lung tissue within 72 hours and slowly decreased with positive lung cultures still present up to 24 days post infection. In contrast, iron deficient animals were bacteremic 5 to 6 days longer and demonstrated slower resolution of their pneumonia than did controls. These data indicate that Hib pneumonia caused a marked impairment in lung anti-Hib defenses within 72 hours of the onset of infection and that while blood clearance was generally accomplished by day 12, pulmonary clearance and resolution of pneumonia took over 3 weeks. Furthermore, this animal model appears to have the potential for *in vivo* evaluation of nutritional modulation on pulmonary host defense mechanisms.

936 IMMUNOLOGIC AND EPIDEMIOLOGIC ASPECTS OF NON-MATERNAL NATURALLY ACQUIRED VARICELLA ZOSTER VIRUS (VZV) INFECTION IN INFANCY. Koichi Baba, Hyakuji Yabuuchi, Michiaki Takahashi, and Pearay L. Ogra, Dept. of Pediatrics, State University of New York at Buffalo, Osaka University, Osaka, and Research Institute for Microbial Diseases, Osaka, Japan.

Employing the techniques of immunofluorescence, neutralization of tissue culture infectivity and dermal response to VZV antigen, the development of VZV specific immune response and evolution of clinical infection was studied in a population of infants under one year of age during three outbreaks of varicella in a semi-closed domiciliary institution for infants in Japan. Over a period of four years, 250 residents ranging in age from 27 days to 32 months were tested for cutaneous reactivity to VZV antigen, and VZV specific antibody activity before, during and after each outbreak of varicella. Of these, 85 subjects developed clinical varicella, with an overall attack rate of 100% for all susceptible subjects. Significantly, however, all infants under two months of age were infected following such exposure, despite the presence of pre-existing maternal antibody. The degree of cutaneous involvement appeared to be milder (<20 vesicles) in infants less than two months old and severe cutaneous disease (with over 300 eruptions or confluent rash) occurred more frequently in subjects 2 to 11 months of age. Pre-existing antibody did not prevent development of illness, or alter the degree of antibody or cellular immune response to subsequent infection. However, the peak cutaneous reactivity to VZV antigen after infection was found to be significantly lower in infants under two months of age.

● **937** IMPAIRED MIGRATORY AND CHEMOTACTIC ACTIVITY OF NEUTROPHILS DURING CYTOMEGALOVIRUS INFECTION OF MICE. James F. Bale, Jr., Earl R. Kern, James C. Overall, Jr., and J. Richard Baringer. Department of Pediatrics, University of Utah School of Medicine, Salt Lake City and Department of Neurology, University of California, San Francisco.

Cytomegalovirus (CMV) infection has been associated with altered host defense and an increased susceptibility to infections. In a murine model, we demonstrated previously an impaired inflammatory response to a subcutaneous challenge with K1 E. coli during the acute phase of a sublethal murine CMV (MCMV) infection. To further define altered neutrophil function, we examined absolute neutrophil counts (ANC) in peripheral blood and in a subcutaneous sponge and the chemotactic ability of neutrophils in the sponge during MCMV infection. Results indicated that ANC in the sponge, but not the peripheral blood, were markedly decreased and neutrophil chemotaxis was depressed on days 1-4. For example, on days 1-2 the following mean values were obtained in MCMV-infected and sham-inoculated mice: peripheral blood ANC of 732 vs 899 (P=0.3), sponge fluid ANC of 1655 vs 5175 (P=0.001), and sponge fluid neutrophil chemotactic index of 1.9 vs 6.2 (P=0.004). These results indicate that the chemotactic ability of neutrophils migrating into subcutaneous tissues of mice is impaired during acute MCMV infection, and strongly suggest that impaired migration of cells from the peripheral blood is at least one mechanism accounting for decreased numbers of neutrophils in tissues. These alterations in host defense may be important in contributing to the development of CMV-related secondary infections.

938 DISTINCTIVE FEATURES OF FUNGAL INFECTIONS IN LOW BIRTH WEIGHT (LBW) INFANTS. J.E.Baley, R.M.Kliegman, A.A.Fanaroff. CWRU, RB&C Hosp., Dept.Peds., Cleve.OH

In recent years 8% of our infants weighing <1.5 kg had documented sepsis, accounting for 14% of the deaths. These include fungal infections which have an insidious onset but dramatic sequelae. To facilitate earlier diagnosis, we report previously poorly recognized but dominant clinical features of fungal infection. In 1979-80, 10 infants with identifiable fungi (9 Candida, 1 Malassezia) representing 2.7% of LBW admissions, had a mean BW of 0.8 kg (0.6-1.1 kg), GA 28 wks and postnatal age of onset at 5 wks. Striking presenting clinical features included pulmonary infiltrates (pneumonia), radiographically indistinguishable from bronchopulmonary dysplasia and resulting in respiratory failure (8/10). Necrotizing enterocolitis was simulated in 7 with abdominal distention, guaiac positive stools, edema of the bowel wall, but absence of pneumatosis. Carbohydrate intolerance and glycosuria necessitating insulin therapy(7) and Candida endophthalmitis(4) were additional features. Predisposing factors included central arterial and venous lines, prolonged broad spectrum antibiotic usage(mean 23 days) for suspected(4) or confirmed bacterial infection(6), and total parenteral nutrition(mean 37 days). Positive cultures for fungus were obtained from blood, urine, CSF and lung biopsy. In 6 infants cultures were intermittently positive. 4 had negative cultures despite microscopically visible fungus in urine and lung. 6 infants died, all responding with oliguria to amphotericin therapy. We conclude that in preterm infants fungal infections have protean manifestations necessitating a high index of suspicion.

939 IDENTIFICATION OF A SUBSET OF STRAINS OF NONTYPABLE HAEMOPHILUS INFLUENZAE ASSOCIATED WITH BACTEREMIA. Stephen J. Barenkamp, Robert S. Munson, Jr. and Dan M. Granoff, Wash U Sch of Med & St. Louis Children's Hosp, St. Louis.

Nontypable Haemophilus influenzae are a frequent cause of otitis media in children and occasionally cause bacteremic illness in neonates and in older immunocompromised patients. The lack of specific strain markers has hampered studies on the relatedness and relative pathogenicity of different isolates. We applied the techniques of biotype determination and SDS-polyacrylamide gel electrophoresis of outer membrane protein (OMP) preparations to 35 epidemiologically-unrelated pathogenic nontypable Haemophilus influenzae isolates. Three of five isolates obtained from the blood of unrelated newborns with sepsis had concordant major OMP profiles and were biotype IV. Two of five isolates obtained from the blood of unrelated older children or adults with bacteremia had concordant major OMP profiles, distinct from the common profile of neonatal strains, and were biotype II. The OMP profiles of the remaining five isolates from blood, two isolates from CSF, and 23 isolates from middle ear aspirates of children with otitis media were unique, although each isolate had peptides with apparent molecular weights of 16,000 and 31,500. No nontypable isolate had an OMP profile identical with that of any of the 256 type b Haemophilus influenzae isolates we have examined. These results suggest that a subset of nontypable isolates associated with bacteremia have distinctive strain markers. Their pathogenicity may relate to a predilection for colonizing the female genital tract in the case of the common neonatal strain, or an increased ability to evade host defenses.

940 DIPHTHERIA-PERTUSSIS-TETANUS VACCINE: REACTIONS AND PROTECTION FROM A HALF DOSE SCHEDULE. Roger M. Barkin, Joel S. Samuelson, Lisa Gotlin (Spon. by James K. Todd). University of Colorado Health Sciences Center, Department of Pediatrics, Denver and Connaught Laboratories, Swiftwater, Pennsylvania.

Diphtheria-pertussis-tetanus (DPT) vaccine has a very high level of reactions when administered according to current recommendations. Reduction of side effects while maintaining adequate protection would enhance acceptance of this product. In a prospective study, patients were randomized to receive standard (0.5 ml) or half (0.25 ml) doses of DPT vaccine for all 3 immunizations administered at 2, 4 and 6 months of age. Side effects and antibody responses were determined in 74 children who completed the entire primary series.

Clinical reactions were determined by questionnaire and home visits. Reactions were categorized into height of temperature, behavioral changes, and local reactions. 3.6% of children in both vaccine groups had temperatures of 102°F or greater and 35.6% had local reactions consisting of a combination of redness, tenderness, and swelling. No differences were noted between the 2 study groups. However, only 47.0% of the reduced dosage group had severe behavioral problems while 64.8% of the standard vaccine recipients had comparable reactions ($p<0.01$). This latter difference was most marked during the third immunization. Patients had serological evidence of protection to diphtheria, pertussis, and tetanus. The decreased reaction and adequate protection of the reduced dosage underlines the need to reevaluate current recommendations.

941 INTRAVENTRICULAR VANCOMYCIN IN THE TREATMENT OF VENTRICULOPERITONEAL (VP) SHUNT INFECTIONS DUE TO METHICILLIN-RESISTANT, GENTAMICIN-RESISTANT (MRGR) *STAPHYLOCOCCUS EPIDERMIDIS (STAPH EPI)*. Douglas L. Bartley, Fred F. Barrett, James C.H. Simmons, Dept. of Ped., Univ. of Tenn. Ctr. for Health Sciences, LeBonheur Children's Med. Ctr., Memphis, TN.

Six patients ranging in age from 3 weeks to 5 months with VP shunt infections due to MRGR strains of *Staph epi* were treated with intraventricular vancomycin (5 mg/day) via the VP shunt (5 cases). In one patient vancomycin (5 mg/day) was injected directly into the ventricles following removal of an infected shunt. All patients had previously received unsuccessful courses of other intraventricular antibiotics prior to vancomycin therapy. Cerebrospinal fluid (CSF) sterility was achieved in all cases within 9 days (avg. 4.5 days); therapy was continued for an average 6 additional days. In 3 cases no simultaneous systemic antibiotics were used. Clinical symptoms and CSF cell counts improved within 3 days in all patients. Neutrophils/ml CSF before $\bar{x} = 161 \pm 138$; neutrophils/ml CSF after 3 days $\bar{x} = 55 \pm 88$ ($\bar{x} \pm SD$). Shunt devices were surgically removed and cultured in all cases upon completion of antibiotic therapy; 2 of 5 (40%) grew the original organism despite persistently negative CSF cultures obtained via the shunt reservoir prior to its removal.

There was no evidence of toxicity during treatment, nor in up to 2 years follow-up. Relapse of infection due to the same organism did not occur although one patient had a new shunt infection (*Staph aureus*) 13 months later.

These data suggest that vancomycin is both safe and effective in the treatment of VP shunt infections due to MRGR *Staph epi* when administered via the shunt. It also appears that in up to 60% of cases bacteriologic cure can be achieved without removing the infected shunt. Complete erradication of the organism, however, can only be guaranteed by removal of the original device.

942 DIRECT DETECTION OF CMV ANTIGEN USING INDIRECT HEMAGGLUTINATION INHIBITION (IHI)-A NEW METHOD OF DETECTION OF VIRAL ANTIGEN. S. Black, M. Raas, L. Mintz, W.L. Drew, H.R. Shinefield. Kaiser Hospital, San Francisco, CA.

A simple and sensitive technique has been developed for detection of CMV (cytomegalovirus) antigen in tissue culture supernatant. The assay is a modification of the indirect hemagglutination assay (IHA) and is capable of detecting 10^3 $TCID_{50}$ of virus in tissue culture fluid. In the performance of the assay, sheep red blood cells are tanned and sensitized with commercial CMV - CF antigen at dilutions determined by checkerboard titration. A lot of commercial CMV antisera having an IHA titer of 1:1024 or higher is chosen. The inhibition assay is performed by incubation of equal volumes of tissue culture fluid to be tested with the dilutions of the antisera of known strength for 15 minutes at room temperature. A 1:100 dilution of the CMV-CF antigen and PBS buffer serve as positive and negative controls respectively. These incubated solutions are then assayed for antibody activity by IHA. A two fold or greater shift to lower titer as compared with the antigen negative control is considered to be a positive test for the presence of viral antigen. The test is specific in that colsely related viruses such as herpes simplex do not interfere with the assay. This IHI assay technique may serve as a tool for screening and identification of tissue culture specimens. It also has potential for use in the direct detection of viral antigen in clinical specimens.

943 USE OF COUNTERIMMUNE ELECTROPHORESIS TO DETECT NONVIABLE STREPTOCOCCUS PNEUMONIAE IN BACTEC BLOOD CULTURE BOTTLES. Joseph A. Bocchini, Jr., Hillary K. Heard, and Ellen D. Rambin, (Sponsored by Joseph A. Little), Dept of Ped and Lab Med, Louisiana State University, Shreveport, LA

BACTEC radiometric systems are used by many laboratories to process blood cultures (BC). In the hypertonic aerobic bottle of this system, S. pneumo will frequently produce a positive growth index (GI), chocolatize the contents and be visible on Gram stain; but will not grow on subculture. The organism is often, but not always, recoverable by subculture from the paired anaerobic BC. During 1978-80, 23% of patients with S. pneumo bacteremia at LSUMC had negative subcultures from aerobic BC's with positive GI's. In 1981 we performed CIE on aliquots from GI positive, chocolatized aerobic BC with Gram positive organisms on smear. A Hyland power pack was used. Pneumo antibody (Omniserum) was obtained from the Statens Seruminstitut, Copenhagen. Of 42 episodes of S. pneumo bacteremia, CIE was positive in all 9 of the cases in which the aerobic BC had a positive GI but S. pneumo failed to grow on subculture. In 7 of these patients, subcultures from the anerobic BC grew S. pneumo and 2 patients had clinical illnesses consistent with pneumococcus. Although nonspecific precipitin bands were occasionally seen near the cathode well, they were easily distinguished from positive bands. No cross reactions have been noted in cultures positive for S. aureus, S. epidermidis or Gp B Strep. CIE can be used to rapidly identify S. pneumo in aerobic BC in which the organisms are no longer viable and can be used to confirm S. pneumo bacteremia in patients whose paired anerobic BC's remain negative.

944 CLOSTRIDIUM DIFFICILE IN PEDIATRIC OUTPATIENTS. Douglas Boenning, Gary Fleisher, Joseph Campos, Christine Hulkower, Robert Quinlan (Spon. by Jean Cortner). The Children's Hospital of Philadelphia, Department of Pediatrics, Division of Microbiology, Philadelphia, Pennsylvania.

Clostridium difficile has been implicated as one cause of hospital-acquired diarrhea in children, yet the prevalence of this organism in outpatient children with diarrhea has not been established. We therefore prospectively studied 306 pediatric outpatients over a 12 month period. Children presenting with diarrhea and controls with non-diarrheal illnesses were cultured for C. difficile and potential bacterial pathogens. C. difficile isolates were identified on a selective medium and confirmed with gas chromatography. Toxin production was detected by counterimmunoelectrophoresis (CIE).

Children ranged in age from 2 weeks to 16 years (median 11 mos). Bacterial pathogens were found in 10.5% of patients with diarrhea (18/171): 12 Salmonella spp., 5 Campylobacter jejuni, and 1 Shigella Grp. B. C. difficile was found in 7.0% of patients with diarrhea (12/171) and 14.8% of controls (20/135). Mean age of the 12 diarrhea patients with C. difficile was 9.8 ± 8.6 mos. vs. 8.2 ± 4.9 mos. for the 20 positive controls (N.S.). Antibiotic exposure during the previous month was found in only 22% of all C. difficile-positive patients (7/32). These 32 patients with C. difficile were clinically indistinguishable from the other study patients. All strains of C. difficile were capable of producing toxin as demonstrated by CIE. C. difficile appears to comprise part of the normal bowel flora in some children despite a negative history of recent antibiotic usage.

945 PERMISSIVENESS OF NEONATAL MONONUCLEAR CELLS FOR INFECTION BY HERPES SIMPLEX VIRUS (HSV) TYPE 2. J.Z. Sullivan-Bolyai, C.B. Wilson, L. Brewer and L. Corey, Dept. of Pediatrics and Laboratory Medicine, University of Washington and Children's Orthopedic Hospital, Seattle, WA.

Disseminated HSV infection occurs more frequently in neonates than adults. To investigate the permissiveness of mononuclear cells for HSV replication, cord and adult peripheral blood mononuclear cells were separated into monocyte and lymphocyte enriched fractions by Ficoll-Hypaque centrifugation and adherence to plastic or fibronectin. Cells were then infected with HSV-2 at a multiplicity of infection (MOI) of 1, washed and serially assayed for HSV using a microtiter method.

Mean HSV-2 titers expressed as $\log_{10}$ TCID50 were:

Day Post Inoculation	0	2	4	6
Cord Blood: Mononuclear cells (n=2)	2.2	2.2	1.7	3.0*
Adherent cells (n=3)	1.9	0.3	<0	<0
Nonadherent cells (n=4)	2.1	1.1	1.6	2.1*
Adult Blood: Nonadherent cells (n=5)	2.6	1.1	0.2	<0
HSV-2 in medium alone (n=1)	2.3	1.4	0.1	<0

* Both $p<0.01$ compared to other preparations on Day 6

A 72 hour incubation time prior to addition of virus or varying the MOI from .001 to 1 did not alter these findings. HSV-2 did not replicate in freeze-thawed cells including the non-adherent cord blood fraction. The data indicate that non-adherent cord blood mononuclear cells are permissive for HSV infection. This observation may partially explain the higher incidence of viremic spread of HSV in the neonate.

946 DEFECTIVE OPSONIZATION OF L. MONOCYTOGENES USING SERUM FROM INFECTED OR NORMAL NEWBORNS. Robert Bortolussi, Dorothy Barnard, Andrew Issekutz, Alan Hudak, Jacqueline Ewing, Alexander Allen, Dora Stinson, and Elihu Rees. (Spon. by Richard B. Goldbloom) Dalhousie University, Halifax, Canada.

During a province-wide outbreak of L. monocytogenes infection, 25 stillborn or live neonates with systemic infection were identified compared to only 7 nonpregnant adults. Although lymphocyte and monocyte immaturity has been suggested as a predisposing cause of newborn illness, we wondered if a humoral defect might also exist. To test this hypothesis, we assessed (i) hemolytic complement by the classical (CCP) and alternative (ACP) pathways (ii) fibronectin (FNC, a nonspecific opsonin) and (iii) opsonization of listeria using a chemiluminescence assay (CL) on samples of blood obtained from 5 control and 5 infected infants during acute illness. Results were expressed as percent of adult controls ± SD.

	CL	CCP	ACP	FNC
Listeria Infants:	6*± 8	104±50	54†±13	24.7*± 4
Control Infants:	11†±20	75±25	65 ±35	57 ±10

*$p<0.01$, †$p<0.05$ vs. adult controls.

Since complement levels were considered adequate, we attributed the poor opsonic activity in newborn sera to other humoral factors which are absent or low such as IgM or FNC. Opsonic activity and FNC levels were partially corrected in the 4 infants given fresh frozen plasma (to 40% of adult control). This study suggests that the susceptibility of newborn infants to listeria may be due, in part to decreased opsonic activity to this organism.

947 TRANSPLACENTAL PASSAGE OF IgG ANTIBODY AGAINST GROUP B STREPTOCOCCUS (GBS) TYPE Ia. Kenneth M. Boyer, Cynthia K. Papierniak, Cecile A. Gadzala, Jeffrey D. Parvin, and Samuel P. Gotoff. Pritzker Sch. of Med., Univ. of Chicago, Dept. of Pediatrics, Michael Reese Hosp., Chicago.

Passive immunization of the fetus by maternal vaccination has been proposed as a means of immunoprophylaxis for neonatal GBS infection. Since attack rates of early-onset infection are increased in premature infants, the kinetics of transplacental antibody passage are critical to the success of such an approach. We measured levels of naturally occurring type-specific IgG antibody against GBS-Ia in paired cord and maternal serum specimens at gestational ages 22 and 41 weeks. A quantitative ELISA technique sensitive to concentrations of specific antibody ≥0.06 ug/ml was used. Twenty-one of 130 maternal sera had IgG anti-GBS Ia concentrations ≥0.25 ug/ml. Ratios of cord:maternal IgG anti-GBS Ia ranged from 0.11 to 1.01. Ratios ≥0.25 were found in 6 of 6 serum pairs at gestational ages ≥36 weeks, 11 of 11 at 30 to 35 weeks, and 2 of 5 (including one pair of twins) at gestational ages <30 weeks. Although antibody against GBS-Ia was not prevalent among the mothers tested, these data suggest that transplacental passage can provide protective levels of IgG anti-GBS Ia to premature as well as full-term newborns born to immune mothers. In an experimental model, antibody levels of 1.5 ug/ml uniformly protect against lethal GBS-Ia infection. Therefore, women with levels ≥ 6 ug/ml, which is achievable with vaccination, should provide adequate antibody for all but the smallest premature infants.

948 VIABILITY OF *Bordetella pertussis* USING TRANSWAB MW 173 (TS). Kenneth Bromberg, Carl R. Gullans, Vincent I. Ahonkhai, Marcelino F. Sierra (Spon. by Leonard Glass). SUNY at Downstate, School of Medicine. Kings County Hospital, Depts. of Pediatrics and Pathology. Brooklyn, New York.

Bordetella pertussis is a difficult bacterium to isolate from clinical specimens. Bedside inoculation of both selective and non-selective growth media provides the highest isolation rate for this organism. A transport medium that would preserve the viability or enhance the growth of *B. pertussis*, however, should allow for the isolation of this organism when bedside inoculation of growth media is not possible or practical.

A commercial charcoal-containing transport medium (CCTM) marketed with a dacron swab as TS (Med. Wire & Equip. Co., Cleveland, OH) was shown to preserve the viability of *B. pertussis* when two positive clinical specimens were each obtained with the swab, inoculated into CCTM, and subsequently incubated on growth medium (CM 119, Oxoid, Columbia, MD). Growth medium was also directly inoculated with dacron swabs at the bedside. Unexpectedly, one of the bedside-inoculated specimens did not yield *B. pertussis*.

To clarify this unexpected observation, the ability of TS to preserve the viability of *B. pertussis* was investigated. The organism was recoverable for up to two days from CCTM inoculated with dacron swabs from a standardized solution of *B. pertussis*.

TS may be a useful alternative to direct specimen inoculation for the recovery of *B. pertussis* from clinical specimens. A clinical trial comparing direct bedside inoculation of growth media to CCTM and subculture to growth medium is needed.

● **949** INCREASED ADHERENCE (AD) OF GROUP B STREPTOCOCCI (GBS) TO BUCCAL EPITHELIAL CELLS (BEC) OF INFECTED NEONATES. Robert A. Broughton and Carol J. Baker. Baylor College of Medicine, Department of Pediatrics, Houston.

AD of GBS to neonatal mucosal surfaces, a potentially important event in the pathogenesis of invasive GBS infection, has not been assessed. An AD assay employing ^{3}H-labeled GBS and adult BEC in a ratio of ~1000 bacteria/cell was developed. AD of several clinical and prototype Ia, II, and III GBS strains to BEC from healthy adults was defined. AD (# GBS/BEC) for the prototype strains was low (mean <1). In contrast, the mean AD was 61 and 73, respectively, for Ia and II isolates from sick neonates. Each of 7 III-GBS isolates from sick neonates adhered poorly to adult BEC (mean 6). BEC from 10 infants with invasive GBS infection (5 early; 5 meningitis; 8 III-GBS) were studied with the infecting GBS isolate, adult BEC-defined strains AD Ia-501 and non-AD III-732, and compared to age-matched controls. The mean AD of GBS infants' BEC (31) for their own isolates was significantly greater than that of control infants' BEC (9) ($p < .03$). 60% of GBS infants but no controls had high AD (>25), whereas 70% of controls' and only 30% of infected infants' BEC, respectively, adhered poorly (<10) ($p < .03$). The AD of III strains to control infants' and adults' BEC was similar. Although Ia-501 also adhered better to BEC of infected infants vs. controls (mean 30 vs. 12), this difference was not significant. No AD of III-732 to either group's BEC was detected. Age of onset or focus of infection did not significantly influence AD. These findings suggest that neonates at risk for invasive GBS infection may have increased BEC receptor sites for certain strains of GBS and/or that GBS may elaborate products which unmask these receptors.

950 ADMINISTRATION OF LIVE VARICELLA VACCINE TO CHILDREN WITH LEUKEMIA-A PROGRESS REPORT. P.A. Brunell, Z. Shehab, C. Geiser, and J. Waugh. Univ. of Tx. Hlth Sc. Ctr., Dept. of Pediatrics, San Antonio, Texas.

Live varicella vaccine was given to 21 susceptible children with acute lymphoblastic leukemia and one child with non-Hodgkin's lymphoma. Ten patients were on chemotherapy and one or more years since remission or diagnosis. The remaining 12 had completed chemotherapy. Antibody was present in all the vaccinees at one month post-immunization and was still detectable in all 13 children tested at one year. Two vaccinees on chemotherapy who developed a biphasic rash were the only patients who failed to develop a blastogenic response to VZ antigen. A third patient on chemotherapy developed an abortive rash following immunization. A sibling of one of the former patients seroconverted probably due to infection with vaccine virus spread from the vaccinee. Neither he or any other of the 18 susceptible or 59 immune household contacts of vaccinees had clinical evidence of varicella. None of the other contacts had rises in VZ antibody following immunization. Four vaccinees had household exposures to chickenpox and one to zoster. This resulted in one mild case of chickenpox 2 years following vaccination. In addition, 2 vaccinees had multiple school exposures and 2 vaccinees other types of exposures with no illness resulting. None of the vaccinees have developed zoster thus far. The vaccine appears to be safe and effective, and routine administration should now be considered for children with leukemia one year or more since diagnosis or remission.

● **951** PROSPECTIVE RANDOMIZED CLINICAL TRIAL EVALUATING THE EFFICACY OF EXPECTANT THERAPY OF OCCULT BACTEREMIA. William L. Carroll, Jonathan I. Singer, Michael K. Farrell, Mary A. Jackson, Jeffrey S. Lobel, Edward D. Lewis, (Spon. by Martin G. Myers). Children's Hospital Medical Center, Cincinnati, Ohio.

Antibiotic therapy for children without foci of infection and at risk for bacteremia is controversial. We conducted a prospective randomized clinical trial using expectant antibiotic therapy in children at risk for bacteremia. Ninety-six children age 6-24 mo., with fever $\geq 40^{\circ}$c, no identifiable source of infection and leukocyte count $\geq$15,000 and/or sedimentation rate $\geq$30 were enrolled. All children had a blood culture, chest x-ray, urinalysis and urine culture. A lumbar puncture was performed if age $\leq$12 mos. Patients were randomized to receive either no antibiotic therapy or CR Bicillin 50,000 U/kg IM followed by Penicillin V 100 mg/kg/day for 3 days. Patients were examined at 24 and 72 hrs. Fifty patients were treated expectantly and 46 received no antibiotic therapy. Ten of the 96 patients were bacteremic (9 S. pneumoniae, 1 H. influenzae). Four of the 5 treated bacteremic cases were improved at the first follow up visit (afebrile and no obvious focus of infection). The 5 untreated patients were unimproved, 4 developed focal infections (2 meningitis, 2 otitis media) ($P \leq 0.05$, Fischer exact test). No complications of expectant therapy were detected. Expectant antibiotic therapy for children who have no obvious source of infection and who meet these criteria associated with occult bacteremia is warranted.

952 SERUM OPSONIC RESPONSE TO H. INFLUENZAE TYPE B (HIB) VACCINE IN 15-18 MONTH OLD CHILDREN. K. Lynn Cates, Lolita Caparas, Martin F. Randolph, J.S.C. Kuo, Christine L. Williams, and Martha L. Lepow, (Spon. by Milton Markowitz). University of Connecticut Health Center, Department of Pediatrics, Farmington; Medical Research Division, American Cyanamid Co., Lederle Laboratories, Pearl River, NY and Albany Medical College, Department of Pediatrics, Albany, NY.

We studied the ability of children immunized with DPT-polyribosylribitol phosphate (PRP) to mount a serum opsonic response to HIB. Twenty-seven children were randomly assigned to receive PRP (GpA, N=12) or DPT booster (GpB, N=15). Serum was obtained before and 1 month after vaccination. HIB opsonic activity was determined using ^{3}H-thymidine-labeled HIB and normal human PMN. Five children in GpA, but only 1 in GpB had a significant rise in serum opsonic activity to HIB ($p < 0.05$). Mean GpA postimmunization opsonic activity, expressed as % phagocytized bacteria, ($\bar{x} \pm$SEM, 60.8±4.1) was significantly higher than that from GpB (47.5±2.8) ($p < 0.05$). Mean opsonic activity in the 5 responders was 64.8. Preimmunization serum from GpA and GpB had similar mean opsonic activity (GpA=52.7± 2.8, GpB=46.6± 2.9). Sera were also tested by radioimmunoassay for anti-PRP antibody. Ten children in GpA, including all 5 with an opsonic response, and none in GpB, had an increase in anti-PRP antibody. The presence of serum bactericidal and anticapsular antibody at the onset of HIB disease in some children suggests that other factors may be necessary for resistance to this organism. We have demonstrated an opsonic response to PRP vaccine which may contribute to host defense against HIB disease.

● **953** NEUTROPHIL PRODUCTION DURING EXPERIMENTAL GROUP B STREPTOCOCCAL SEPSIS. Robert D. Christensen, Jane Macfarlane, Nancy Taylor, Harry R. Hill and Gerald Rothstein, University of Utah School of Medicine, S.L.C., Utah.

Neutrophilia usually accompanies bacterial infection in adults but infected neonates frequently develop neutropenia. In an attempt to explain this difference, we studied neutrophil(neut) production and marrow pool sizes in groups of 6-9 adult and neonatal rats inoculated with 3×10^6 type II group B strep(GBS)/gm body wt. All infected adults survived, developing neutrophilia with a peak count of 340±18% of control(x±SEM, $p < .001$). In contrast, infected neonates developed profound neutropenia (9±3% of control, $p < .001$) and 88% died. In adults the neut storage pool (NSP=all PMN+bands+metamyelocytes within the marrow) diminished to 65±4% of control, but the neonates' NSP became almost completely depleted(9±2%, $p < .001$). Infected adults increased their granulocytic stem cells(CFUc) by 320±20%($p < .001$) and their CFUc proliferative rate (determined by tridiated thymidine suicide) by 95±4%($p < .001$). In the face of neutropenia and NSP depletion, however, infected neonates had decreased CFUc(48±8%, $p < .001$) and CFUc proliferation did not increase. Thus, adult rats responded to GBS infection with neutrophilia, a modest temporary reduction in NSP, and an increase in stem cell number and proliferative rate. In contrast, infected neonates developed profound neutropenia, an exhausted NSP and did not increase stem cell number or proliferative rate. It appears that both exhaustion of the NSP and inability to accelerate neut production result in the neutropenia in neonatal GBS sepsis. The deficient neut supply which results may contribute to the high mortality in this condition.

954 INCREASED OPSONIC ACTIVITY IN SICKLE CELL PATIENTS AFTER PNEUMOCOCCAL IMMUNIZATION. David S. Chudwin, Mary H. Caulfield, Arthur J. Ammann, Diane W. Wara, University of California, Department of Pediatrics, San Francisco.

Sickle cell disease patients (SCD) produce antibodies after pneumococcal polysaccharide (PPS) immunization, but increased opsonic activity has not been demonstrated. We studied the correlation between a rise in S. pneumoniae type 7 PPS antibodies (αPPS-7), measured by RIA (Dr. G. Schiffman), and increased opsonization in vitro. We measured the uptake at 30 min by human neutrophils of radiolabelled type 7 bacteria opsonized with the test serum. A 2 fold increase (FI) was defined as a positive antibody response, and a 1.45 FI as a positive opsonic response (>2 x coefficient of variation). Sera from 18 SCD >2 yrs, 6 SCD <2 yrs, and 6 controls before and after PPS immunization were tested:

	αPPS-7 ng Ab N/ml		>2	% Uptake		>1.45
	Pre	Post	FI	Pre	Post	FI
SCD >2 yrs	337±288	1051±392	13/18	36±27	70±27	11/18
SCD <2 yrs	79±31	537±475	4/6	12±4	15±7	3/6
Controls	877±1263	2061±1074	5/6	57±24	73±17	2/6

SCD >2 yrs had significant increases in mean antibody ($p < .001$) and opsonic ($p < .001$) levels after immunization. SCD <2 yrs had borderline antibody ($p = .06$) and opsonic ($p = .12$) responses. Mean antibody amounts and opsonic activity pre- and post-immunization were significantly greater in SCD >2 yrs than SCD <2 yrs ($.042 > p > .001$). In all, 17/24 SCD (71%) had a positive antibody response; 14/17 (82%) of them had a corresponding increase in opsonic activity. Thus, most but not all SCD who responded to PPS immunization had a concomitant increase in opsonic activity for type 7.

● **955** AMP^R PLASMID DNA INTEGRATED INTO THE CHROMOSOME OF HAEMOPHILUS INFLUENZAE (HI): CLINICAL AND EVOLUTIONARY IMPLICATIONS. M. Murphey-Corb, M.A. Willard, R.S. Daum, Dept. of Peds, Tulane U., New Orleans, Louisiana.

The majority of amp^R Hi clinical isolates are free of physically demonstrable extrachromosomal DNA. Properties of these "plasmid-free" (pf) strains include stability of the β-lactamase phenotype and conjugal transfer of amp resistance determinants to amp^S recipients at low frequency. Moreover, amp^R transconjugants obtained from such crosses uniformly contain plasmids. These observations suggest that plasmid DNA in pf strains may be physically integrated into the bacterial chromosome. To test this hypothesis, we utilized the transfer technique of Southern to visualize plasmid specific DNA sequences in the chromosome of pf amp^R Hi. Total cellular DNA from pf amp^R donor, amp^S recipient, and plasmid containing transconjugants was digested with SacI restriction endonuclease. The resulting fragments were fractionated by agarose gel electrophoresis and transferred to nitrocellulose where plasmid specific sequences were visualized by autoradiography after hybridization to ^{32}P labeled plasmid DNA. These results demonstrate conclusively that maintenance of plasmid sequences in pf strains occurs via integration into the host genome. The clinical significance of the recognition of 2 modes of R factor carriage in Hi is derived from known evolutionary advantages enjoyed by bacterial strains with genetic elements of this versatility. Extrachromosomal R factors in Hi are easily lost in the absence of antibiotic pressure but are readily transferred to other strains. Conversely, integration of R factors allows uniform stability of resistance determinants but inefficient dissemination in the species.

956 EFFECT OF ORAL ANTIBIOTICS ON THE OUTCOME OF SEROUS OTITIS MEDIA (SOM). Michael J. Corwin, Leonard B. Weiner, Daniel A. Daniels (Spon. by Frank A. Oski). SUNY Upstate Medical Center, Dept. of Pediatrics, Syracuse, N.Y.

SOM is a frequent residual of acute otitis media (AOM). This study was undertaken to determine the effect of oral antibiotics on the outcome of this residual SOM. The study was conducted in a private pediatric practice where pneumatic otoscopy and tympanometry were performed on all patients 30 days following the diagnosis of AOM. Patients were eligible for enrollment in the study if they were found to have SOM at this followup visit. Following enrollment, subjects were randomly assigned to either treatment with a combination of sulfisoxazole (150 mg/kg/day) and erythromycin ethylsuccinate (50 mg/kg/day) for 10 days or no treatment. Repeat pneumatic otoscopy and tympanometry was scheduled every 30 days for 4 months. Followup examiners were unaware of the initial treatment regimen. Seventy subjects (50% treated) have been enrolled with a mean age of 3.5 years (range 0.8-11 years). At the first followup visit SOM was resolved in 31 subjects (58% treated) and persistent in 20 (55% treated). Nineteen patients returned with AOM prior to the first followup visit. Only 32% of these 19 patients were in the treatment group. Followup of the 20 patients with persistent SOM at 30 days post enrollment revealed 9 patients (44% treated) with persistent SOM at 60 days, 5 patients (60% treated) at 90 days and only 2 patients (50% treated) at 120 days. These data support the view that oral antibiotics will not hasten the resolution of SOM but may reduce the recurrence of AOM.

957 PREVENTION OF GROUP B STREPTOCOCCAL (GBS) COLONIZATION IN NEWBORN MICE WITH TOPICALLY APPLIED LIPOTEICHOIC ACID (LTA). Frederick Cox (Spon. by Alex F. Robertson). Medical College of Georgia, Department of Pediatrics, Augusta, Georgia.

A mouse model of maternal-newborn (M-N) transmission of GBS colonization was developed. Pregnant Swiss-Webster mice were colonized daily for 3 days before delivery with approximately 10^8 type III GBS delivered to the vaginal canal, oral cavity and nipples. Cultures from the mouth, perineum and nape of newborn mice were obtained at birth in Todd-Hewitt broth containing naladixic acid and gentamicin. LTA (2 mg/ml), prepared from type III GBS, or phosphate buffered saline (PBS) was then applied topically to the 3 sites.

Repeat cultures at 3 days of age revealed 35/75 (47%) PBS treated mice and 0/79 LTA treated mice were colonized if 2 doses of LTA were applied. No obvious toxicity was noted.

In separate experiments, 0.5 mg/ml of LTA was protective in the M-N model and prevented colonization with 60,000 GBS in the oral cavity of newborn mice. LTA from type III organisms also protected against colonization with type I or II GBS.

This is the first in vivo evidence that colonization with GBS can be prevented by a substance known to interfere with their adherence to epithelial surfaces. This may be a useful method of prophylaxis against GBS infection in neonates if it is nontoxic.

958 VARIATION IN GROUP B STREPTOCOCCAL (GBS) ADHERENCE WITH GESTATIONAL AGE (GA). Frederick Cox (Spon. by Alex F. Robertson). Medical College of Georgia, Department of Pediatrics, Augusta, Georgia.

Adherence of GBS to buccal epithelial cells (BEC) was tested by mixing 10^8 GBS/ml and 10^5 BEC/ml under standard conditions and determining the mean number of GBS/cell. Testing was performed in 33 infants with different GA during the first 24 hours of life.

	Mean Number of GBS/BEC (No. Patients)							
GA	<32	35-32	36	37	38	39	40	41
	42(3)	40(2)	31(5)	23(3)	15(5)	11(5)	9(5)	8(5)
Range	40-46	38-41	29-35	21-24	12-18	10-14	8-10	6-9

Results revealed a curvilinear relationship between adherence and GA with a significant decrease in adherence with increasing GA. The polynomial regression model: adherence = $-44.3844 + 7.6767\,(GA) - 0.1582\,(GA^2)$ was found to predict 92% ($r = -.96$) of the variance in adherence. Background bacterial counts before addition of GBS were zero in all patients. In 5 healthy adult controls, 88 GBS adhered/cell. Pre-treatment of adult BEC with amniotic fluid from a normal term pregnancy for 72 hours reduced adherence to 80 GBS/cell.

This data suggests that an inhibitor to GBS adherence develops late in gestation. This may be a normal protective mechanism for the first few days of life in term infants. Increased adherence in premature infants may explain, in part, their higher incidence of GBS infection. This is the first report of GBS adherence in premature infants.

959 IN VIVO EFFECT OF BREAST MILK INHIBITION OF BACTERIAL ADHERENCE. Alice H. Cushing, University of New Mexico School of Medicine, Department of Pediatrics, Albuquerque.

Enterotoxigenic E. coli, in order to cause diarrhea, must also adhere to mucosal surfaces. In man, two of these adherence-mediating surface materials, called colonization factor antigens (CFA), have been defined. They may be presumptively identified by the organisms' ability to agglutinate red blood cells from different animal species in the presence of mannose. Antibodies to CFA and non-antibody adherence-inhibiting materials have been demonstrated in human breast milk in vitro but their efficacy in vivo has not been reported.

We compared episodes of diarrhea following fecal carriage of toxigenic-CFA+ bacteria in breast fed babies with the ability of their breast milk to inhibit CFA+ agglutination. Results were as follows:

	Inhibition	No inhibition
Diarrhea	0	3
No diarrhea	8	1

Results in this small number of subjects suggests that breast milk inhibition of bacterial adherence correlated with the babies' capacity to carry toxigenic-CFA+ organisms and not have diarrhea. Secretory antibody to toxin, on the other hand, showed no such association.

960 UNSUSPECTED MENINGOCOCCAL BACTEREMIA (UMB). Barry Dashefsky, David W. Teele, and Jerome O. Klein. Boston University School of Medicine, Boston City Hospital (BCH), Department of Pediatrics, Boston.

To determine the incidence and clinical course of UMB in children we reviewed charts of all 23 children at BCH with meningococcemia from Sept. 1971 to Dec. 1981. Of these, 13 (mean age = 18 mo., range = 2-70 mo.) were initially treated parenterally for sepsis (6), meningitis (4), pneumonia (2), and arthritis (1). Ten (mean age = 10.5 mo., range = 5-20 mo.) were considered well enough to be sent home.

Eight of these 10 received oral antibiotics for otitis media (6) or pneumonia (2). At recall, of these 8, 1 with a previously normal lumbar puncture (LP) and 1 without prior LP had meningitis, 4 were afebrile and without focus of infection, and 2 were still febrile with the same focus. Six were hospitalized and treated parenterally; 2 were continued on oral therapy as outpatients. All 8 recovered without further complications.

At first visit, 2 without focal infection were not treated. On recall, 1 was treated orally for otitis media; 1 was treated parenterally for meningococcemia. Both recovered uneventfully.

Meningococcemia has been considered an ominous event. These data show that UMB occurred in mildly to moderately ill children and accounted for 46% of cases of meningococcemia. Like unsuspected bacteremia due to Streptococcus pneumoniae and Haemophilus influenzae, the outcome of UMB in children initially untreated or treated with oral antibiotics varied but included development of meningitis (20%).

961 PATHOGENIC EFFICIENCY OF PLASMID CONTAINING (R^+), AMPICILLIN RESISTANT (AMP^R) H. INFLUENZAE TYPE B (HIB) R S Daum, M Zutter, E J Johnson and J E Willard. Dept. of Pediatrics, Tulane University, New Orleans, LA.

Genes that code for ampicillin resistance in Hib are carried on extrachromosomal plasmids in 10/37 (27%) of strains. To assess the possibility that R^+, amp^R strains of Hib are at a selective disadvantage relative to genetically related amp^S strains, we used the infant rat model to study infection in 277 pups inoculated with one of four strains. Strains studied included Eagan (R^-, amp^S), A/Eagan (R^+, amp^R) - a laboratory derived transconjugant containing plasmid DNA encoding for amp^R, C_{306}(R^+, amp^R)- a clinical isolate and C_{306}(R^-, amp^S)- a blood isolate from an animal inoculated with C_{306}(R^+, amp^R). Major outer membrane proteins were analyzed by SDS-polyacrylamide gel electrophoresis and were identical between pair strains. R^+ and R^- strains readily colonized the nasopharynx. The incidence of bacteremia was greater in R^- inoculated animals but this difference was not significant. However, the geometric mean number of bacteria in blood was significantly ($p<.05$) less in R^+ inoculated animals as was the incidence of meningitis ($p<.03$). β-lactamase elaboration by R^+ strains was unstable and associated with loss of detectable plasmid DNA at variable frequency. We conclude that in the infant rat model, strains of Hib containing 30 Md amp^R plasmids are at a subtle selective disadvantage relative to genetically related, plasmid free strains and that such R^+ amp^R strains are less efficient pathogens.

● **962** CYTOMEGALOVIRUS (CMV) IN BREAST MILK AND TRANSMISSION TO THE INFANT. M. Dworsky, M. Yow, S. Stagno, R. Pass, C. Alford. University of Alabama in Birmingham, Department of Pediatrics, Birmingham, Alabama.

We assessed the relative importance of maternal excretion of CMV in milk and other sites for transmission in 47 breast feeding mother-infant pairs. The 13 seronegative women, (mean follow-up 10 months, age 23 years, months breast feeding 4.0) did not excrete virus at any time and none of their infants acquired CMV. In contrast, 12 infants born to 34 seropositive women (mean follow-up 9.5 months, age 25 years, months breast feeding 3.2) acquired CMV between 1 and 6 months ($p=0.01$). None of the eleven infants who nursed less than 1 month became infected. Twelve of 23 infants who nursed longer than 1 month did so ($p=0.002$), indicating that increased duration of breast feeding increases the likelihood of infant acquisition. Eleven (31%) women shed CMV into their milk, 4 (11%) into their vaginal tract, 3 (9%) into their urine and 1 (3%) into saliva. Shedding at each maternal site (mean number of cultures per woman for milk 2.8, vagina 4.6, throat 4.7, urine 4.4) was intermittent. Nine of 11 (82%) infants born to mothers who excreted CMV into breast milk became infected. Only 3 infants (13%) became infected who were born to the 23 mothers who excreted CMV from other sites or in whom CMV was not demonstrated. Clearly seropositive women who excrete CMV into their milk are more prone to infect their infants ($p\leq0.001$) and this appears to be the most common source of CMV for breast fed infants. Protracted pneumonitis of moderate severity associated with the onset of viruria in 2 infants co-infected with C. trachomatis has been the only adverse sequelae in the brief follow-up period.

● **963** DEFICIENT CLASSICAL PATHWAY (CP)-MEDIATED OPSONOPHAGOCYTOSIS (OP) OF TYPE Ia GROUP B STREPTOCOCCI (GBS) IN NEONATAL SERA. Morven S. Edwards, Gregory J. Buffone, and Carol J. Baker. Baylor College of Medicine, Departments of Pediatrics and Pathology, Houston.

We have shown previously that OP activity of adult sera for fresh clinical Ia GBS isolates is mediated by the CP in a non-antibody dependent fashion. The present study was designed to determine the influence of opsonins other than type-specific antibody (TSA) which might be critical for efficient OP of Ia GBS by neonates. Sera collected to preserve endogenous complement were obtained from 20 term neonates <72 hrs. old and their mothers. OP activity for a clinical Ia GBS strain (515) was determined in an assay requiring human leukocytes, serum and $3x10^6$ Ia GBS. Significant OP (bactericidal index [BI] ≥75% was observed in 12 neonatal sera (mean 91%, range 75-98%), while 8 had deficient OP (mean 19%, range 0-37%). Chelation of high BI sera with MgEGTA inhibited CP-mediated OP. OP was not influenced by TSA level (median 2.1μg/ml, both groups). However, the mean CH_{50} for high BI sera (300 IU/ml) was significantly greater than that for low BI sera (mean 227, range 195-278) ($p<.001$). Mean CH_{50} values for maternal sera of high vs. low BI neonates were similar (493 vs. 481, respectively). Low BI neonates had lower mean titers of each complement component assessed (C1,C4,C2,C3 hemolytic titers; C1q,C4, C3, B, C3bINA immunodiffusion titers) than high BI neonates. C1q immunodiffusion and C4 hemolytic titers were significantly lower for low BI sera than representative high BI sera ($p<.05$). These results suggest that inadequate functional levels of one or more CP components could be a critical factor predisposing certain neonates to invasive type Ia GBS infection.

964 DEFECTIVE PHAGOCYTIC CELL FUNCTION IN TWO INFANTS WITH SEVERE GRAM-NEGATIVE ABSCESS DISEASE. Greg R. Elliott, Jon S. Abramson, Warren E. Regelmann, Henri Verbrugh, Paul G. Quie, Univ. of Minnesota, Dept. of Pediatrics, Minneapolis.

Two infants developed life-threatening polymicrobial gram-negative abscess disease during the first year of life. Both infants had perianal abscesses and responded with leukemoid reactions (WBC ≥ 70,000). One infant was the product of a consanguineous relationship; neither had family history of recurrent infections. Both infants had normal immunoglobulins and complement levels, and one infant had moderately depressed lymphocytic proliferation to mitogens. These infants showed a marked delay in polymorphonuclear leukocyte (PMN) chemiluminescence (CL) response to opsonized zymosan and one had a depressed PMN CL response, as well. Monocyte (MNC) CL to opsonized zymosan was depressed and delayed in each infant. In contrast, phorbol myristate acetate (PMA), a soluble stimulator, elicited normal PMN and MNC CL responses in each infant. PMN phagocytosis of E. coli was severely depressed in both infants as was their bactericidal capacity for this organism. Their PMN staining for myeloperoxidase and leukocyte alkaline phosphatase was normal. Each infant had depressed PMN chemotaxis to zymosan activated serum, but PMN ultrastructure and adherence was normal in the one infant studied.

The abnormal CL response to zymosan with normal response to PMA associated with abnormal chemotaxis and phagocytosis suggest a phagocytic cell membrane or receptor defect resulting in depressed killing of gram-negative bacteria. Severe gram-negative abscess disease in infants may be clinical evidence of phagocytic cell dysfunction.

965 THE ROLE OF CYTOMEGALOVIRUS (CMV)-SPECIFIC CELLULAR IMMUNITY IN GENITOURINARY CMV INFECTIONS OF ADOLESCENT WOMEN. Roger G. Faix, Sherrie E. Zweig, John F. Kummer, Donald Moore, David J. Lang (Spon. by R. P. Kelch), Duke University Med. Ctr., Durham, N.C.

Since genitourinary CMV infection occurs despite the presence of specific antibody, a role for CMV-specific cellular immunity in control of infection has been postulated. We studied 92 healthy sexually active nonpregnant adolescent women with CMV cultures (cervix, urine, saliva, leukocytes), complement-fixing (CF) CMV antibodies, general measures of cellular immunity and CMV-specific lymphocyte blastogenesis. 20 women were culture- and seropositive (V+), 39 were culture negative but seropositive (S+) and 33 were culture- and seronegative (S-). There were no significant differences among the 3 groups for E-rosettes or mitogen stimulation. There was no significant difference in frequency of CMV-specific lymphocyte reactivity (stimulation index >3.0 and net cpm >10,000) between V+ (12/20) and S+ (28/39) though both were significantly more often reactive than S- (3/33) ($p<.001$). Mean values for SI/net cpm were V+: 7.02±0.76/16547±2702; S+: 7.79±0.72/16789±3387; S-: 3.20±0.64/4854±948. There was no significant difference between V+ and S+ though both were significantly greater than S- ($p<.001$). Lack of viral contact with systemic immunocytes does not seem responsible for the lack of difference in systemic cellular immunity between V+ and S+ since the geometric mean CF titer of V+ (74.0±16.9) was significantly greater ($p<.02$) than that of S+ (37.3±6.4). We could not demonstrate that systemic CMV-specific cellular immunity is an important factor in genitourinary CMV infections.

966 CYTOMEGALOVIRUS (CMV)-SPECIFIC LYMPHOCYTE BLASTOGENESIS IN UNINFECTED NEWBORNS. Roger G. Faix, John F. Kummer, Sherrie E. Zweig, Donald Moore, David J. Lang (Spon. by R.P. Kelch), Duke University Med. Ctr., Dept. of Pediatrics, Durham, N.C.

Most infants born to CMV-shedding women are not congenitally infected. It is unknown if such uninfected infants are exposed to CMV in utero. We studied infants of 59 adolescent women followed through pregnancy with CMV cultures (cervix, urine, saliva, leukocytes), complement-fixing (CF) CMV antibodies, CMV-specific lymphocyte blastogenesis and general measures of cellular immunity. 16 mothers shed virus while pregnant (V+), 29 were virus negative but seropositive (S+) and 14 were virus and seronegative (S-). Infants were studied with CMV cultures (cord blood, urine), cord CF-CMV antibodies, CMV-specific cord lymphocyte blastogenesis and general measures of cellular immunity. No significant differences were found among infants of the 3 groups for E-rosette number or mitogen stimulation. Geometric mean CF-CMV titer for infants of V+ (121.0±34.5) was significantly greater ($p<.001$) than for infants of S+ (32.3±6.0). The one congenitally infected infant (mother V+) had CMV-reactive lymphocytes (stimulation index>3.0 and net cpm>10,000). 7 of the 15 uninfected infants of V+ had CMV-reactive lymphocytes, as did 7 of 29 infants of S+ and 0 of 14 infants of S-. Since 5 of 14 mothers whose uninfected infants had CMV-reactive lymphocytes lacked reactive lymphocytes themselves at delivery, passive transfer of reactivity at delivery is unlikely. Some S+ mothers may have shed CMV at times not studied. We suggest that CMV-reactive cord lymphocytes in uninfected infants may reflect intrauterine CMV contact.

967 CYTOMEGALOVIRUS (CMV)-SPECIFIC CELLULAR IMMUNITY DURING PREGNANCY IN ADOLESCENTS. Roger G. Faix, Sherrie E. Zweig, John F. Kummer, Donald T. Moore, David J. Lang (Spon. by R.P. Kelch), Duke University Med. Ctr., Dept. of Pediatrics, Durham, N.C.

Since preexisting CMV antibodies do not prevent CMV shedding in pregnancy, a role for cellular immunity in determination of viral excretion has been postulated. We studied 59 pregnant adolescent women prospectively with CMV cultures (cervix, urine, saliva and leukocytes), complement-fixing CMV antibodies, general measures of cellular immunity and CMV-specific lymphocyte blastogenesis. These studies were performed a mean of 3.95 times through delivery for each subject. Results were analyzed for these gestational times: <20wks, 20-30wks, 30-40wks, delivery, postpartum. 16 women were virus-positive during pregnancy (V+), 29 were virus-negative but seropositive (S+) and 14 were virus and seronegative (S-). No seroconversions occurred. No abnormalities in mitogen stimulation or E-rosette number were noted. There was no significant difference between V+ and S+ overall or at any gestational time for frequency of CMV-specific lymphocyte reactivity (stimulation index>3.0 and net cpm>10,000). There were downward trends for mean net cpm through gestation for both V+ and S+ though they failed to reach significance. Mean SI and mean net cpm for V+ and S+ were greater than for S- throughout; this was significant at all times except for V+ net cpm at 20-30wks and postpartum. No significant differences were noted between V+ and S+. One mother (V+) had a congenitally infected newborn. We suggest that maternal viral shedding during pregnancy may not be related to systemic CMV-specific cellular immunity.

968 EPSTEIN BARR VIRUS (EBV) INFECTIONS DURING PREGNANCY. Gary Fleisher. University of Pennsylvania School of Medicine, Children's Hospital of Philadelphia, Department of Pediatrics, Phildelaphia, PA.

A prospective study of EBV infection in pregnant females was undertaken with 3 objectives: 1) To define the current epidemiology of EBV in this population and compare it with data collected previously 2) to test for serological evidence of reactivation of the latent, persistent carrier state and 3) to assess the effect of infection on the fetus. We measured antibodies from early and mid (20% of the women) pregnancy and cord sera to viral capsid antigen (VCA), early antigen (EA), and EB nuclear antigen (EBNA) using immunofluorescent assays. Thus far, 2000 women have been tested: 1386 in a clinic group (CG) and 614 in a private practice group (PG). Among the 1386 women in the CG, there were 8 (0.6%) seronegative [≤20 yrs, 5/650 (0.8%); 21-30 yrs, 3/648 (0.5%); and ≥31 yrs, 0/88 (0%)]; 18 (2.9%) of the women in the PG were seronegative [≤20, 2/42 (4.8%); 21-30 yrs, 12/388 (3.0%), and ≥31 yrs, 4/184 (2.3%)]. By comparison, 17 (9%) of 185 pregnant women bled in 1959-1965 were seronegative ($p<0.01$). Titrations of 200 complete sets of sera have shown only occasional evidence of reactivation. Two infants born to women with asymptomatic primary seroconversions were normal and showed declining antibody titers in follow-up (Table). An additional woman with first trimester infectious mononucleosis, caused by EBV, is under observation.

	1st Trimester				Cord				Infant 3-5mos			
No.	M-VCA	G-VCA	EA	EBNA	M-VCA	G-VCA	EA	EBNA	M-VCA	G-VCA	EA	EBNA
1	<10	<10	<10	<2	<10	320	40R	40	<10	40	<10	5
2	<10	<10	<10	<2	<10	320	160R	5	<10	20	<10	2

969 LIVE ATTENUATED CYTOMEGALOVIRUS (CMV) VACCINE: FURTHER STUDIES. Gary Fleisher, Stuart Starr, Stanley Plotkin, University of Pennsylvania School of Medicine, Children's Hospital of Phila., Dept. of Pediatrics, Phila., PA.

Further studies have been performed with live attenuated Towne strain CMV vaccine to determine: (1) the response to various dilutions (dil) and (2) the persistence of immunity beyond 1 yr and in vaccinees who become pregnant. (1) Volunteers (vol) who received 1:2, 1:5, and 1:10 dilutions of vaccine ($10^{3.5}$pfu undiluted) were tested for complement fixing (CF) and anticomplement immunofluorescent (ACIF) antibodies to CMV and for specific lymphocyte proliferation (LP). Peak antibody responses (Table) and the magnitude of the local reaction were compared with those seen in women previously receiving undiluted vaccine. All vaccinees developed an LP response which was of similar magnitude regardless of the vaccine dose. There was some diminution in the local reaction at dilution of 1:10. (2) 5 vol, followed for 19-28 mos after receiving undiluted vaccine, had detectable antibodies by ACIF (GMT 16) and all 4 tested had a LP response (mean 4117 cpm). 3 vol have become pregnant 6, 8, and 12 mos after vaccination and have maintained detectable responses by the CF, ACIF, and LP assays 4 to 8 mos into gestation. Dilutions (1:10, 1:5, 1:2) of CMV vaccine were immunogenic but had decreased potency for the development of humoral immunity. Following immunization with Towne strain vaccine, immunity appears to persist for more than 2 yrs and remains through gestation.

No	Dil	CF:No.pos.(GMT)	ACIF:No.pos.(GMT)
4	1:10	4(16)	4(23)
6	1:5	5(32)	6(36)
2	1:2	2(16)	2(64)
10	1:1	10(39)	10(97)

970 TRIMETHOPRIM-SULPHAMETHOXAZOLE (TMP-SMX) PROPHYLAXIS IN NINE PATIENTS WITH CHRONIC GRANULOMATOUS DISEASE (CGD). H. Frayha, R. Gold, C.G. Prober and W.D. Biggar. Division of Infectious Diseases, The Hospital for Sick Children, University of Toronto, Canada.

CGD is a genetic disorder of bacterial killing by blood neutrophils (PMN). Patients usually present in the first 2 yrs of life with severe, chronic and recurrent bacterial infections. Approximately one third of reported patients die of infection before 7 yrs of age. Because of their susceptibility to infection we give all CGD patients TMP-SMX prophylaxis (2mg TMP/kgm/day) once daily. Our experience since 1972 includes 9 male patients given TMP-SMX for a mean of 5.6 yrs with a total patient experience of 51 patient yrs. Their mean age is 15 yrs (range 4-22). The diagnosis was established in each case by the failure of PMN to reduce nitroblue tetrazolium dye and to kill Staphylococcus aureus normally in vitro. Five of 9 patients have been free of infection during 15 yrs of observation. Of the 4 remaining patients, there have been 6 infections over 35 yrs of observation. One patient, followed for 6 yrs, had a dental abscess. One patient, followed for 10 yrs, had a perianal abscess and has occasional skin pustules. One patient, followed for 10 yrs, had a perianal abscess and a liver abscess. The ninth patient, followed for 9 yrs, had one episode of a paronychia, a skin abscess and died following an 8-month illness characterized by fever, an elevated ESR and weight loss without demonstrating any focus of infection. We have not observed any side effects of TMP-SMX prophylaxis. Compared to published reports, our patients appear to have fewer infections while taking TMP-SMX and have a better prognosis.

971 VIRAL SPECIFIC CELL MEDIATED IMMUNITY, SUPPRESSOR CELLS, PREGNANCY, AND HEALTH CARE WORKERS. Lawrence D. Frenkel, Ruth E. Alteneder, Deanna F. Cedargren, Tina R. Petok. Medical College of Ohio, Department of Pediatrics, Toledo.

Female health care workers are a largely middle class, young (median age 26 yrs.), and fertile group (average gravidity 2.4); many (48%) are cytomegalovirus (CMV) seronegative. Although primary acquisition of CMV infection during pregnancy has been accepted as the main contributor to congenital affliction, the role of reactivation of maternal CMV in congenital infection has not been completely elucidated. Health care workers, especially those caring for neonates, are thought to be at high risk for exposure to CMV. One hundred and fifty pregnant and nonpregnant women with direct patient contact (DPC) and without (NDPC) were matched for age, gravidity, parity, number of sexual partners, and age at initial sexual activity. These individuals were followed for up to 3 years and evaluated for CMV and HSV specific humoral and cell mediated immunity (CMI), cervical and urine viral excretion, and suppresion of CMI by serum and cellular factors. No significant differences were noted between DPC and NDPC groups in terms of viral excretion, CMV or HSV seroconversion, or CMV or HSV geometric mean titers. Pregnant women demonstrated significant suppression of specific cell mediated immunity to CMV and HSV in all trimesters, particularly the third. This specific suppression is not related to serum factors but does seem to be related to a suppressor cell subpopulation.

● **972** VARICELLA VACCINE: USE IN CHILDREN WITH LEUKEMIA. Anne Gershon, Sharon Steinberg, William Borkowsky, & NIH Collab. Study Gp. Dept. Pediatrics, NYU Med. Ctr., NY, NY.

Natural varicella may be severe or fatal in children with leukemia. We therefore immunized 63 children with leukemia in remission with 1000 pfu of live attenuated varicella (Oka) vaccine, to induce primary immunity to varicella-zoster (VZ) virus. Twenty-seven of these children had received no chemotherapy for 1-12 months (mean 6) prior to vaccination. Maintenance chemotherapy was suspended for 2 weeks in 36 vaccinees. All tested seroconverted and developed cellular immunity (CMI) to VZ virus in 3-8 weeks.

In children whose chemotherapy was finished the VZ fluorescent antibody to membrane antigen (FAMA) geometric mean titer (GMT) 8 weeks after immunization was 1:11; 3% had mild rash. In children with chemotherapy suspended the VZ-FAMA-GMT 8 weeks after vaccination was 1:8; the incidence of mild to moderate rash was 54%. Rashes appeared 7-54 days (mean 28) after vaccination. VZ virus was isolated from a rash in 1 child. The VZ-FAMA-GMT of children with rash was higher than in those without rash. There was no spread of varicella to susceptible siblings or other virus shedding. Four vaccinees with household exposures to VZ virus did not become ill. These preliminary data confirm that VZ vaccine is safe for leukemic children in remission and that vaccine induces antibody and CMI to VZ virus.

973 PENICILLIN (PEN) EFFECT ON NEONATAL FLORA. K. Ghaey, M. Tolpin, K. Nelson, B. Kontelas, N. McMahon, C. Chakinis, V. Schauf; Depts. of Pediatrics and Preventive Medicine, Univ. of Ill.; Chicago.

PEN is effective in preventing ophthalmia neonatorum and in reducing group B streptococcal (GBS) infection in term infants. Prophylactic PEN also reduces neonatal GBS colonization. However, PEN's impact on the development of the infant's other flora is unknown. We characterized the mucocutaneous and gastrointestinal flora of 51 infants in a randomized, double-blind study of placebo vs prophylactic aqueous PEN G (100,000 U) IM at delivery. At birth (ADM) and discharge (DIS) cultures were obtained from ear canal, nasopharynx, umbilicus and rectum. There were no differences in colonization between the 2 groups, by the organisms shown in the table:

	PEN (25 INFANTS)		PLACEBO (26 INFANTS)	
No. Isolates	ADM	DIS	ADM	DIS
Enterobacteriaceae	27	42	27	40
Streptococci				
α-non Group D	7	25	3	22
Group D enterococci	3	8	9	7
Group D non-enterococci	0	0	0	4
S. epidermidis	16	46	20	54
S. aureus	5	8	8	3
Hemophilus species	2	8	4	10
Anaerobes	20	18	19	23

Widespread PEN prophylaxis may be feasible since it reduces GBS colonization without significantly altering the infant's other flora.

974 RELATIONSHIP OF NASOPHARYNGEAL (NP) COLONIZATION WITH H. INFLUENZAE, TYPE b, (Hib) TO PROTECTION AGAINST SYSTEMIC BACTEREMIA IN RATS. Janet R. Gilsdorf and Patricia Ferrieri, Univ. of Minnesota Medical School, Dept. of Pediatrics, Minneapolis, MN.

The relationship between asymptomatic np carriage of Hib and protection against invasive Hib disease is unknown. The role of Hib np colonization, with and without bacteremia, in protecting against systemic Hib bacteremia was investigated in rats. Rats, intranasally colonized at age 10 days with 2-5 x 10^6 cfu Hib, were challenged at age 112 to 120 days with 6-26 x 10^6 cfu Hib intraperitoneally (ip). Among 31 rats who became bacteremic during np colonization (C-B), 1(3.2%) was bacteremic upon ip challenge. Among 14 colonized but nonbacteremic (C-NB) rats, 12 (85.7%) were bacteremic after challenge. Of 14 noncolonized and nonbacteremic (NC-NB) control rats, 10 (71.4%) were bacteremic after challenge. There was no difference in duration of bacteremia nor in peak bacteremic levels post-challenge between C-NB and NC-NB rats ($p > 0.05$, rank sum test). Among C-NB rats, rates of bacteremia after ip challenge were identical (85.7%) in both heavily and lightly colonized animals. Likewise, in C-NB rats there was no correlation between either duration ($r = -0.224$) or degree ($r = -0.41$) of bacteremia after challenge, and duration of earlier np carriage (range = 2 to 28 days) of Hib.

Thus, Hib np colonization of infant rats without systemic bacteremia did not appear to protect these animals against subsequent ip bacterial challenge. However, other protective mechanisms may be evoked by np colonization.

975 NOSOCOMIAL INFECTION AND DEATH IN A NEONATAL INTENSIVE CARE UNIT. Donald A. Goldmann, Jonathan Freeman, and William A. Durbin (Spon. by Kenneth McIntosh), Harvard Medical School, Children's Hospital Medical Center, Dept. of Medicine, and Channing Laboratory, Boston.

Based on 5 years of prospective surveillance in a neonatal intensive care unit (NICU), we investigated the association of nosocomial infection (NI) with death during hospitalization for 911 infants who remained in the NICU for ≥ 48 hours. Low birthweight and the diagnosis of patent ductus arteriosis (PDA) were the variables most strongly associated with NI, and after stratification for these variables there was a persistent ($p=0.03$) overall effect of NI on mortality. The presence of PDA significantly ($p=0.02$) modified the effect of NI on mortality. In infants without PDA there was a substantial effect of NI on mortality ($\hat{RR}$ = 3.42, 95% confidence interval 1.68-6.95), whereas there was no effect in infants with PDA. Relocation of the NICU to a facility with improved infection control features and a 50% increase in staff was associated with a dramatic fall in the adjusted NI rate ($\hat{RR}$, old NICU/new NICU = 9.73, 95% confidence interval 4.30-22.0). This was accompanied by a slight, not statistically significant decline in the adjusted mortality rate ($\hat{RR}$, old NICU/new NICU = 1.03, 95% confidence interval 0.68-1.58). Although infection control programs may have a substantial impact on the endemic risk of NI and its attendant morbidity, the number of lives saved in intensive care settings such as ours may be small.

● **976** ZOSTER IN CHILDREN WITH CANCER: IMMUNOPRECIPITATION PROFILES. Charles Grose, Univ. Texas Hlth. Sci. Ctr., Depts. of Pediatrics and Microbiology, San Antonio.

Twenty children with cancer who developed zoster were enrolled in a long-term study of their humoral response to varicella-zoster virus (VZV) antigens. The immunoprecipitation profiles of acute zoster sera were easily distinguished and very similar to those of high titer VZV xenoantisera; they contained a mean of 16 polypeptides, which ranged in mol. wt. from 32 to >>200 kilodaltons (kd) and included the major VZV capsid polypeptide (155 kd), three major glycoproteins (118, 98 and 62 kd), actin (45 kd) and a low mol. wt. polypeptide. In comparison with post-zoster sera, pre-zoster sera were selectively deficient in precipitating two higher mol. wt. polypeptides (145 kd and 174 kd), one smaller polypeptide (32 kd), and all 3 major VZV glycoproteins. Longitudinal analyses detected elevated human antibodies to VZV-specific glycoprotein antigens up to one year after zoster, while the humoral response as measured against non-glycosylated determinants fell within a few months. Occasional reappearance of the characteristic "zoster profile" in sera drawn during late convalescence presumably represented subclinical VZV reactivation. In summary, radioimmune precipitation is a sensitive technique by which to characterize the humoral immune response to individual VZV-specific polypeptides.

977 TREATMENT OF INFANTS OF HEPATITIS B SURFACE ANTIGEN (HB_sAg) POSITIVE MOTHERS WITH HEPATITIS B IMMUNE GLOBULIN (HBIG). Madhu B. Gudavalli and Catherine M.P. Kierney. (Sponsored by Robert G. Schacht.) New York University School of Medicine, New York Infirmary-Beekman Downtown Hospital, Department of Pediatrics, New York.

59 infants born to pregnant women of Chinese extraction known to be HB_sAg positive, were screened at birth and found to be HB_sAg negative. They received 0.5-1 ml HBIG within 48 hours of birth and 53 (90%) received a dose at 3 months of age. 57 (97%) were followed for a mean of 7.2 months (range 1-14) and 4 (7%) were found to be HB_sAg positive at a mean age of 4.5 months, representing 17% of infants of the 'e' antigen positive mothers, a significantly lower incidence of positivity than 85% reported for untreated infants. 3 of the 4 infants had normal LFTs while the fourth had both clinical and biochemical evidence of hepatitis. Thus HBIG decreases, but does not abolish, the incidence of chronic carrier state in infants of HB_sAg positive mothers, further study using Hepatitis B vaccine is being carried out.

● **978** THE ROLE OF PILI IN H. INFLUENZAE ADHERENCE TO PHARYNGEAL CELLS. Nicholas G. Guerina, Solomon Langermann, Herbert W. Clegg, T. Woodrow Kessler and Donald A. Goldmann (Spon. by Kenneth McIntosh), Harvard Medical School, Children's Hospital Medical Center, Dept. of Medicine, Boston.

We have discovered pili on isolates of H. influenzae and found that strains possessing these filamentous surface antigens adhere strongly to isolated human pharyngeal cells. In vitro adherence assays were conducted using a pair of H. influenzae type B isolates cultured from the CSF and pharynx of the same patient. Both isolates were found to possess the same outer membrane proteins but the pharyngeal isolate strongly hemagglutinated (HA) human O RBCs whereas the CSF isolate did not. Electronmicroscopy (EM) revealed the presence of pili only on the surface of the pharyngeal isolate. Representative values for the adherence of these strains to isolated human pharyngeal cells are presented below.

Strain	Culture site	HA	Piliation	Bacteria/cell (mean±SD)
AO1	CSF	-	no	4 ± 10
AO2	pharynx	+++	yes	161 ± 91

A strongly HA nontypable isolate also adhered well to pharyngeal cells (mean adherent bacteria/epithelial cell 189±95).

We have examined additional clinical isolates to determine the prevalence of pili. Under routine culture conditions the proportion of cells in the piliated phase was below the limits of detection by HA or EM, but piliated subpopulations were isolated from 9 of 11 strains tested by selective absorption to human O RBCs. These results suggest that most, if not all, strains of H. influenzae are capable of expressing pili which may be important in colonization and infection.

● **979** REINFECTION AND DURATION OF IMMUNITY TO RESPIRATORY SYNCYTIAL VIRUS (RSV). Caroline B.Hall, R. Gordon Douglas, Jr. University of Rochester Medical Center, Department of Pediatrics, Rochester, New York

To determine the duration of immunity to RSV and factors associated with reinfection, 15 young healthy adults with natural RSV infection were subsequently followed for over 2 years and challenged with RSV (NIH safety-tested pool) at increasing intervals (=2,4,8,14,20,26 months from time of natural infection). Thirteen (87%) became reinfected within 20 months, 12 (80%) within 8 months. Two (13%) remained immune. Of 13 reinfected, 7 (54%) acquired a third infection after mean interval of 18 months (range 12-24 months). Initial natural infections tended to be more severe than challenge reinfection, with third infections mildest. Asymptomatic infections occurred in 0/15 initial, 3/13 second, and 4/7 third infections. The titer and duration of RSV shedding diminished from second to third infections. The level of nasal or serum antibody did not correlate with the risk of infection. Serum antibody rose 4-fold (by ELISA, Neut or CF) in 55% of infections. Mean nasal antibody titer tended to increase with infection or sometimes with inoculation without other evidence of infection. These findings suggest that immunity to RSV after natural infection is often of short duration, or that important antigenic differences exist among RSV strains. But after ≥ two infections, immunity lengthens and infections become less symptomatic, along with diminished viral shedding. Successful immunization may thus require 2 or more inoculations and may provide protection only for a limited time, hopefully of sufficient duration to provide immunity for the period of greatest risk for an infant.

980 COAGULASE NEGATIVE STAPHYLOCOCCAL BACTEREMIA IN THE CRITICALLY ILL NEONATE. Susan E. Hall, Stephen Baumgart, Joseph M. Campos, Richard A. Polin. Dept. of Peds., Univ. of Pa. Sch. of Med., and Children's Hospital of Philadelphia, Philadelphia, PA.

Coagulase negative staphylococci (CNS) can be responsible for life-threatening infections in the critically ill neonate. During 1978, 416 infants were admitted to the ICN. Fifty (12%) had blood cultures reported positive for CNS. Fourteen cultures (13 infants birthweight 1.91 ± 1.13 SD kg; gestational age 33.6 ± 5.6 wks) were identified as true episodes of CNS bacteremia defined as pure growth of CNS in both bottles of one or more blood cultures exhibiting identical antibiotic sensitivities. Mean age onset CNS bacteremia was 49 days, range 2-253. At the time of diagnosis, 4 infants had been mechanically ventilated for 17 ± 11 days. Similarly, 7 infants had central venous and/or arterial catheters in place prior to CNS bacteremia onset (duration umbilical arterial catheter 13 ± 3 days, central jugular venous catheter 13 ± 6 days). All infants had 1 or more clinical signs of sepsis. At the time of positive culture, 11/14 infants (79%) had an abnormal WBC (Manroe et al, J. Peds., 1979). After blood culture and sensitivity results were reported, infants were treated with a semi-synthetic penicillinase-resistant penicillin, cephalosporin, or chloramphenicol. Nine organisms (65%) were resistant to semi-synthetic penicillinase-resistant penicillins whereas all were sensitive to cephalosporins and vancomycin. Two infants died (15%). In conclusion: (1) critically ill neonates are susceptible to CNS bacteremia with significant mortality, (2) CNS bacteremia is a late onset, nosocomial event frequently associated with indwelling catheters, (3) cephalosporins or vancomycin may be preferred antibiotics in treatment of CNS bacteremia when organisms are resistant to penicillinase-resistant penicillins.

981 IMIDAZOLE THERAPY OF COCCIDIOIDAL MENINGITIS IN CHILDREN. H. Robert Harrison, E. Russell Alexander, Allan D. Friedman, John N. Galgiani. Arizona Health Sciences Ctr. and V.A.M.C., Depts. of Pediatrics and Medicine, Tucson.

Coccidioidal meningitis (CM) is an often fatal form of infection due to Coccidioides immitis. Standard therapy with systemic and intrathecal amphotericin B (AMB) has limited efficacy and major toxicity. We are now treating 5 children with CM, aged 2 - 6 1/2 yrs., with intraventricular miconazole and oral ketoconazole (MCZ/KTC). All presented with hydrocephalus at 19-62 mos. of age. Two had fungi isolated from ventricular and lumbar fluid. All patients had ventriculoperitoneal (VP) shunts placed for hydrocephalus and local therapy. The four with noncommunicating hydrocephalus had cisternal Ommaya reservoirs placed, but all became non-functional within 6 months.

Three were first treated with intraventricular, intracisternal, and intravenous AMB and switched to MCZ/KTC, two when cisternal access was lost, and the third for drug toxicity and persistently positive ventricular fungal cultures. Two received MCZ/KTC from the first. All are now on intraventricular MCZ via VP shunt 1-2 times/week, 3-5mg/instillation, and oral KTC 15-22 mg/Kg/D. After 8-22 mos. of MCZ/KTC therapy all are well with normal ventricular fluid and negative fungal cultures. Serum CF titers have decreased 4, 8, 16, and 16-fold in 4 patients and are stable in one. Ventricular titers have dropped from 4-16 fold and are now negative in 4 of 5. In no patient has toxicity limited therapy.

MCZ/KTC may be an effective and less toxic therapy for CM than amphotericin B and may be most useful when local drug instillation is difficult.

982 SELECTION OF TEMPERATURE-SENSITIVE MUTANTS IN PERSISTENT INFECTION BY PARAINFLUENZA VIRUS TYPE 3. David S. Hodes. Columbia University College of Physicians and Surgeons, The Babies Hospital, Department of Pediatrics, New York, N.Y. 10032.

Because of evidence indicating that the epidemiology of parainfluenza virus type 3 (para 3) may be influenced by persistent infection (PI) of individuals, we have developed an in vitro model of para 3 PI in Vero cells. Previous work had indicated that the mechanism of initiation of PI in this system involved the production of a soluble virus gene product that prevented the development of viral cytopathic effects. This product could not be implicated, however, in the maintenance of PI since it was undetectable after a few passages. We therefore sought to determine whether the mechanism of maintenance involved the selection of temperature-sensitive (ts) mutants, a factor implicated in several other systems of PI. Clones were isolated from the virus population that initiated the PI and from the virus population being shed into the supernatant fluid after 6 months of PI. The former population contained no ts mutant clones whereas 25 of 26 clones isolated from the latter showed a yield ratio $39^{\circ}C/35^{\circ}C$ of 10^{-1} or less. The ts mutants tended to be unstable with 12 clones reverting to a ts^{+} phenotype and 2 more showing a significant increase in $39^{\circ}C/35^{\circ}C$ yield ratios after 2 passages at $35^{\circ}C$. Complementation studies on the stable clones indicated that thye all shared a common lesion. The maintenance of our para 3 PI thus appears to involve the selection of ts mutants of a specific sort, but that the lesion may be readily reversible.

● **983** MODE OF ACQUISITION FOR DE NOVO PNEUMOCYSTIS CARINII INFECTION. Walter T. Hughes, St. Jude Children's Research Hospital, Division of Infectious Diseases, Memphis.

P. carinii pneumonitis is believed to occur in the immunocompromised host from reactivation of a latent infection. The mode of acquisition for the primary infection is unknown. Axenic rats maintained in germfree isolators were found to be free of *P. carinii* after three months of immunosuppression with dexamethasone. This *P. carinii*-free rat model was used to identify the mode of acquisition of *P. carinii* from the natural environment. The germfree rats were exposed in a selective manner to potential sources of *P. carinii*, including air, water and food. Animals exposed in the isolator with filtered (sterile) air and to regular (unsterile) water and food did not acquire *P. carinii*. Rats exposed in open cages to room air but maintained on sterile water and food acquired the infection. Duplicate experiments done in laboratories over 900 miles apart (Memphis and Baltimore) yielded similar results. Animals fed *P. carinii* infected lungs did not acquire the infection. Serial sacrifice of cesarean-section originated, barrier-sustained rats, exposed to room air revealed *P. carinii* infection to be evident by 9 weeks of age and all of the rats were infected by the age of 14 weeks. These findings show that *P. carinii* is naturally acquired as a *de novo* infection from airborne organisms.

984 PROVOCATION OF PNEUMOCYSTIS CARINII PNEUMONIA WITH A T- LYMPHOCYTE INHIBITOR (CYCLOSPORIN A). Walter T. Hughes, St. Jude Children's Research Hospital, Division of Infectious Diseases, Memphis.

Pneumocystis carinii pneumonitis occurs almost exclusively in the immunocompromised host while the organism is believed to be prevalent as a latent infection in the immunocompetent human and lower animals. The latency can be unmasked in the rat model by broad-spectrum suppression of the immune responses with corticosteroid administration. A fungal metabolite, cyclosporin A, has recently been discovered to selectively inhibit subsets of T lymphocytes. This compound was used as a probe to learn whether or not selective T cell inhibition would permit activation of *P. carinii* infection. Using the rat model *P. carinii* infection was provoked in 10 per cent of animals receiving 5.0 mg/kg./day of cyclosporin A and in 50 per cent of those receiving 20.0 mg/kg./day of the drug, while the organism was not detected in untreated control animals. More extensive immunosuppression with dexamethasone evoked the pneumonitis in all of the animals so treated. These findings indicate that the T lymphocyte has an active role in the control of *P. carinii* infection. Reasonable speculation leads to the expectation that clinical usage of cyclosporin A may be associated with *P. carinii* pneumonitis, but to a lesser extent than with corticosteroid therapy.

985 THE EFFECT OF IMMUNE SERUM AND POLYMYXIN B ON ESCHERICHIA COLI INDUCED INFLAMMATION AND VASCULAR INJURY. Andrew C. Issekutz, Shabir Bhimji and Robert Bortolussi. (Spon. by Richard B. Goldbloom). Dalhousie University, Izaak Walton Killam Hospital for Children, Halifax, Canada.

Bacterial invasion normally stimulates an inflammatory reaction which limits the spread of the microorganisms. However, inflammation may also have deleterious effects leading to tissue injury and vascular damage. We studied inflammation induced in the skin of rabbits by the intradermal injection of live or killed E. coli. Protein exudation (using ^{125}I labelled albumin), blood flow (using ^{86}RbCl), leukocyte infiltration (using ^{51}Cr labelled leukocytes) and hemorrhage (using ^{59}Fe labelled RBC's) were measured in the lesions. Severe inflammation, normally induced by injection of killed or live E. coli was significantly diminished by treating the E. coli with immune serum: protein exudation by 30% ($p<.05$), blood flow by 30% ($p<.05$), leukocyte infiltration by 36-54% ($p<.01$), hemorrhage by 56-74% ($p<.005$). Cross-over experiments with four different E. coli serotypes and four different antisera indicated that antibody to specific O antigens, but not to K or H antigen was important for modifying the inflammatory response. Treatment of 4 E. coli serotypes with antiserum to "core" glycolipid inhibited the inflammatory response to all four killed E. coli serotypes. Finally, treatment of killed E. coli with polymyxin B also inhibited their inflammation inducing potential. The results suggest that inflammation and vascular injury at the sites of E. coli infection is diminished by polymyxin B or by antibody to endotoxin. Such a decrease in tissue and vascular damage may improve survival in E. coli infections.

986 HOSPITALIZATION IN NEONATAL ENTEROVIRUS INFECTION. Jerri A. Jenista, Marilyn A. Menegus, and Keith R. Powell (Spon. by David H. Smith). Univ. of Rochester, Strong Memorial Hospital, Dept. of Pediatrics, Rochester, NY.

Hospitalization for possible sepsis is common in young infants. Often no etiology is found for the suspected infection and the child is discharged with the diagnosis "probable viral syndrome." We prospectively followed infants from birth through the first month of life to determine: rate of and reason for admission, risk factors predicting admission, and the role of enterovirus infections. 588 residents of Monroe County, NY born at Strong Memorial Hosp. from June 24 through Sept. 30, 1981 were studied. Of these, 24 (4%) were admitted. Diagnoses were: suspected sepsis (17), hyperbilirubinemia (2), and pneumonia, apnea, seizures, irritability, and abdominal mass (1 each). Hospitalization was associated with lower socioeconomic status, fever, lethargy or poor feeding, maternal concern sufficient to contact a physician, and the week of the year (all $p<.01$). There was no correlation with breast feeding, neonatal or maternal hospital course, or infant exposure to illness in the home or elsewhere (all $p>.05$). 66% of the hospitalized group (82% of those admitted for possible sepsis) were culture positive (throat-rectal ± CSF) for non-polio enterovirus on admission. 4 had culture-proven aseptic meningitis. No bacterial pathogens were isolated and no infants died. 75% of the admissions (81% of the enterovirus-positive admissions) occurred from mid-Aug. through Sept. Admission rates ranged from 0 to 4% per week per infant at risk. Thus, during the late summer, neonates are at high risk for hospital admission with enterovirus infection.

987 THE ANTISTREPTOLYSIN O (ASO) RESPONSE IN THE HYPERCHOLESTEROLEMIC RABBIT: FURTHER IN VIVO EVIDENCE FOR A BIOLOGIC EFFECT OF CHOLESTEROL ON THE IMMUNE RESPONSE TO THIS EXTRACELLULAR ANTIGEN. Edward L. Kaplan, Univ. of Minnesota Dept. of Pediatrics, Minneapolis. (Spon. by L.W. Wannamaker).

Cholesterol (C) and similar lipids may modify several biologic properties of streptolysin O (SO). In addition to neutralizing the hemolytic effect of SO, we showed that in-vitro preincubation of SO with cholesterol modifies the antigenicity as well as the myocardial cytotoxicity in tissue culture of this streptococcal extracellular antigen (SEA). We have now studied the biologic effects of hypercholesterolemia on the immune response to this SEA in the rabbit.

Thirty-eight rabbits fed a 1% cholesterol diet (CR) and 39 animals fed a normal diet (NR) were immunized intravenously with 35 units of SO twice weekly for 18 weeks; 502 serum samples were obtained at regular intervals. Mean serum cholesterol levels in CR rabbits rose to almost 2 gm% as compared with < 100 mg% for NR; the proportion of free and esterified cholesterol in NR and CR sera were similar. After 7 weeks of immunization, geometric mean ASO titers (log) were significantly higher for NR than for CR animals: e.g., 1.90 vs 1.76 at 7 wks, $p<.01$; 1.99 vs 1.84 at 11 wks, $p<.02$; 2.07 vs 1.87 at 18 wks, $p<.01$ (students' T test).

These data indicate suppression of the ASO response in the CR rabbit and provide additional evidence for a biologically significant role of cholesterol in the in-vivo modification of the host immune response to a known streptococcal antigen. They are compatible with theories suggesting a more extensive influence for C on the immunology of streptococcal infection and its sequelae.

988 PROSPECTIVE COMPARATIVE TRIAL OF MOXALACTAM (MOX) VS. AMPICILLIN (AMP)/CHLORAMPHENICOL (CHLORO) FOR THE TREATMENT OF HAEMOPHILUS INFLUENZAE TYPE B (HiTb) MENINGITIS: PRELIMINARY REPORT. Sheldon L. Kaplan, Edward O. Mason, Jr., Sally J. Kvernland, Elaine M. Loiselle, Francis I. Catlin, Rita T. Lee, Murdina M. Desmond, & Ralph D. Feigin. Baylor College of Medicine & Texas Children's Hospital, Dept of Pediatrics, Houston, TX

The treatment of HiTb meningitis has been compared to date in 15 children (mean age 15.8 mon) who received Mox (200 mg/kg/day) vs. 17 children (mean age 16.3 mon) who received Amp or Chloro. Three isolates in each group were Amp-resistant. The MIC of Mox for all isolates was ≤0.03 µg/ml. The median initial cerebrospinal fluid-polyribosephosphate quantity in both groups was 0.08 µg/ml. Two in the Mox group and 3 in the Amp/Chloro group received greater than 10 days of parenteral therapy; all others received 10 days. The mean ± SD duration of fever in the Mox group was 6.1 ± 4 days (range 2-16 d) compared to 5.8 ± 3.8 d (range 2-12 d) for the Amp/Chloro group. Selected clinical features:

Number with:	Seizures after admission	Subdural effusion	Prolonged fever	Any sequelae
Moxalactam	5	2	3	0
Amp/Chloro	4	0	5	1*

*Initial CSF-PRP quantity = 20.48 µg/ml

Adverse reactions in the Mox group included neutropenia-2, eosinophilia-4, thrombocytosis-4, elevated SGOT/SGPT-1. Neutropenia and thrombocytosis each were noted in 2 children in the Amp/Chloro group. Mox appears to be as safe and effective as Amp/Chloro in the treatment of HiTb meningitis in children.

989 **EPIDEMIOLOGY OF ACUTE OTITIS MEDIA (AOM) DUE TO HAEMOPHILUS INFLUENZAE (HI): BIOTYPES IN CHILDREN WITH RECURRENT DISEASE.** **Raymond B. Karasic, Patricia E. Brooks, Paul A. Shurin, David W. Teele, Stephen I. Pelton (Spon. by Jerome O. Klein). Boston University School of Medicine, Boston City Hospital, Department of Pediatrics, Boston.**

We used biotyping to study the epidemiology of AOM due to HI. Using macro- and microchemical technics, we determined the biotype (Bt) of 78 middle ear (ME) isolates of HI: Bt-I 10(13%); Bt-II 39(50%); Bt-III 21 (27%); Bt-IV 0(0%); Bt-V 6(8%); unclassified 2(3%). Six (8%) strains were serotypable (5-b, 1-f); 13(17%) were β-lactamase (β-lac) positive. No correlation was found between Bt and β-lac production.

Using isolates from children who had serial ME and nasopharyngeal (NP) cultures positive for HI, we observed the following: 1)Right and left ME isolates in bilateral AOM yielded the same Bt in all 9 children tested. 2)Simultaneous NP and ME isolates were of identical Bt in each of 6 determinations. 3)Repeat ME cultures from 8 children with a 2nd episode of AOM showed a change in Bt in 4 cases.

These data demonstrate that: 1)Biotyping of HI is a useful technic for studying the epidemiology of ME disease, and perhaps other diseases caused by non-typable HI. 2)Recurrent attacks of AOM due to HI result from acquisition of a new strain in some cases, implying that reinfection is important in recurrent ME disease.

990 BIOLOGIC CHARACTERIZATION OF A RECOMBINANT DNA HUMAN INTERFERON. Douglas K. Kelsey, Kenneth M. Kosak, Bruce A. Braaten and Lowell A. Glasgow. University of Utah School of Medicine. Department of Pediatrics. Salt Lake City.

Recombinant DNA technology has resulted in the production of highly purified human interferon (HuIFN) preparations which are being evaluated as potential antiviral and antitumor agents in humans. We determined the biologic properties of a recombinant DNA interferon HuIFNα-2 (Schering Corp.), in vitro and in vivo: (1) antiviral activity was documented by inhibition of CMV, SFV, VSV, HSV 1 and 2 and vaccinia virus in WISH, human embryonic lung, foreskin fibroblast and osteosarcoma cells; (2) species specificity was indicated by a >1000-fold reduction in anti-viral activity in murine cells in vitro; 3) immunomodulator activity was documented by augmentation of human NK cells and activation of human monocytes to be cytotoxic for human tumor cells; (4) antiproliferative activity was determined by inhibition of growth of human osteosarcoma cells (HOS) in vitro and prevention of growth of transplanted HOS tumors in athymic mice.

In summary, HuIFN -2 was found to have antiviral, immunomodulatory, and antiproliferative activity characteristic of standard reference preparations of HuIFN. The feasibility of large scale production of pure preparations of HuIFN using recombinant DNA technology offers potential in the treatment of malignancies and viral infections of man.

991 TRANSMISSION OF CLOSTRIDIUM DIFFICILE (Cd) AMONG CHILDREN ATTENDING DAY CARE CENTERS (DCC). Kyung-Hee Kim, Herbert L. DuPont, Larry K. Pickering. University of Texas Medical School, Program in Infectious Diseases and Clinical Microbiology, Houston, Tx.

We evaluated the occurrence of Cd and its association with diarrhea in 3 DCCs caring for children <2 yrs of age. Stools were collected from children during diarrhea outbreaks and 1-3 times a week thereafter. Environmental cultures for Cd were obtained before, during, and after outbreaks. DCC 1 was enrolled when diarrhea was not a problem and 1 of 13 children had Cd in stool. Within 1 month, 6 other children became colonized with Cd (none had received antibiotics). 4 of the 7 children with Cd developed diarrhea 2-4 weeks later at which time Cd was recovered from diaper change area pads as well as from other sites i.e., linen, sinks, and hands of a teacher and 2 children. DCC 2 and 3 were studied during and after diarrhea outbreaks. In DCC 2, 1 of 4 children with diarrhea and 0 of 4 children without diarrhea had Cd in stool. Within 3 weeks, the other 3 children with diarrhea became positive (2 had been given antibiotics). Cd was recovered from hands of 1 asymptomatic child and from the classroom floor. In DCC 3, 2 of 5 children with diarrhea and 2 of 14 children without diarrhea had Cd in stool; a third child with diarrhea became positive on day 5. Cd was recovered from hands of 1 child with Cd and diarrhea and environmental contamination was demonstrated. All colonized children in the 3 DCCs continued to excrete Cd during a 3 1/2 month period of observation. These results show that Cd can be detected commonly in DCCs and that transmission occurs probably by direct contact.

992 IN VIVO BACTERICIDAL EFFECT OF TRIMETHOPRIM/SULFAMETHOXAZOLE (TMP/SMZ) AGAINST AMPICILLIN-RESISTANT H. INFLUENZAE TYPE b (Hib). Kwang Sik Kim, Marian Manocchio, Joel Ward and Bascom F. Anthony. UCLA School of Medicine, Harbor-UCLA Medical Center, Dept. of Peds, Torrance, CA.

We have evaluated TMP/SMZ in vitro and in vivo against a β-lactamase-positive Hib. In vitro, bacterial killing was complete in 24 hours with 2 & 38 µg/ml of TMP & SMZ, respectively. In vivo, we used the newborn rat model of Hib bacteremia and meningitis following intraperitoneal injection. TMP/SMZ given subcutaneously in a dose of 5 mg/kg of TMP twice daily produced serum levels of 0.5-2 µg/ml of TMP in 2 hours, comparable to clinical values. Bacterial counts in blood and cerebrospinal fluid (CSF) were determined at the beginning of therapy and daily thereafter for 3 days. Bacteremia and meningitis were produced in 100% of animals. The results are summarized below:

	Initial bacterial counts (log 10 CFU/ml)	Δ Bacterial counts (log 10CFU/ml) day 1	day 2	day 3
Blood				
Control	5.34±0.81	0.45±1.15	0.40±1.29	0.24±1.44
TMP/SMZ	5.45±0.90	-2.98±1.78	-3.95±1.32	-4.48±1.52
p value	>0.5	<0.001	<0.001	<0.001
CSF				
Control	5.30±1.35	1.41±2.72	0.42±2.56	-0.69±3.12
TMP/SMZ	5.64±1.24	-3.02±2.65	-3.65±2.27	-4.27±2.46
p value	>0.5	<0.001	<0.001	<0.01

This experimental study illustrates that TMP/SMZ is an effective agent in vivo against ampicillin-resistant Hib and warrants further investigation.

993 PARADOX OF THE IN VITRO AND IN VIVO RESPONSE OF E. COLI TO AMPICILLIN (A) AND CHLORAMPHENICOL (C). Kwang Sik Kim, Marian Manocchio and Bascom F. Anthony, Department of Pediatrics, UCLA School of Medicine, Harbor-UCLA Medical Center, Torrance, CA.

At present, there are no consistently effective antimicrobial regimens for neonatal gram-negative meningitis (usually E. coli). We have evaluated the combination of A and C in vitro and in vivo against a K_1 strain of E. coli. The minimal inhibitory and bactericidal concentrations were 2 and 4 µg/ml for A and 4 and 32 µg/ml for C. In vitro experiments indicated antagonism with the combination by both isobolograms and killing curves.

In vivo, we used the newborn rat model of E. coli bacteremia and meningitis following intraperitoneal injection. Bacterial counts in blood and cerebrospinal fluid (CSF) were determined daily and mortality recorded. A and C subcutaneously, 50 mg/kg twice daily, resulted in peak serum levels of 45±20 µg/ml and 20±12 µg/ml, respectively (mean±S.D.). Mean CSF/serum levels were 7.7% for ampicillin and 77.5% for chloramphenicol. Bacterial clearance was inversely related to the mortality, which is summarized below:

	A	C	A+C	Saline (control)
No. rats	23	22	25	23
No. deaths	14	18	4	23
Mortality	60%	81%	16%	100%
p value	<0.01	<.001		

This study illustrates that in vitro results are not necessarily predictive of in vivo responses and that the combination of A&C is an effective regimen against E. coli in this model.

994 THE ROLE OF PILI IN PHARYNGEAL COLONIZATION WITH E. COLI K1. Herbert W. Clegg, Nicholas G. Guerina, Solomon Langermann, T. Woodrow Kessler, and Donald A. Goldmann (Spon. by Kenneth McIntosh), Harvard Medical School, Children's Hospital Medical Center, Dept. of Medicine, Boston.

We have studied the role of pili in E. coli K1 colonization of the pharynx both in a neonatal rat model and in humans. Experiments were performed with a clinical strain which had been separated into 2 phases based on colonial morphology, hemagglutination (HA), and electron microscopy: 1) a piliated (P+) phase which produced mannose-sensitive HA, and 2) a non-piliated (P-) phase. The P+ and P- phases were incubated with pharyngeal cells, and the P+ phase adhered in significantly greater numbers than the P- phase:

Source of cells	Bacteria/cell (mean ± SD) P+	P-
Neonatal rat	71 ± 44	5 ± 6
Pre-term neonate	119 ± 59	2 ± 2
Term neonate	86 ± 45	2 ± 2
Adult	45 ± 21	4 ± 3

The same difference in adherence was observed with P+ and P- phases of an acapsular mutant of the K1 strain, confirming that pili, not capsule, are of paramount importance in adherence.

When neonatal rats were fed 10^6 cfu of E. coli K1 in either the P+ or P- phase, only P+ bacteria were recovered from the pharynx 24 hr and 7 d after feeding, regardless of the challenge phase. Both challenge phases produced 100% colonization rates and 26-29% bacteremia rates. Our results suggest that pilus-dependent adherence to pharyngeal epithelium may be important in the pathogenesis of E. coli K1 colonization and infection.

995 FOMITES AND HERPES SIMPLEX VIRUS: THE TOILET SEAT REVISITED. T. Larson, Y. Bryson; UCLA Sch. Med., Dept. Pediatrics, Los Angeles, Ca.

The role of fomites in transmission of genital or oral herpes simplex infections (HSV) is undefined. It has been believed that HSV does not remain viable for any length of time at room temperature unless inoculated into specific transport media. We therefore examined the ability of HSV obtained directly from patient's genital lesions to remain viable on various surfaces. Samples included dry cotton gauze pressed to lesions, plastic gloves and speculum used in pelvic exams, fingerprints from gloves pressed on plastic petri dishes and cotton swabs from lesions. After collection from 10 patients, all samples were kept dry at room temperature in non-sterile conditions. Swabs and some gauze specimens were rubbed on a ceramic toilet seat and a patient with HSV lesions sat on the toilet seat to test HSV survival on this surface. Samples were cultured initially and at various time intervals post-collection (0-90 hrs). Cultures were taken from samples by rubbing a moistened cotton swab over the contact area (gloves, petri dish, speculum and toilet seat) or mixing small pieces of exposed gauze in media and inoculating samples into WI38 cells. Results showed that HSV was recoverable from gloves and petri dish fingerprints after 1 hr, speculum after 18 hrs, and on dry gauze after 88 hrs. HSV was cultured from the toilet seat up to 1½ hrs after both gauze contact and direct patient contact. The survival of HSV on fomite materials for hours to days gives rise to the speculation of possible non-venereal transmission of HSV to susceptible patients in the setting of the clinic exam room, hospital or during routine daily activities.

● **996** BENEFICIAL PERINATAL IMMUNIZATION WITHOUT IMMUNOLOGIC TOLERANCE. Rosemary D. Leake, Terrence A. Payne, Larry J. Baraff, Charles R. Manclark, Christopher C. Cody, and Joseph W. St. Geme, Jr., UCLA School of Medicine, Harbor/UCLA Medical Center, Dept. of Pediatrics, Torrance; and Bureau of Biologics, National Institutes of Health, Bethesda.

Concerned that DTP immunizations are often delayed but aware that early immunization may produce immunologic tolerance, we examined antibody titers by the ELISA technique following traditional DTP immunization (Wyeth) at 2, 4 and 6 months (N=18 infants) or experimental DTP immunization at time of discharge from the nursery (mean=3.5 days), plus 2, 4 and 6 months (N=17). IgG, IgA and IgM values were measured for filamentous hemagglutinin antigen (FHA) - the respiratory attachment factor, lymphocyte promoting factor (LPF) - the probable pertussis toxin, agglutinin antigen (AA), and pertussis agglutinins (by standard agglutination technique) in blind coded sera from cord blood as well as sera from 4, 6 and 9 months of age.

Cord blood showed comparable antibody levels in the traditional and experimental groups. There was a significant antibody advantage to early immunization at 4 and 6 months in FHA/IgM only ($p<0.05$; student t test). Final antibody titers at 9 months did not vary in the 2 groups in any respect. There was a significant correlation of pertussis agglutinin antigen and anti IgGMA (3 combined immunologic classes vs. pertussis agglutinins; $p<0.05$).

Thus: 1) Initiating DTP immunization at nursery discharge does not produce evidence of immunologic tolerance, and 2) produces higher mean titers of IgM antibody which may reflect greater protection to pertussis.

997 SAFETY AND IMMUNOGENICITY OF A SINGLE DOSE OF AN H. INFLUENZAE B (HIB) VACCINE, COMBINED WITH DIPHTHERIA-PERTUSSIS-TETANUS (DPT) IN 15-18 MONTH OLD CHILDREN. Martha L. Lepow, Martin F. Randolph, Daniel L. Mayer, J.S.C. Kuo, and Christine L. Williams, Albany Medical College, Department of Pediatrics, Albany, NY and Medical Research Division, American Cyanamid Co., Lederle Laboratories, Pearl River, NY

Thirty-five children 15-18 months were randomly assigned to receive a DPT-polyribosylribitol phosphate (PRP) (Gp. A) or DPT booster (18) (Gp. B). Febrile, local and systemic reactions were monitored. Pre and 1 month post immunization throat and rectal swabs were tested for presence of HIB or cross-reacting bacteria. Sera obtained at the same times were tested by radioimmunoassay for anti-PRP antibody (J. Immunol. Methods 1981:43:33-47). An antibody concentration of $\geq$ 0/15 µg/ml is considered protective. Fever to $\leq$ 103°F (R) occurred in 4 of each group at 6 and 24 hours in different subjects. Local reactions occurred in 1/3 and systemic reactions in half of each group. None was severe. One child in each group had HIB in the pre-immunization throat swab: both had initial antibody titers > 0/15 µg/ml. Twelve of Gp. A and 10 of Gp. B had initial antibody levels of < 0/15 µg/ml. Nine of Gp. A reached the protective level post immunization, and 12/17 had either a twofold increase in anti-PRP or the final concentration of $\geq$ 0/15 µg/ml. Geometric mean titer increased from 0/10 to 0/89. No change occurred in anti-PRP titers in Gp. B. The addition of PRP to DPT results in no significant increase in reactions compared with DPT alone and a protective level of antibody to PRP was achieved in 70% with a single dose.

● **998** POLYCLONAL ACTIVATION OF PERIPHERAL BLOOD B LYMPHOCYTES IN INFANTS WITH CHLAMYDIAL PNEUMONIA. Daniel Levitt, Marc O. Beem, Richard W. Newcomb. The University of Chicago, Department of Pediatrics, and La Rabida Children's Hospital and Research Center, Chicago.

Infants with lower respiratory infections caused by *Chlamydia trachomatis* have elevated serum IgM and IgG, but not IgE levels. Cellular concomitants of the hyperglobulinemia were studied by enumerating B cell and T cell numbers in peripheral blood mononuclear cells (PBMC) from infected babies. Seven infants, 3-10 weeks old, with chlamydial pneumonia contained 34.3 ± 9.7% surface IgM bearing B cells in their PBMC fraction compared to 8.7 ± 3.3% of normal adult PBMC and 14.0 ± 6.6% of PBMC from infants (< 6 months) with various other infections. Numbers of cells with surface IgD and IgG were also increased. Plasma cells with cytoplasmic IgM, IgG and IgA constituted more than 8% of PBMC compared to < 0.8% in control infants and adults. Except for a modest decrease in total T cell proportions, no gross abnormalities of T cells were revealed by enumerating cells stained with the monoclonal anti T cell antibodies OKT3, OKT4 and OKT8. When cultured *in vitro* without added mitogen, PBMC from 3 infants with chlamydial pneumonia secreted as much immunoglobulin as adult cells treated with pokeweed or *S. aureus* mitogens and more than 20-fold greater than control infant PBMC either stimulated or unstimulated. These results suggest that B lymphocytes are polyclonally expanded and activated during *C. trachomatis* pneumonia.

999 EXPERIMENTAL CONGENITAL DISEASE WITH SIMIAN CYTOMEGALOVIRUS IN RHESUS MACAQUES. William T.London, William C. Wallen, Sidney A. Houff, Blanche L. Curfman, Renee G. Traub, John L. Sever, A. Julio Martinez. NIH, NINCDS, Infectious Diseases Branch, Bethesda, Maryland and University of Pittsburgh, Department of Neuropathology, Presbyterian-University Hospital.

We have been able to produce congenital infection and disease in fetal rhesus macaques after intrauterine inoculation of rhesus cytomegalovirus (Rh-CMV) in seropositive mothers. At 80 days gestation, 11 rhesus macaque fetuses were inoculated intracerebrally by laparotomy of the mother and trans uterine injection into the fetus with 0.20 ml of Rh-CMV inoculum ($10^{4.25}$). At birth five animals showed hydrocephalus. Large intranuclear eosinophilic inclusion bodies were seen in periventricular neurons of all 11 fetuses. At 50 days gestation intraamniotic inoculation with 0.25 ml of the inoculum resulted in hydrocephalus in two of nine additonal animals. All fetuses inoculated with Rh-CMV had CMV antibodies at birth as detected by immunofluorescence, whereas uninoculated controls had little or no CMV antibody. The Rh-CMV was isolated from various fetal tissues, as well as placenta and amniotic fluid. Placentas from virus-inoculated animals showed placentitis, with intranuclear inclusion bodies consistent with CMV. Eight controls did not develop congenital disease nor did CMV antibody titers rise in the mothers. These studies demonstrate rhesus macaque fetal susceptibility to CMV infection and the induction of congenital disease.

● **1000** THE EFFECT OF VACCINATION ON PNEUMOCOCCAL OTITIS MEDIA - INFANTS VACCINATED WHEN 6-9 MONTHS OLD. P.Helena Mäkelä[1], Pekka Karma[2], Seppo Pöntynen[3], Markku Sipilä[2] and Matti Timonen[4], [1]National Institute of Public Health, Helsinki; [2]Institute of Clinical Sciences, University of Tampere, Tampere; [3]Central Hospital of Lapland, Rovaniemi; and [4]Department of Pediatrics, University Central Hospital, Oulu, Finland.

3800 infants received in a double blind fashion 14-valent pneumococcal vaccine or saline placebo at the age of 6 (15%), 7 (60%), 8 (20%) or 9 (5%) months. The vaccinations were performed at the local health centers as part of the routine vaccination program. A booster dose was given appr. 5 months later. The serum antibody response was monitored in a cohort of 100 infants by radio- and enzyme-immunoassay. The families were informed of symptoms and signs suggestive of acute otitis media (AOM) and told to bring the infant to the project clinic when suspecting AOM. After clinical examination, middle ear exudate was obtained for culture and typing of pneumococci. The patient was treated with antimicrobials, and followed until the exudate had cleared. The data from a period of 12 to 23 months after vaccination show that prevention of AOM was specific for the pneumococcal types evoking a serum antibody response. However, the response to most of the polysaccharides was poor at this early age.

1001 ACUTE RESPIRATORY ILLNESSES IN SURVIVORS OF INFANT RESPIRATORY DISTRESS SYNDROME (RDS). Martin G. Myers, Gail McGuinness, Franklin Koontz, Peter A.Lachenbruch, Dan B. Olson and Rachel Hollingshead.Children's Hospital Research Foundation, Cincinnati, Ohio and the University of Iowa,Iowa City

Infant survivors of RDS are believed to develop residua which predispose them to increased respiratory illness (RI) morbidity. The frequency, severity and etiologies of acute RI were evaluated prospectively in 17 survivors of RDS and 10 pre-term infants who did not have RDS. They were compared to normal,full-term infants who were matched for sex and season of birth. For 12 months following discharge of the affected child, children were evaluated at three-week intervals by history, examination and nasal wash culture for viruses, mycoplasmata, *Chlamydia trachomatis*, and aerobic bacteria.

The total numbers of RI and non-respiratory illnesses were similar for the pre-term infants,with and without RDS, and their controls. The frequency of lower RI was greater in children surviving RDS, but this difference was not significant($p=0.11$).However, the co-variates of duration of hospitalization for RDS and the duration of acidemia were related to the number of subsequent RI. Gestational age, duration of hypoxemia and duration of mechanical ventilation did not correlate with subsequent RI. The organisms associated with RI were similar in all infant groups.

Although we did not detect increased RI morbidity for pre-term infants, subsequent RI morbidity in RDS survivors may be related to duration of acidemia and factors related to the duration of the initial hospitalization.The data imply that any increased RI morbidity is related to increased severity of infection by the same organisms which cause RI morbidity among control infants.

1002 DOSE RESPONSE OF COLONIZATION FACTOR ANTIGEN (CFA) POSITIVE ENTEROTOXIGENIC E.COLI (ETEC) IN THE INFANT RABBIT ASSAY. Richard E. McClead, Susan Gregory (Spon. by Grant Morrow), OSU, Children's Hospital, Dept. Peds, Cols, Oh.

Fluid secretion by the intestinal epithelium of the infant rabbit is a model for evaluating the toxin production by ETEC. In vivo toxin production by ETEC requires attachment to and colonization of the small bowel. The host specificity of the attachment/colonization process of some ETEC in man is attributed to CFA. In this study, we evaluated the dose response of CFA(+) and CFA(-) ETEC in the infant rabbit model. Varying concentrations of CFA(+) and CFA(-) organisms in 1 ml saline were injected into the small bowel of individual infant rabbits. After 18 hours of in vivo incubation, the small intestines were removed and the fluid accumulation index (FAI=gm fluid/gm intestine) determined. Fluid data from animals who died post-incubation were excluded.

FLUID SECRETION IN THE INFANT RABBIT MODEL (mean ± SEM, g/g)

E.coli	10^4 org/ml	10^5 org/ml	10^6 org/ml	10^8 org/ml
CFA(+)	1.09 ± 0.12	1.98 ± 0.29*	1.82 ± 0.15*	1.83 ± 0.18*
(n=)	(7)	(12)	(10)	(11)
CFA(-)	0.78 ± 0.16	1.00 ± 0.18	0.87 ± 0.10	1.16 ± 0.10
(n=)	(8)	(9)	(13)	(13)

Saline control: 0.95 ± 0.13 (11); *$p < 0.01$

The group mortality rate of CFA(+) ETEC 10^6 and 10^8 was greater than all other groups ($p < 0.01$).

Conclusions: The optimum inoculum concentration in this model is 10^5 organisms/ml of CFA(+) ETEC. Greater concentrations of CFA(+) organisms result in a high group mortality rate. The response of CFA(-) ETEC is the same as saline controls.

1003 DECREASED IgG IN NEONATES WITH GROUP B STREPTOCOCCAL (GBS) SEPSIS. Scott A. McGeary, Bascom F. Anthony, Penelope G. Shackelford, UCLA Sch.of Med., Harbor-UCLA Med.Ctr., Dept. of Peds., Torrance, CA; Washington Univ. Sch. of Med., St. Louis Children's Hosp., St. Louis.

In previous studies which demonstrated an absence of detectable type-specific antibody in cord or acute illness sera of 30 infants with type III GBS sepsis, we observed that total serum IgG levels in the septic infants were distinctly less than those in the cord sera of healthy newborns. We therefore compared serum IgG levels (using radial immunodiffusion) in 14 infants < 7 days old with GBS sepsis and 14 well infants matched for birthweight (within 100 gm), gestational age (within 1 wk), and postnatal age (within 1 d). IgG levels were significantly less ($p < .02$) in the septic infants compared to the controls (901±473 mg/100ml vs. 1305±268 mg/100ml). Total protein in the two groups was not significantly different (5.3±.9 gm/100ml vs. 5.7±.7 gm/100ml), indicating that the difference was not due to a generalized increase in protein catabolism in sepsis. Maternal sera, available for 8 of the septic newborns, did not have a corresponding decrease in IgG (1082±260 mg/100ml vs. 716±296 mg/100ml in their infants). The IgG levels of three septic infants > 30 days old were not significantly different from those of matched controls (457±55 mg/100ml vs 580±101 mg/100ml). These findings suggest that serum IgG is depleted in the course of neonatal GBS sepsis. Whether this occurs in other bacterial infections or in older infants is unknown. This suggests a rationale for the use of fresh frozen plasma or immune globulin in the treatment of newborn sepsis.

1004 PROTEIN KINASE ACTIVITY ASSOCIATED WITH MEASLES VIRUS. Cody Meissner and Bernard N. Fields (Sponsored by Richard C. Talamo). Tufts-New England Medical Center, Department of Pediatrics and Department of Microbiology and Molecular Genetics, Harvard Medical School, Boston, Mass.

Measles virus and five strains of SSPE virus were found to contain a virion associated protein kinase activity. Purified virus phosphorylated two of the known measles phosphoproteins, P and NP, in vitro, as well as an exogenous phosphate acceptor, the μ1C polypeptide of reovirus. The cyclic nucleotide independent kinase showed a broad temperature and pH range. The P polypeptide contained phosphoserine as the only phosphoamino acid, while NP contained phosphoserine and phosphothreonine. Enzyme activity was retained after solubilizing the viral envelope, indicating an association of this activity with the nucleocapsid.

● 1005 NEW STREPTOCOCCAL EPIDERMOLYTIC TOXIN RESPONSIBLE FOR BULLAE IN CELLULITIS AND ERYSIPELAS. Marian E. Melish, Mieko S. Murata, University of Hawaii School of Medicine, Department of Pediatrics, Honolulu, Hawaii.

Bullae and vesicles are commonly found in lesions in streptococcal cellulitis and erysipelas. We have discovered a protein exotoxin, streptococcal epidermolytic toxin (Strep ET) elaborated by strains of Streptococcus pyogenes causing erysipelas. Strep ET was sequentially purified from Todd Hewitt broth culture filtrates by 80% saturated $(NH_4)_2SO_4$ precipitation, Ultrogel AcA 54 chromatography and isoelectric focussing. The resulting preparation migrates as a single band in SDS gel electrophoresis with an estimated molecular weight of 30,000 daltons. Analytical isoelectric focussing reveals the major pI to be at pH 8.8 with three closely associated minor bands. Strep ET is not hemolytic and chemically different from known extracellular streptococcal products. Both live toxigenic streptococci and purified Strep ET cause blister formation after subcutaneous injection in newborn mice. Histologically Strep ET causes separation of cells of the upper epidermis similar to that caused by staphylococcal epidermolytic toxin. Strep ET was found in 84% of 50 group A beta hemolytic streptococcal throat isolates, 92% of 30 skin isolates and all of 8 cellulitis isolates tested. It can be detected in the bulla fluid of patients with streptococcal cellulitis and erysipelas. Strep ET, produced locally at the infectious site, appears to be responsible for bulla formation in these patients as skin biopsy shows cleavage plane identical to the mouse model. At present unlike Staph ET, Strep ET is not known to cause any generalized toxemic disease.

1006 EFFECT OF VIRAL INFECTION ON NASAL COLONIZATION OF INFANT RATS WITH HAEMOPHILUS INFLUENZAE TYPE B (HIB) Richard H. Michaels and Richard L. Myerowitz University of Pittsburgh, Departments of Pediatrics and Pathology and Children's Hospital of Pittsburgh, Pittsburgh PA

Viral infection might be a factor in spread of HIB in families and day care centers by enhancing nasal HIB colonization. An animal model was used to examine this possibility. We had previously shown that the intranasal dose of HIB required to produce meningitis in infant rats is significantly reduced if the animals are pre-infected with influenza A virus. Sendai (parainfluenza 1) virus and rat coronavirus have similar effects.

In the present study, all three of these respiratory viruses were found to potentiate nasal HIB colonization in infant rats. In virus-infected animals an intranasal dose of 200,000 cfu HIB results in nasal HIB titers at least 100-fold higher than in controls during the first two weeks after HIB inoculation, and as much as 10,000-fold higher during the first week.

Children with cough, sneezing or rhinorrhea could be effective disseminators of HIB if they were as heavily and persistently colonized as these virus-infected animals.

HIB Titer of Nasal Washings at Indicated Day after HIB Inoculation

Inoculum	3d	5d	7d	11d	14d	18d	24d
Sendai virus	*4.0	4.0	4.1	3.9	3.0	0.2	<0.1
Normal saline	1.2	0.3	<0.1	<0.1	0.4	<0.1	<0.1
Rat coronavirus	4.2	4.3	4.2	4.3	3.9	3.5	2.6
Normal saline	<0.1	<0.1	<0.1	<0.1	1.6	2.0	0.4

*Geometric mean titer expressed as log 10 cfu/μl (N=15 animals)

1007 ACYCLOVIR THERAPY IN 129 IMMUNOCOMPROMISED PATIENTS WITH HERPESVIRUS INFECTIONS. Charles D. Mitchell, Bonnie Bean, Gregory W. Sachs, Henry H. Balfour, Jr. University of Minnesota Medical School, University Hospitals, Depts. Laboratory Medicine/Pathology and Pediatrics, Minneapolis.

During the last 2 years, 129 immunocompromised patients, including 42 children, at the University of Minnesota Hospitals have completed intravenous acyclovir (ACV) treatment protocols for symptomatic herpes simplex (HSV), cytomegalovirus (CMV), and varicella-zoster (VZV) infections. Sixty-two patients, 15 of them children, were enrolled in a randomized, double-blind, placebo-controlled protocol. Analysis of the 25 patients with mucocutaneous HSV infections demonstrated that the 12 ACV recipients experienced significantly more rapid resolution of pain ($p = 0.032$) and termination of viral shedding ($p = 0.004$). In the group of 16 patients who could be analyzed for CMV disease, 9 ACV recipients had a significantly faster rate of improvement ($p = 0.0437$) and a more rapid rate of defervescence ($p = 0.0208$). Of 17 zoster patients, the 8 who received ACV had more rapid healing and a shorter period of pain but these differences were not statistically significant. An additional 67 patients (27 under age 18) subsequently were enrolled in open-label studies. ACV was well tolerated by patients on both double-blind and open protocols. Children did not demonstrate transient increases in serum creatinine occasionally seen among adults. We conclude that ACV is a safe and efficacious therapy for HSV. CMV disease and zoster appeared to respond, but further study is needed to define the role of ACV in these infections.

●1008 INCORPORATION OF CLONED DNA INTO A CAPSULE-DEFICIENT HAEMOPHILUS INFLUENZAE (H.i.) YIELDS VIRULENT TYPE b TRANSFORMANTS. E.R. Moxon, R. A. Deich, C. Connelly, Johns Hopkins Hospital, Department of Pediatrics, Baltimore, Maryland and NCI-Frederick Cancer Research Facility, Fort Detrick, Frederick, Maryland.

Strains of H.i. which cause systemic infections in humans usually elaborate type b capsular polysaccharide. It was shown previously that type b, but not type d, transformants (average size of donor DNA ~ 40 kb) of a capsule-deficient H.i. caused bacteremia and meningitis in rats following intranasal inoculation. To characterize further the molecular basis of type b capsule elaboration and virulence of H.i., a gene library was constructed. DNA from the H.i. type b transformant was partially digested with pancreatic DNAse. Fragments (~ 10-16 kb) were cloned into the lambda vector Charon 4 and amplified in E. coli (strain KH 802) to yield 24,000 independent clones. Groups of 10^3 individual phages were amplified in E. coli and DNA from these pools was assayed for its ability to transform a capsule-deficient, avirulent H.i. strain to yield irridescent, type b colonies. From those pools yielding positive assays, single phage clones were amplified and assayed in similar manner. Two independent type b transforming clones were isolated. Type b transformants generated by the cloned DNA produced bacteremia and meningitis in rats whereas the untransformed H.i. did not cause invasive infection. Thus, pieces of DNA have been cloned which can mediate both type b capsule elaboration and virulence of H.i. Further investigation of these and other clones should further characterize the molecular basis of H.i. pathogenicity.

1009 RESPIRATORY ILLNESSES IN BREAST AND FORMULA-FED INFANTS: A PROSPECTIVE STUDY OF MATCHED INFANT PAIRS. Martin G. Myers, Samuel J. Fomon, Franklin P. Koontz, Gail A. McGuinness, Peter A. Lachenbruch and Rachel Hollingshead. Children's Hospital Research Foundation, Cincinnati, Ohio and the University of Iowa Hospitals, Iowa City, Iowa.

Both the frequency and severity of respiratory illnesses have been reported to be lower in breast-fed than in formula-fed infants. Ten pairs of infants, exclusively breast or formula-fed, were evaluated prospectively for the frequencies of respiratory and gastrointestinal illnesses and for the etiologies of respiratory infections. The infants were matched for sex and birth within one month. Infants were evaluated every 14 days for the first 112 days of life. At each visit, illness history and a nasal wash culture for viruses, mycoplasmata, Chlamydia trachomatis, and aerobic bacteria were obtained.

Breast-fed infants had more exposure to children less than twelve years of age in the family, but were less likely to be exposed to other infants in day-care settings. Family size, maternal age and maternal education were similar in both groups. However, breast-fed infants were exposed to less tobacco smoke and their fathers were more educated than the formula-fed infants. Although significantly more gastrointestinal illnesses occurred among the formula-fed infants ($p<0.03$), there were more respiratory illnesses in the breast-fed infants but this difference was not significant.

During the first four months, we were unable to demonstrate less repiratory illness morbidity in breast-fed infants than formula-fed infants.

1010 INHALED CEPHALORIDINE IN CYSTIC FIBROSIS. Geraldine Nolan, Penelope A. McIvor, Ronald Gold, Henry Levison, and Mary Corey. University of Toronto, The Hospital for Sick Children, Department of Pediatrics, Toronto, Ontario.

The use of prophylactic antibiotics in cystic fibrosis is controversial. The effect of prophylactic inhaled cephaloridine on bacterial colonization of the respiratory tract and on the general progression of the disease was studied in a 2 year prospective study. 47 patients (24 males and 23 females; mean age 13 years) with mild to moderate pulmonary disease participated. Balanced groups were formed after stratification by age, sex, and pulmonary function. One group received inhaled cephaloridine and the other received no inhaled antibiotic. Both groups received oral cloxacillin. No significant differences between outcome variables of the 2 groups were observed. Quantitative sputum cultures showed that 90% of patients carried Pseudomonas aeruginosa, 36% carried P. cepacia, 20% carried Staphylococcus aureus. No hospital admission was associated with S. aureus infection. There were no differences between the annual incidence of respiratory tract infections (4.3 vs 5.7) or hospital admissions (0.4 vs 0.7). Girls had higher rates than boys for both these variables. Schwachman scores, Xray scores and pulmonary function showed no differences between the groups in the expected deterioration over time. We conclude that anti-staphylococcal prophylaxis with inhaled cephaloridine has no additional benefit to oral cloxacillin and is not indicated in the management of cystic fibrosis.

1011 PROSPECTIVE STUDY OF SPUTUM BACTERIOLOGY IN CHILDREN WITH CYSTIC FIBROSIS (CF). Geraldine Nolan, Penelope A. McIvor, Ronald Gold, Henry Levison, and Mary Corey. University of Toronto, The Hospital for Sick Children, Department of Pediatrics, Toronto, Ontario.

47 CF patients (mean age 13.7) with mild to moderate pulmonary disease, were followed for 2 years with monthly quantitative sputum cultures. Carriage was considered chronic if 75% or more of monthly cultures were positive ($>10^4$ colonies/ml), intermittent if 25-74% were positive, and transient if 1-24% were positive. 53% of children were chronic carriers of Pseudomonas aeruginosa (PA) for 2 years. 15% became chronic carriers of PA during the 2nd year; 21-24% were intermittent or transient carriers. Only 11% of children were free of PA during the 2 years. The 2nd most common bacteria carried was P. cepacia (PC). Carriage increased from 15% to 38% during the 2 years. Carriage of PC tended to be transient or intermittent compared to PA: only 6% of children were chronic PC carriers. The mean age of acquisition of PA was 6.9 years; for PC, 12.5 years. Carrier rates for Staph. aureus, Haemophilus influenzae, Escherichia coli, Klebsiella species, and Proteus species ranged between 11-30%. Carriage of these organisms was usually transient or intermittent. Staph. aureus is no longer the major pathogen in children with CF. The most common pathogen in the older child is PA. The prevalence of PC is increasing. Such an increase may have major clinical implications as PC is usually resistant to most antibiotics.

1012 RECURRENT GENITAL HERPES: DEVELOPMENT OF AN ANIMAL MODEL. James C. Overall, Jr., Lawrence R. Stanberry, Vera C. Salmon, and Earl R. Kern. University of Utah School of Medicine, Department of Pediatrics, Salt Lake City, Utah 84132

Our laboratory described previously a model of primary genital herpes simplex virus (HSV) infection in 200 g female, Hartley guinea pigs. We now report features of recurrent genital herpes in this same animal model. After intravaginal inoculation with 10^5 pfu of HSV (MS strain), over 95% of animals developed primary genital infection with peak lesion severity and lesion virus titers on days 5-8 and healing by days 12-15. Mortality due to the primary disease was low (0-20%). Recurrent lesions (1-2 mm vesicles with erythematous bases) appeared spontaneously on the external genital skin in 80-100% of animals. Lesions seldom persisted more than 24 hrs. Mean time the first recurrence was day 26 (range 22 to 41 days). Recurrences were frequent with a mean of 3.5 per animal (range 2-9) through day 50. Recurrent lesions continued to appear after day 50, but less frequently. HSV (confirmed by neutralization) was recovered from approximately 10% of recurrent lesions sampled (swab and biopsy). Eight (47%) of 17 animals with recurrent lesions had latent HSV recovered from sacral ganglia. This model of spontaneous recurrent genital HSV infection should be useful in expanding our understanding of the pathogenesis and in evaluating potential antiviral therapy or immunization for recurrent disease in humans.

1013 MULTIPLE AGENTS ASSOCIATED WITH ACUTE LOWER RESPIRATORY ILLNESSES (ALRI) IN YOUNG CHILDREN. J. Paisley, B. Lauer, K. McIntosh, M. Glode, J. Schachter, and C. Rumack. University of Colorado School of Medicine, Denver, and Hooper Foundation, University of California, San Francisco.

We prospectively studied the etiology of ALRI in 102 children < 5 years old hospitalized over a 9 month period. Viruses (V), Chlamydia (C), B. pertussis and bacteria (B) were identified by standard cultural and serologic methods. Counter-immuno-electrophoresis (CIE) of nasal secretions and urine was used to detect antigens of S. pneumoniae (Sp) and H. influenzae b. The age distribution was 0-5 m (77), 6-12 m (13) and 13-60 m (12). Pathogens were detected in 87 cases; mixed infection occurred in 33 of these. A total of 80 V, 10 C and 32 B were detected. The V included respiratory syncytial (61), rhino (7), parainfluenza (5), CMV (4), adeno (2) and influenza A (1). Four patients had double viral infections. The B included Sp (23), H. influenzae (5), B. pertussis (2), S. aureus (1), and K. pneumoniae (1). B were detected more often by CIE (22) than by culture of blood (5) or tracheal aspirate (3). In only 8 (all Sp) of the 32 B patients was a B the sole pathogen (1/5 with bacteremia). Characteristics of the C cases included age ≤ 3 m (10), absence of fever (9), and mixed infection (9: 7 with V, 2 with Sp by CIE). Compared to children with only V or C detected, those with B more often had fever (17/29 vs 11/58, $p < .001$), band form counts > 2000/mm^3 (13/29 vs 11/58, $p < .05$) and radiographic consolidation (16/29 vs 11/58, $p < .001$). In this study, ALRI was usually associated with V, often with multiple pathogens, and not with C after 3 months of age.

● 1014 CYTOMEGALOVIRUS INFECTION IN A DAY CARE CENTER. Robert F. Pass, Anna M. August, Meyer E. Dworsky, David W. Reynolds. The University of Alabama in Birmingham, Department of Pediatrics, Birmingham, Alabama.

The prevalence of cytomegalovirus (CMV) excretion among children in a day care center was assessed in order to determine the effect of grouping young children upon transmission of CMV and to define the exposure to CMV experienced by female workers. Seventy of 75 (93%) children attending participated. Urine was obtained from 68 and mouth swabs from 33. Serum was available from 37 mothers and 16 employees. The children's ages ranged from 3 to 65 months; 94% were caucasian. Median age at entry to day care was 6 months; 59% had been breast fed. The mean number of siblings was 0.5, and parental ages were 29.4 ± 3 for mothers and 31.6 ± 4 for fathers. Parents averaged over 16 years of formal education. CMV shedding was found in 51% of children and was related to age:

Age (mo.)	0-12	13-24	25-36	37-48	49-50
+ve (%)	1/11 (9)	15/18 (83)	10/15 (67)	3/14 (21)	7/12 (58)

Nineteen of 37 (51%) mothers were seropositive; 25 (68%) of their children shed CMV. Excretion was not related to maternal serology or to breast feeding. Four of 36 excretors and 0 of 34 nonexcretors had experienced serious bacterial infection (2 meningitis, 1 bacteremia, 1 facial cellulitis), $p < 0.05$. Twelve of 13 (92%) children under 2 with viruria who were sampled at both sites were also positive in the mouth. CMV was isolated from 4 plastic toys mouthed by toddlers, suggesting a possible means of transmission. Ten of 16 workers were seropositive. Transmission of CMV among children in a day care occurs readily; virus excreting children may be a source of infection for employees and mothers.

● 1015 FACTORS INFLUENCING *IN-VITRO* ATTACHMENT OF *HAEMOPHILUS INFLUENZAE* TYPE B (HIB) TO HUMAN EPITHELIAL CELLS (EC). Michael E. Pichichero (Spon. by David H. Smith). Univ. of Rochester School of Medicine, N.Y. Department of Pediatrics.

Attachment of Hib to the nasopharyngeal surface is thought to be the initial event in pathogenesis of systemic disease. The adhesive component(s) of Hib and mechanism(s) of adherence were studied. Attachment of ^{3}H-labeled Hib (Eagon) to EC was quantitated following removal of unattached Hib by differental centrifugation. Buccal EC were used in most experiments; however, similar results but greater binding were observed with pharyngeal EC. Candidate "adhesins" isolated from the Hib cell surface included the capsular polysaccharide (PRP), lipopolysaccharide (LPS), and purified outer membrane (OM).

Preincubation of EC with PRP did not inhibit subsequent attachment of Hib. However, adherence of PRP to EC was observed if divalent cations were present at concentrations found in nasal mucus. A mouse monoclonal anti-PRP antibody caused agglutination of Hib and completely inhibited attachment. Preincubation of EC with LPS did not inhibit Hib attachment, although high concentrations caused non-specific agglutination of Hib. Unexpectedly, preincubation of EC and/or Hib with OM resulted in enhanced attachment of Hib to EC, suggesting a role for OM protein. Enhanced attachment was not a non-specific protein effect nor was it attributable to LPS contamination. The effect was reversed by heat denaturation of OM and did not occur with untypable Hi. Further study of the mechanisms of Hib adherence is relevant to understanding the pathogenesis of systemic Hib disease and the role of mucosal antibody in human immunity.

1016 EXCRETION OF GIARDIA LAMBLIA BY INFANTS AND YOUNG CHILDREN IN DAY CARE CENTERS (DCC). Larry K. Pickering, William E. Woodward, Herbert L. DuPont, Peggy S. Sullivan. University of Texas Medical School, Program in Infectious Diseases and Clinical Microbiology, Houston, Tx.

We prospectively evaluated the excretion of G. lamblia cysts (C) and trophozoites (T) by 72 young children in a DCC over a 12 month period. Excretion by age was: 0-6 months = none; 7-30 months = 44% excreted C and 16% excreted T; over 30 months = 13% excreted C. Eight children between 7 and 30 months of age continously excreted C and/or T for periods of 3 to 10 months. These children were generally asymptomatic, had normal appearing stools, and normal height and weight increments. We have initiated a survey of approximately 400 children from 0-24 months of age in 30 randomly selected DCC's to determine the prevalence of G. lamblia. Results from 12 centers collected thus far show that 32% of 112 children have G. lamblia C and 8% T in their stool specimens. The frequency is highest in children between 13 and 24 months of age (40%) and of similar occurrence in males and females. Preliminary results suggest that excretion of G. lamblia is greater in children who have been in their DCC for over one month (36% C, 9% T) when compared to those enrolled for less than one month (7% C, 0% T). The prevalence of diarrhea within the preceding month in children who excreted C and/or T was greater (60%) than in non excretors (40%) ($p<0.05$). Children in DCC's may be a major reservoir for G. lamblia. The importance of these observations to DCC children, their families and the community at large remains to be determined.

1017 ACYCLOVIR (ACV) THERAPY OF CHICKENPOX IN IMMUNOSUPPRESSED CHILDREN. Charles G. Prober, L.E. Kirk, and R.E. Keeney. (Spon. by R. Gold). University of Toronto, The Hospital for Sick Children, Toronto, Ontario and Burroughs Wellcome Co., Research Triangle Park, NC.

A double-blind, placebo-controlled, multi-center investigation was conducted to assess the usefulness of ACV in the treatment of immunosuppressed children with chickenpox. Twelve patients received placebo and 8 received ACV (500mg/m^2/dose every 8 hours x 21 doses). If clinical deterioration became evident patients could be removed from the study to receive antiviral therapy. Eighteen patients had skin lesions < 96 hours upon admission to the study. Nineteen patients had malignancies. The 2 groups of patients were similar in age, concomitant or preceding immunosuppressive therapy, status of malignancy, and presenting granulocyte and lymphocyte counts. Zoster immune globulin or plasma had been given to 50% of the placebo group but only 25% of the ACV group. Two patients in the ACV group and 1 in the placebo group had lung and/or liver (SGOT > 100 units) involvement at entry. Of the patients without systemic involvement at entry 6 of the 11 placebo patients compared with 0 of the 6 ACV patients developed lung and/or liver disease ($p = .037$). No ACV patient was removed from the trial to receive known antiviral therapy whereas 5 of the placebo group were so removed. The removal of these patients prohibited a comparison of lesion progression and duration of fever. The overall clinical impression of therapy however was rated beneficial in 6 of 8 ACV patients compared to 3 of 12 placebo patients ($p = .04$). No evidence of toxicity related to ACV was observed. These findings support the usefulness of ACV as an antiviral agent for chickenpox in immunosuppressed children.

1018 THE ETIOLOGY OF MENINGITIS IN EARLY INFANCY. David K Stephure, Charles G Prober (Spon. by R. Gold) University of Toronto, The Hospital for Sick Children, Toronto, Ontario

The charts of all infants < 16 wk. of age who had meningitis at our hospital between 1976 and 1980 were reviewed. Of the 122 charts reviewed, there were 76 cases of bacterial meningitis (BM). The remaining 46 cases (38%) had sterile cerebrospinal fluid(CSF); 6 of these had received antibiotics before the CSF was obtained. Eleven infants with BM (14%) had an external communication with the CSF (10) or an immuno-deficiency (1). The bacterial etiology of the remaining 65 patients is shown below.

BACTERIA	POST NATAL AGE 0-4 WK	5-8 WK	9-12 WK	13-16 WK
ENTERICS	26	0	1	0
GROUP B STREPTOCOCCUS (GBS)	14	1	3	0
HAEMOPHILUS (H)	0	1	4	3
NON-GBS STREPTOCOCCUS (S)	1	3	3	2
MENINGOCOCCUS (M)	0	1	0	1
LISTERIA	1	0	0	0

E. coli and GBS accounted for 83% of the cases of BM < 4 wk. of age. Only 1 case of enteric meningitis occurred at > 4 wk. This infant had been born prematurely and contracted his meningitis while still in the intensive care nursery. H, S, or M accounted for all other cases of BM in infants > 4 wk. of age. Choice of empiric antibiotics for presumed BM need not consider enteric organisms in infants > 4 wk. of age unless there is an external communication with the CSF, an immuno-deficiency or unless the meningitis is acquired in hospital. Beyond 4 wk. of age, coverage for S, H, and M should be provided.

● 1019 EARLY PENICILLIN IN INFANTS ≤2000 GMS WITH EARLY ONSET GBS (EOGBS): IS IT EFFECTIVE? S.P. Pyati, R.S. Pildes, N.M. Jacobs, R. Ramamurthy, T.F. Yeh, D. Raval and P. Amma. Cook County Hosp., Dept. of Pediatr., Chgo, Ill.

During a 52 month period, 1187 neonates ≤2000 gm were randomized into two groups: early Rx (100,000u Pen. G. IM within 60 min. of birth) or C (control, no early Rx). An initial blood culture (IB) was taken from a peripheral vein in all 1187 infants within 60 min. of birth; repeat blood cultures (RB) were taken when indicated. EOGBS disease was diagnosed if the infant was symptomatic and if the I.B. or R.B. culture (≤5 days) was positive.

	No.	Pos.GBS I.B.Culture	Pos.GBS R.B.Culture	Total EOGBS	Inf. Rate	P
Rx	589	9	1	10	17/1000 L.B.	n.s.
C	598	12	2	14	23/1000 L.B.	n.s.

There were no sign. diff. between the 10Rx and 14 C in BW (mean±S.D. 1.40±0.48 vs. 1.25±0.46 kg.), Apgars ≤5 (7/10 vs. 8/14), ROM ≥12 hrs. (7/10 vs. 7/14) or RDS (6/10 vs. 8/14). The only difference was the time of Rx (.8±.4vs.12.9±9.6hr. $p<0.001$). Four of the 10 (40%) Rx and 6 of the 14 C (34%) survived (p,n.s). The survivors (4Rx, 6C) weighed more ($p<0.001$), had less incidence of low Apgar ($p<0.01$) and less ($p<0.001$) RDS than the 14 (6Rx, 8C) non-survivors. All EOGBS neonates ≤1500 gms with RDS expired. The presence of early bacteremia and symptoms suggests that in infants ≤2000 gms invasive infection is usually well established prior to the first hour of postnatal life. Early Pen Rx. does not prevent infection nor decrease mortality in LBW infants <2000 gm.

1020 INITIATION OF CHLORAMPHENICOL THERAPY IN NEONATES. P.Rajchgot, C.Prober, S.Soldin, F.Good, E.Harding and S.Macleod (Spon by D.Biggar), Hospital for Sick Children, Toronto.

Because of its excellent CNS penetration, chloramphenicol (C) may be a useful drug in the treatment of neonatal sepsis. Concentrations of C, measured by HPLC, were studied at approximately 2 and 12 hr. following the first dose of C which was given by a syringe pump infusion over 1/2 hr. Thirteen infants ranging in postnatal age from 1-23 days with mean gestational age 31±4.2 wks (m±SD), were studied after the first dose. Ten of these received the recommended unit dose of 12.5mg/kg with the following results

Hrs. after first dose	2	12
Sample size	n=9	n=7
Concentration of C (mcg/ml)	9.6±3.8	7.5±3.8

Three infants were studied following a loading dose of 20mg/kg. Peak concentrations in this group were 19.8,21.7 and 17.8mcg/ml. One had serum concentrations at 1 1/2,7 1/2 and 11 1/2 hr of 12.9,21.7 and 14.7mcg/ml. The data from all neonates showed that for infants less than 1 day of age (n=5) the 12 hr. concentration was 118±42% of the 2 hr. concentration. For the older infants (>3 days of age) the 12 hr. value was 47±18% of the 2 hr. level. The delayed rise of serum concentrations on the first day of life may reflect both slow C elimination and delayed hydrolysis of C succinate. The latter possibility is currently being assessed with a new assay for C succinate. Attainment of adequate serum concentrations (peak >15mcg/ml) during the early critical hours of therapy requires a loading dose particularly in young neonates in whom bioavailability of C from C succinate may be delayed.

1021 DISSEMINATED LEGIONELLOSIS IN A PATIENT WITH SEVERE COMBINED IMMUNE DEFICIENCY. C. Pandu Rao, Ernest Cutz, Paul S. Thorner, Sandu Toma, Ronald Gold and Erwin W. Gelfand. Depts. Immunology, Pathology and Infectious Diseases, Hospital for Sick Children, Toronto, Canada.

A 5 month old male infant presented with a six week history of bronchopneumonia refractory to antibiotics. He was suspected of having an underlying immunodeficiency and investigations revealed normal to low absolute lymphocyte count, 3% E-rosetting T lymphocytes, absent proliferative responses to phytohemagglutinin and concanavalin A, and markedly reduced serum immunoglobulins. Red cell adenosine deaminase and nucleoside phosphorylase enzyme activities were normal. His respiratory condition progressively deteriorated with the development of pulmonary pneumatoceles and empyema and he required assisted ventilation. Open lung biopsy showed a heavy infestation of Pneumocystis carinii; a Dieterle stain was positive and Parainfluenza type 3 was cultured. Despite treatment, his condition worsened and he expired.

At autopsy, the lung was noted to be consolidated and contained many cavitating abscesses. Microabscesses were found in the liver and the brain stem. Legionella pneumophilia type 6 was cultured from the lung, and direct immunofluorescence examination of the lung, liver, spleen and brain was positive for Legionella pneumophilia type 6. Because of their heightened susceptibility, immunocompromised patients appear to be at the highest risk. Since many of these patients develop mixed infections, Legionella pneumophilia should be included in the differential diagnosis when confronted with progressive respiratory failure of unknown etiology.

1022 TETANUS TOXOID ANTIBODIES IN MATERNAL, CORD AND PREMATURE BLOOD BY ELISA AND LATEX AGGLUTINATION TECHNIQUES. Stanley E. Read, Husn Frayha, Ari Eisen and Greg Hannigan. The Hospital for Sick Children, Toronto, Ontario.

Levels of IgG antibody to tetanus toxoid were measured in paired maternal and full-term cord blood samples, as well as in premature peripheral blood using an enzyme-linked immunosorbant assay (ELISA) and a latex agglutination technique. Both methods were found to be sensitive in detecting antibody levels well below the 0.01 I.U./ml considered to be the minimum protective level. Based on a standard of 280 I.U./ml (Connaught Laboratories, Toronto), the mean antibody level in 20 maternal samples was 0.53 I.U./ml (range: 0.037-2.29). In the 20 paired cord blood samples, the mean level was 0.60 I.U./ml (range: 0.050-2.50). In 55% of cases, the cord blood levels were higher than the maternal levels (0.75 ±0.87 vs. 0.56±0.68). In 13 prematures weighing <2000g the mean antibody level was 0.44 I.U./ml (range 0.053-2.45) which was significantly lower than the level in full-term infants ($p<0.001$). These results provide further evidence for an active transport of antibodies across the placenta during pregnancy and indicate that, since prematures have signficantly lower levels of tetanus antibody than full-term infants, those whose mothers have borderline low protective levels (e.g. 0.03 I.U./ml) may not be passively protected against tetanus in the neonatal period.

● **1023** INTERFERON-ASSOCIATED ENZYME (2'-5'A SYNTHETASE) LEVELS IN INFECTION AND ALTERED IMMUNE STATES. Stanley E. Read and Bryan R.G. Williams. The Hospital for Sick Children, Toronto, Ontario.

The production of 2'-5'A synthetase is stimulated by interferon (IFN) and may play a role in its antiviral, antiproliferative and immunomodulating functions. 2'-5'A synthetase is detectable in the lymphocytes of healthy adult controls at a level of 60±40 pmoles/hr/A_{260}. Of 17 patients with proven bacterial meningitis and/or sepsis, only 2 patients had levels which were greater than 2 S.D. above the mean control level. In contrast, 8 of 10 cases of clinical aseptic meningitis had elevated levels (2 cases with increased levels proven by viral culture). In addition, 5 neonates with proven viral infections (2 disseminated herpes, 2 cytomegalovirus and 1 rubella) had elevated synthetase levels. In 3 normal children with varicella, elevated lymphocyte synthetase was detected on day 2 after appearance of the rash and persisted for 14-21 days. Synthetase was also detected in the vesicle fluid and was greatest at the end of appearance of new lesions. Eight ALL patients in remission who developed varicella showed a delayed rise in lymphocyte synthetase levels.

Lymphocyte levels of 2'-5'A synthetase can normally be boosted in vitro by IFN. In contrast, the enzyme levels in lymphocytes of children with severe combined immunodeficiency (SCID) cannot be enhanced by IFN treatment. Furthermore, unlike normal mononuclear cells, the natural killer cell subpopulation of SCID patients was refractory to IFN stimulation. Whether this reflects the absence of an IFN-reactive lymphocyte subpopulation or the lack of IFN receptors is under investigation.

1024 MATERNAL-INFANT TRANSFER OF NON-ANTIBODY MEDIATED IMMUNITY TO INFLUENZA IN THE MOUSE. Peter D. Reuman, Richard M. Kris, Elia M. Ayoub, Parker A. Small, Jr. Department of Pediatrics, University of Florida, Gainesville, FL.

Previous studies have shown that recovery from influenza involves both humoral and non-antibody mediated (NAMI). To look for evidence of transmission of influenza specific non-serum antibody mediated immunity (NAMI) from mother to infant mouse, we studied five groups of infant mice: (1) CONTROL: born of non-immune control mothers (NIM); (2) IMMUNE: born of fully influenza A (H_3N_2) immune mothers (I+AbM); and (3) BOTH: born of H_3N_2 immune mothers in whom influenza specific serum antibody was suppressed by passive antibody received one day prior to non-lethal influenza infection (I-AbM). In addition, two other groups of infant mice were cross-fostered to determine the route of transmission of NAMI: (4) BREAST: infants of NIM suckled on I-AbM; (5) PLACENTA: infants of I-AbM suckled on NIM. At four weeks of age there was no detectable maternal HI antibody in any sera except sera of fully immune mothers. At four weeks infant mice were separated from their mothers, infected with 100 LD_{50} of H_3N_2 virus, and followed for mortality:

	TRANSFER OF NAMI BY				
	(1)CONTROL	(2)IMMUNE	(3)BOTH	(4)BREAST	(5)PLACENTA
DIED/TOTAL	10/14	0/28	1/12	2/18	5/15
P vs CONTROL	--	<0.001	<0.001	<0.001	<0.05

These data show that influenza specific NAMI (1) is transferred from mother to infant by breast and probably by placenta and (2) protects against death in mice up to 4 weeks of age.

● **1025** USE OF ELECTROPHORESIS OF ROTAVIRAL RNA TO ESTABLISH THE IDENTITY OF STRAINS INVOLVED IN A TERTIARY CARE NURSERY OUTBREAK. Wm. J. Rodriguez, Hyun W. Kim, Carl D. Brandt, Mary K. Gardner & Robt. H. Parrott. Research Fnd of Children's Hospital and GWU School of Medicine & the Health Sciences, Washington, D.C.

Electrophoresis (EP) of rotaviral (RV) genomes was employed to identify RV strains found in nosocomial outbreaks in a tertiary care nursery, in which 22 of 102 infants had RV infection. Enough nucleic acid (RNA) for EP was recovered from viruses in the stools of 17/22 (77%). The time sequence and proximity of RV infected infants in the nursery rooms had suggested two distinct outbreaks with baby-to-baby spread of a single RV strain. However, when RV RNA patterns were analyzed, five distinct patterns were found among viruses from different patients. There were four different RNA electropherotypes identified during each outbreak period. We had evidence of baby-to-baby spread of two distinct RNA electropherotypes in each outbreak period. RNA patterns of these nursery RV strains were similar ("long" gel pattern) to those previously seen in patients from the community. In brief: a) infants hospitalized in a tertiary care nursery can become infected with different RV strains, some similar to those prevalent in the community; and b) secondary spread of individual strains can be traced with considerable accuracy by RNA EP.

● 1026 FIMBRIAE ON TYPE II AND TYPE III GROUP B STREPTOCOCCI: ASSOCIATION WITH VIRULENCE. Neal S. Rote, Ann O. Shigeoka, Sandra R. Kaplan, Harry R. Hill. Univ. of Utah School of Medicine, Depts. of Path., Ob/Gyn, Peds. Salt Lake City, Utah.

Although type-specific carbohydrate antigens induce protective immunologic responses against group B streptococcal infection, other factors also contribute to the virulence of these organisms. We and others have previously reported strain differences within the same serotype in opsonic requirements and virulence. Some strains (R) are relatively resistant to opsonization by antibody and express increased virulence, while other strains (S) are sensitive to opsonization and are less virulent. Neuraminidase decreases the virulence of both type III_S and III_R strains while not affecting II_S or II_R strains. Loss of virulence is associated with the removal of 70% of cellular sialic acid. We examined II_S, II_R, III_S and III_R strains (N=12) by electron microscopy to determine if S and R strains could be differentiated morphologically and if neuraminidase altered the surface topography of these organisms. In 9 of 12 strains hair-like fimbriae were observed extending from the surface. The presence of fimbriae was independent of serotype or S/R type. When fimbriae were present neuraminidase-induced changes in virulence were associated with the complete loss of these structures. Thus, 1) this is the first indication that some strains of serotype II and III group B streptococci express fimbriae on their cell surface, 2) the fimbriae may (type III) or may not (type II) be removed by neuraminidase, and 3) when fimbriae are expressed, their removal is associated with neuraminidase-induced decrease in virulence. These structures may have a critical role in the group B streptococci/host defense interaction.

1027 ANTIMICROBIAL THERAPY(AMT) DURING LABOR: MATERNAL BENEFIT VS NEONATAL RISKS. Charles R. Rosenfeld, Ralph T. DePalma, F. Gary Cunningham, Ken J. Leveno, Micki Roark. Southwestern Med Sch, Depts. Ped & OB/GYN, Dallas, TX.

Maternal intrapartum AMT is of concern to pediatricians as it may mask bacterial infection, inhibit growth in cultures, or lead to empirical AMT in neonates. At Parkland Hospital ~90% of women undergoing Cesarean delivery at term for cephalopelvic disproportion after ≥6h rupture of membranes develop serious uterine infection unless given perioperative antibiotics. We have analyzed pregnancy outcome in 2 groups of such women given AMT before (n=421) or after (n=152) cord occlusion, to determine risk in the neonate for sepsis or empirical AMT, and maternal outcome. Physician concern for neonatal infection, reflected by blood cultures and/or differential cell count, was evident in 23/152 (15%) infants not exposed to AMT in utero compared to 115/412 (28%) infants exposed in utero, p=.01; there was no difference in the incidence of PROM, jaundice, or AMT. Upon evaluation of these 138 infants there was no difference in the incidence of risk factors in the AMT exposed and unexposed infants, and no positive cultures. The economic impact was significant with excess hospital costs in exposed, $248±237 ($\bar{X}$±SD, n=11), and unexposed, but evaluated infants, $156±102 (n=18), significantly greater than infants unexposed and not evaluated, $64±87 (n=30), p<.025. No difference was seen in the incidence of uterine infection between AMT given before, 24%, or after, 21%, delivery. Extrapolating these results to the ~.7 million Cesarean deliveries each year, many coupled with perioperative AMT, excessive hospital costs could be staggering; thus, we recommend that maternal AMT await cord occlusion.

1028 PROGNOSTIC VALUE OF SERIAL ANTIGEN QUANTITATION IN H. INFLUENZAE TYPE B (HIB) MENINGITIS. R. Russell, F. Mather, G. Siber, G. Rosenberg and R. Daum, Dept. of Pediatrics, Tulane University, New Orleans, LA.

To clarify whether capsular antigen concentration in body fluids at admission or rate of antigen clearance during therapy predicts severity of illness in Hib meningitis, we employed the sensitive (≥0.5 ng/ml) latex agglutination assay to study antigen kinetics in 68 patients. Hospital course was classified as mild (Mi) moderate (Mo) or severe (S). Comparisons of admission geometric mean CSF PRP concentrations (Mi 40, Mo 329, S 304 ng/ml) revealed differences of borderline significance (Mi vs S, p=.04) as did urinary PRP concentrations (Mi vs S, p=.04). Admission blood PRP concentration (Mi 20, Mo 43, S 86) did not significantly differ. However, comparisons of highest observed or "peak" blood concentrations which in 25% occurred after admission (Mi 26 Mo 74, S 170) revealed significant differences (Mi vs S, p=.009). All 8 patients with highest observed blood concentrations <1.0 ng/ml had Mi or Mo courses. The duration of antigenemia in days (Mi 13, Mo 13, S 17) did not differ significantly. However, duration of antigenuria increased with severity of disease (Mi 12, Mo 13, S 20) (Mi vs S, p=.003) and best correlated with clinical course. Moreover, all 6 patients with ≤5 days of antigenuria had Mi or Mo courses while all 6 with ≥26 days of antigenuria had S courses. Intermediate duration of antigenuria was without prognostic significance. We conclude that low peak blood concentration, antigenuria of short duration and antigenuria of prolonged duration are correlated with severity of hospital course.

1029 PREVENTION OF H. INFLUENZAE TYPE B (HIB) DISEASE IN INFANT RATS WITH HUMAN HYPERIMMUNE GLOBULIN (HIG). John R. Schreiber, Donna M. Ambrosino, Robert S. Daum and George R. Siber (Spon. by Kenneth McIntosh). Harvard Medical School, Sidney Farber Cancer Institute, Department of Clinical Microbiology, Boston, MA.

From the pooled plasma of 55 adult donors immunized with Hib capsular antigen (PRP) we prepared HIG with 600µg/ml anti-PRP antibody (PRP-Ab) and compared its protective activity in infant rats with that of conventional immune globulin (IG) containing 66 µg/ml PRP-Ab. One day after an ip dose of 0.13cc globulin or saline, serum for PRP-Ab was obtained and 4 doses of 10^5 Hib were given intranasally q12h. Nasal colonization remained 100% in all groups; cumulative bacteremia (cultured d 4, 6 & 8) and meningitis (cultured d 6 & 8) were:

	HIG	HIG	IG	IG	HIG-A*	Saline
Globulin dil.	1/20	1/60	1/2	1/6	1/20	-
PRP-Ab dose (µg)	3.9	1.3	4.3	1.4	0.03	0
No. of pups	28	20	8	9	10	28
Day 1 PRP-Ab (ng/ml)	887	260	549	280	< 100	< 100
Bacteremia (%)	28	60	25	63	100	100
Meningitis (%)	12	30	13	38	70	86
Death (%)	0	10	13	11	10	25

(*Absorbed with PRP). Pups maintaining serum PRP-Ab >50ng/ml to day 8 (n=16) vs pups with < 50ng/ml (n=117) had 19% and 86% bacteremia respectively (p< .001) and 6% and 44% meningitis (p< .01). We conclude that HIG contains ten times more protective activity than IG and that protection is due to PRP-Ab. HIG may be useful in the prophylaxis of Hib disease in high-risk children.

● 1030 ROLE OF CAPSULAR AND NONCAPSULAR ANTIBODIES IN PROTECTION AGAINST EXPERIMENTAL HAEMOPHILUS INFLUENZAE TYPE b INFECTION. Jerry L. Shenep, Stephen J. Barenkamp, Robert S. Munson, Jr. and Dan M. Granoff, Wash. Univ. Sch. of Med., St. Louis Children's Hosp., St. Louis.

Antibodies (Ab) to capsular and noncapsular antigens of Haemophilus influenzae type b (Hib) confer protection against experimental Hib disase. However, the antigenic specificities of protective noncapsular Ab have not been defined. Hib rabbit antisera were sequentially absorbed with type b capsule (PRP) and Hib lipopolysaccharide (LPS), both coupled to sepharose 4B. Affinity purified Ab were eluted from the solid phase. Adequacy of serum absorption and titers of affinity purified Ab were monitored by RIA or ELISA. Affinity purified anticapsular Ab, anti-LPS Ab, and immune serum absorbed to remove LPS and PRP Ab but containing high titers of Ab to outer membrane proteins, were all bactericidal in vitro. Infant rats were passively protected (absence of bacteremia in 30% of animals following IP challenge) by as little as 90-250 ng of PRP Ab per rat. In contrast, 1000 fold more affinity purified anti-LPS Ab (or anti-LPS Ab in hyperimmune serum prepared against boiled bacterial cells) failed to prevent bacteremia (10^3-10^5 cfu/ml blood). But immune serum absorbed with PRP and LPS and containing Ab to outer membrane proteins was highly protective. Protection by the latter could be removed by absorption with Hib outer membrane. In conclusion, Ab against PRP and outer membrane proteins are bactericidal and protective. However, anti-LPS Ab, although bactericidal, is not protective. These results support the inclusion of outer membrane proteins in experimental vaccines for prevention of Hib disease in children.

1031 FAILURE PROOF SUPRAPUBIC BLADDER ASPIRATION. Shyan Sun, Kamtorn Vangvanichyakorn, Zaneida Aranda, Anita Baldemero. (Spon. F. Behrle) New Jersey Med. School Dept. Neonatology, Newark, New Jersey

Despite refinements in the counting technique of urine for bacteria and white cells, there are many difficulties in obtaining voided specimens which are uncontaminated, particularly with infants. These can lead to major problems in interpretation. Percutaneous suprapubic aspiration of the urinary bladder has proved to be easy, safe and a useful method of obtaining urine for accurate diagnosis of urinary tract infection. It has been our impression that the failure rate was quite high among junior house staff. An in-house survey of 25 pediatric residents (1st year to 3rd year) revealed a surprisingly high failure rate ranging from 100% to at least 20%. The general consensus among the house staff was that the major cause of failure was tapping an empty bladder. Since a bedside real time ultrasonography machine (ATL Mark III) became available a year ago, we have routinely scanned the urinary bladder just above the symphysis pubis area before the procedure. Suprapubic tap was performed only after the bladder was identified and full. After more than a dozen procedures, the failure rate was zero. The technique is easy and simple. A full bladder is clearly defined on the screen and the needle is visible when it is being introduced. The obvious danger is perforation of viscera near the bladder. This risk is best avoided by ensuring that the bladder is full by ultrasonography. Unnecessary time, effort, trauma, and pain can be saved by performing bedside urinary bladder ultrasound scanning prior to suprapubic bladder aspiration.

1032 SIBLINGS OF PATIENTS WITH HAEMOPHILUS (HIB) MENINGITIS SHOW IMPAIRED IgG AND IgM ANTIBODY RESPONSES TO HAEMOPHILUS VACCINE. Janet Squires, Dan M. Granoff, Robert S. Munson, Jr., Brian Suarez, and Wm. Hankins, Wash. Univ., St. Louis Children's Hospital and Connaught Labs.

In a preliminary study (ICAAC), type b (PRP) Ab responses to PRP-pertussis vaccine (Lederle) were found to be impaired in siblings (S) of patients with Hib meningitis. In the present study, the sample size has been increased and we present data on total Ab to PRP (by RIA), IgG and IgM Ab to PRP (by SPRIA), and the IgG responses to pertussis (by SPRIA). 21 sibs, ages 9-23 mos, were immunized (2 injections separated by 1 mo). The Ab responses of the S were compared to the responses of 21 immunized controls (C) matched for age and race but without a family history of Hib disease. S were divided into 2 groups, those who were born after the case and who were not exposed to Hib disease (S1, N=13), and those who were alive at the time of the case (S2, N=8).

		Antibody to PRP (Median, ng/ml by RIA)			Fold Increases in Ab (Geo Mean, 2 Mos)			
Group	N	Pre	1 Mo	2 Mos	Anti PRP		Anti Pertussis	
C	21	28	430	1128	24.0	p=.03	4.0	
S-1	13	29	230	204	6.8		4.0	N.S.
S-2	8	244	544	519	1.6		2.7	

1/3 of the responses to PRP were restricted to the IgM class and 2/3 were both IgM & IgG. At 2 mo, the geo. mean fold increases in IgG & IgM Ab were greater for C than S (IgG:3.6 compared to 1.4 & 1.2 for S1 & S2; IgM:2.6 compared to 1.1 & 1.0 in S1 & S2, $p<.05$). In conclusion, S show normal Ab to pertussis but not to PRP. The deficiency in S appears to reflect both IgG & IgM responses.

1033 INFANTS AND CHILDREN PRODUCE IgG TO SPECIFIC OUTER MEMBRANE PROTEINS (OMP) OF HAEMOPHILUS INFLUENZAE b (Hib). David H. Smith, Marilyn R. Loeb. University of Rochester, Dept. of Pediatrics, Rochester, NY 14642.

Earlier studies indicated that antibodies to non-capsular antigens of Hib are widely distributed among humans, bactericidal (BC) in vitro and protective in an infant rat model of Hib meningitis. We have been studying the role of Hib OMP in pathogenicity and of specific antibodies in human immunity. The composition of Hib OMP as assessed by SDS-PAGE electrophoresis shows strain variation but 3 of the 7 major proteins appear to be constant.

The IgG response to specific OM proteins has been analyzed using a radioimmune assay of SDS-PAGE gels of the OMP of a single Hib isolated in 1972 in Boston. Ten of 11 healthy children and adults had specific antibodies; the number and type of antibodies varied with patient age. All 23 patients ($17<2$ yrs, $6\geq 2$ yrs) from various communities recuperating from systemic Hib disease produced antibodies to Hib OMP; those younger than 2 years produced an average of 8 antibodies; older patients produced an average of 14 antibody types. All patients produced IgG to at least 1 of the common OMP. Continuing studies with monoclonal antibodies indicate that some antibodies to OMP are BC in vitro.

These data indicate a wide cross-reactivity of these proteins, that infants who are poor producers of antibody to Hib capsule can make antibodies to Hib OMP and suggest further studies of certain of the common OMP as potential vaccine constituents.

1034 ANTIBODY RESPONSES OF TWO-YEAR-OLD CHILDREN TO TWO *HAEMOPHILUS INFLUENZAE* B VACCINES: CAPSULAR POLYSACCHARIDE (PRP) AND PC, A PROTEIN-PRP COMPLEX FROM THE BACTERIAL MEMBRANE. David H. Smith, Pari Farsad, Porter Anderson, Richard A. Insel, Thomas Petrusick and Mathuram Santosham. Univ. of Rochester School of Medicine, N.Y.; Univ. of Texas Medical School at Galveston; Baltimore City Hospital. Depts. of Pediatrics.

The antibody (Ab) response of infants to purified (p)PRP vaccine is inadequate for protection until about age 18 mo. In weanling rabbits (also unresponsive to pPRP) PC had been shown to induce a vigorous anti-PRP response in a "booster"pattern.

The immunogenicity of pPRP and PC were compared in 2-yr-old children, in which an immature but measurable response to pPRP is expected. Two s.c. injections of pPRP (10 µg) or PC (50 µg protein, 2.5 µg PRP) were given 2 mo apart to 17 and 18 subjects respectively. Adverse reactions were negligible. With pPRP there was a primary (1°) response but no significant secondary (2°). With PC there were significant anti-PRP responses to both 1° and 2° injections.

	Geometric mean anti-PRP Ab, ng/ml		
Vaccine	Pre-immunization	Post-1°	Post-2°
pPRP	140[a]	580[b]	750[c]
PC	92[d]	520[e]	950[f]

significant at $p < 0.05$ by paired t test: a vs b, d vs e, e vs f.

Increases in Ab to the somatic components of PC were found in most subjects, but bactericidal Ab responses after PC were all PRP-directed. The booster response observed with PC encourages further study of the concept of presenting PRP with carrier protein for immunoprotection of the immature human.

1035 SYSTEMIC INFECTION WITH MULTIPLE STRAINS OF CYTOMEGALOVIRUS ASSESSED BY RESTRICTION ENZYME DIGESTION ANALYSES: Stephen A. Spector (Spon.by James D. Connor) University of California, Department of Pediatrics, San Diego.

Restriction endonuclease digestion analyses (REDA) of the human CMV genome have demonstrated marked heterogeneity among epidemiologically unrelated CMV isolates. REDA of longitudinal CMV cervical isolates suggest that women can have cervical infections with multiple strains of CMV. It is unknown if individuals may have a systemic infection with more than one CMV strain. To help answer this question, premature identical twins who acquired CMV infections while hospitalized during their first 2 months of life were studied. REDA of their original CMV isolates indicated that the infants were infected with different strains of CMV. Following discharge home of the babies at 3 months of age, they slept in the same crib, shared the same toys and were in frequent close contact with each other. Longitudinal assessment of the infants indicated that they continued to excrete CMV in their urine for at least 2 yrs following their initial infection. REDA of the twins' viral isolates at 2 yrs indicated that they maintained their initial CMV strains and that there was no evidence of viral transmission between the children. Follow-up of the twins' mother, however, indicated that 3 months following the infants discharge home that she developed a primary CMV infection. REDA of her viral isolate indicated that she was infected with the identical strain as one of her twins. These findings suggest that normal individuals do not develop concomitant systemic infections with multiple strains of CMV, and that it should be possible to develop an effective CMV vaccine.

1036 STUDIES OF ALPHA (∝) HEMOLYTIC STREPTOCOCCI (∝-S) IN ICU NEONATES IMPLANTED WITH STRAIN 215 OF∝-S. K. Sprunt, G. Leidy, W. Redman, Dept. Pediatrics, College of Physicians & Surgeons, Columbia University, New York, N.Y. 10032.

Conversion of abnormal oropharyngeal colonization to "normal" in ICU neonates by pharyngeal implantation of strain 215 from a normal neonate was reported. Strain 215 in competition with other strains of∝-s as they arose in vivo was studied in detail in 5 infants who yielded only the implant strain following the procedure (4-18 days). Strain 215 comprised at least 90% of the ∝-s populations in 2 infants for approximately two weeks with another strain yielding 10% or less. 3 infants showed a rapid rise to dominance of a strain other than 215: the subsidence of this 2nd strain with rapid emergence to dominance of a 3rd was shown for 2 of the 3 infants. Strains arising subsequent to implantation differed from strain 215 in at least 2 markers.

The effect of antibiotic therapy (Rx) subsequent to implantation was studied in 3 infants. In∝-s populations, dominance of strain 215 prior to, during and subsequent to Rx was shown for one infant, decline of 215 to undetected levels and reemergence to dominance after Rx was shown in another infant, and its dominance subsequent to Rx occurred in a 3rd infant who had 20% or less of strain 215 in mixed ∝-s populations after implantation.

Competition of the implant strain with another strain varies in vivo. Antibiotic Rx subsequent to successful implantation allows dominance or reemergence to dominance of 215.

1037 LOSS OF VACCINE INDUCED ANTIPNEUMOCOCCAL ANTIBODY IN CHILDREN WITH NEPHROTIC SYNDROME. John S. Spika, G. Scott Giebink, Chap T. Lee, Neal A. Halsey, Brian A. Lauer and Gerald Schiffman, Depts. Pediatrics and Biometry, Univ. of Minnesota, Minneapolis, Dept. Pediatrics, Univ. of Colorado, Denver, and Dept. Microbiology, Downstate Med. Ctr., Brooklyn.

Twenty-five patients with steroid responsive idiopathic nephrotic syndrome (SRNS) were vaccinated with a polyvalent pneumococcal vaccine. Serum was obtained pre-vaccination, 1,6 and 12 months after vaccination and during disease relapse. Total type-specific pneumococcal antibody concentration (ABY), measured by radioimmunoassay, was expressed as ng of anticapsular antibody nitrogen (ngN)/ml.

Patients were divided into three groups(gr): gr I-no relapse (n=11), gr II-relapse during the study period but serum not obtained within three weeks of relapse(n=10), gr III-serum obtained at the time of relapse (n=7). Linear regression lines were determined for each anticapsular-type antibody for each patient. An average slope was calculated for each anticapsular type within a patient group. No differences were found between gr I and II with regard to rate of antibody decline, but at one year gr II patients had mean ABY <200 ngN/ml against types 4,7,8,14 and 19. Gr. III had a more rapid decline in ABY against types 6A, 8 and 19 ($P<0.03$), and types 1,4,7,9 and 18 ($P<0.1$). At one year, ABY for gr III was <200 ngN/ml against types 4,6A,7,8,19 and 23.

Patients with SRNS may not maintain protective levels of antibody (≥200 ngN/ml) against many vaccine polysaccharide types during relapse and those who have relapsed may not have protective levels of antibody at one year while in remission.

1038 SINGLE DOSE PHARMACOKINETICS OF CEFTRIAXONE IN NEONATES, INFANTS, AND CHILDREN. Russell W. Steele, Linda B. Eyre, Robert W. Bradsher. Dept. of Pediatrics and Medicine, University of Arkansas for Medical Sciences and Arkansas Children's Hospital, Little Rock, Arkansas.

Thirty pediatric patients with bacterial meningitis were enrolled in a study designed to determine serum and cerebrospinal fluid concentrations of ceftriaxone after a single intravenous dose. The safety and tolerance of single dose administration was also evaluated. Drug was given 2-5 days into conventional treatment when the patient was considered stable. Without alteration of the antimicrobial regimen, either a 50 or 75 mg/kg dose of ceftriaxone was infused over 10-15 min. This study was randomized so that half of the patients received each dose. Plasma samples were obtained at times 0, 15 min, 30 min, 1 hr, 2 hr, 6 hr, and 12 hr, and CSF 1-8 hr after administration and assayed by specific HPLC methodology. Analysis of data is currently being completed. The mean ± S.D. values of pharmacokinetic parameters were maximum plasma conc., 216±66 µg/ml; elimination half life, 5.5±2.0 hr; plasma clearance, 55±23 ml/hr/kg; and apparent volume of distribution 395±55 ml/kg. Both plasma clearance and volume distribution were approximately 3-fold larger than the corresponding parameters observed in healthy adult subjects receiving a 27 mg/kg dose of ceftriaxone. The CSF concentrations measured 2-8 hr after the dose varied considerably but usually exceeded by many fold the susceptibilities of all organisms except for two isolates of Listeria. No untoward side-effects were noted except some local discomfort during the infusion.

1039 QUANTITATIVE CORRELATION BETWEEN PULMONARY H_2 ELIMINATION AND BACTERIAL COLONIZATION OF THE GUT IN PRETERM INFANTS. David K. Stevenson, Susan M. Shahin, Clinton R. Ostrander, Ronald S. Cohen, and Anne S. Yeager. Dept. of Ped., Stanford Univ. Sch. of Med., Stanford, CA

Since H_2 is only produced by bacteria colonizing the gut and is excreted via the lungs in proportion to total production, the amount of H_2 in breath when the intake of carbohydrate is constant might be expected to correlate with the quantity of H_2-producing colonic bacteria. We observed changes in breath H_2 in infants without apparent changes in carbohydrate tolerance. Eleven preterm infants who were not receiving antibiotics and who were tolerating a constant carbohydrate load/feeding were studied. The change (Δ) in end-tidal H_2 concentration (ETH_2) was correlated with the bacterial colony count in stool. Stools were collected on a swab using a standardized method. The swabs were either innoculated onto anaerobic media at the bedside or transported in PBS for innoculation on aerobic plates. Colony counts were expressed as total bacteria/sample. No stools contained anaerobic bacteria. There was a significant correlation ($p<.001$) between the Δ in ETH_2 and the Δ in absolute number of aerobic gram negative bacteria ($y=.96 \times -4.5$; $n=27$; $r=.73$). Seven of 9 infants with increases in $ETH_2 \geq 20$ ppm also had increases in colony counts $\geq 10^6$. All of 3 infants who had decreases in $ETH_2 \geq 20$ ppm also had decreases in colony counts $\geq 10^6$. These data are consistent with the hypothesis that changes in the number of H_2-producing bacteria in the gut contribute to changes in the pulmonary elimination of H_2 in preterm infants who do not have clinical evidence of carbohydrate intolerance.

1040 DIMINISHED BACTERICIDAL CAPACITY FOR GROUP B STREPTOCOCCUS IN "STRESSED" AND NON-STRESSED NEONATES. J. Stroobant, M.C. Harris, C. Cody, S.D. Douglas, R.A. Polin. Univ. of Pa. Sch. of Med., Dept. of Peds., Children's Hospital of Philadelphia, Philadelphia, PA.

The increased susceptibility of the newborn infant to bacterial infection is primarily due to impaired host defenses. Stress may be an additional factor which can further compromise immune function. The purpose of this study was 1) to compare neutrophil (PMN) killing in newborn infants and adults; 2) to determine the effect of stress on the bactericidal capacity of neonatal PMNs. PMNs were obtained from 3 groups: 26 adults, 13 healthy neonates (B.W. 3239.2 ± 208.9 g (m ± SD), GA 38.8 ± 1.3 wk.), and 29 "stressed" neonates (B.W 1935.8 ± 891.1 g, GA 32.9 ± 4.3 wk.). The "stressed" population included infants with RDS (n=24), aspiration syndromes (n=3), and sepsis (n=2). 28 of 29 required mechanical ventilation. PMN monolayers on coverslips were incubated with type Ic group B streptococcus (GBS) in 10% adult serum. Coverslips were stained with acridine orange, and bacterial killing was assessed using a fluorochrome microassay. Killing was expressed as number of dead organisms/total number phagocytosed X 100. PMNs from "stressed" infants killed significantly fewer GBS than adult PMNs: (60 min., "stressed" 48.3 ± 10.4, adult 57.0 ± 9.3, $p < .001$; 90 min., "stressed" 56.3 ± 11.0, adult 67.5 ± 10.1, $p<<.001$). PMNs from healthy infants demonstrated reduced killing vs. adults: (60 min., healthy 47.7 ± 7.5, adults 53.7 ± 6.4, $p < .005$; 90 min., healthy 55.2 ± 10.4, adult 66.6 ± 7.9, $p<<.001$. There was no significant difference between "stressed" and healthy neonates. In summary, the bactericidal capacity of neonatal PMNs is diminished; however, it is not further compromised by stress.

● **1041** EPSTEIN-BARR VIRUS-INDUCED INFECTIOUS MONONUCLEOSIS IN INFANTS AND PRESCHOOL CHILDREN. Ciro V. Sumaya and Yasmin Ench. University of Texas Health Science Center, Department of Pediatrics, San Antonio, Texas.

Our ongoing prospective study of EBV-induced infectious mononucleosis in children has revealed that this disease is not uncommon in infants and preschoolers. This paper will focus on the frequency, clinical manifestations, heterophile antibody responses, EBV-specific antibody responses, and EBV excretion observed in these very young patients. Sixty of 139 children diagnosed to have EBV-induced infectious mononucleosis over a 5-year period were less than 6 years old; 8 other young patients had a similar clinical illness unassociated with an EBV infection. In addition to the usual typical cases, atypical syndromes with prominent manifestations in other organ systems, histiocytosis-like skin eruption, or failure to thrive pictures were occasionally documented. Heterophile antibody responses increased stepwise from 0% in infants less than 1 year old to adult-type rates of 80% by 4 year olds. The young patients had more transient IgM antibody responses to EBV-capsid antigen, a low but still higher rate of antibodies directed to restricted component of EBV-early antige and an earlier onset of antibodies to EBV-nuclear antigen than older children and adults. EBV was present in oropharyngeal secretions in 44 (73%) young children sampled during the acute phase, a rate similar to that in adult patients. It appears that EBV-induced infectious mononucleosis is not a rare entity in the very young. Since heterophile antibody frequently may not be detected in these age groups, EBV-specific antibody responses may be necessary for making the diagnosis.

1042 NK OBSERVATIONS DURING A DOUBLE-BLIND COMPARISON OF BID VS. QID CEPHALEXIN FOR GROUP A STREPTOCOCCUS PHARYNGITIS. Martha Tarpay, Stephen A. Chartrand, Cathy Hopkins, Alan Cox, and Melvin I. Marks. University of Oklahoma Health Sciences Center, Dept. of Pediatrics, Oklahoma City, OK.

Fifty-six children 3-21 years of age with culture proven group A Streptococcus pharyngotonsillitis were treated with cephalexin bid vs. qid in a double-blind fashion. Patients were seen at the beginning of treatment, 10 and 24 days later. Initial throat cultures were processed for group A Streptococcus, virus, chlamydia, mycoplasma and B-lactamase producing bacteria; throat cultures for strep and blood for ASO, anti-DNase and streptozyme were obtained on each visit. Compliance was evaluated by counting residual medicine and by M. lutea bioinhibition of urine.

Herpes simplex was isolated in 1 patient; all other viral, chlamydial and mycoplasma cultures were negative. B-lactamase producing organisms were present in all except 1 throat culture and represented < 1 up to 97% of the nonstrep throat flora. A total of 38 patients returned for all 3 visits. Antibiotic treatment was initiated within 72 hours after onset of symptoms in 22/38, and at 96 hours or later in 16/38. There were no significant differences in the geometric means of the anti-DNase B-titers between early and late treatment groups at the onset of therapy and on followup evaluation. Significant increases (a rise of 2 dilution increments or ≥ 0.2 log) in anti-DNase B occurred in 13% of the patients with early therapy and 58% with delayed treatment ($p = 0.05$). Compliance was good in 76% of patients and poor in 8%. Bacteriologic failure occurred in only 1 of 56 patients.

1043 PERSISTENCE OF PROTECTIVE PNEUMOCOCCAL ANTIBODY FOLLOWING VACCINATION IN PATIENTS WITH THE NEPHROTIC SYNDROME. A. Tejani, K. Gurumurthy, S. Fikrig, and G. Schiffman, SUNY, Downstate Medical Center, Departments of Pediatrics and Microbiology, Brooklyn, N.Y.

We have determined the level of persisting pneumococcal antibody in a group of nephrotic children vaccinated by us 5 years ago. (Fikrig et al., J. Infect. Dis. 137:818, 1978). Of the 19 vaccinated children, 2 have died, and one has moved away. Sera from the remaining 16 patients were examined by radioimmunoassay to determine the antibody response to 11 of the 14 types contained in the polyvalent pneumococcal vaccine. The lowest protective level of geometric mean titre (GMT) of antibody in our laboratory (G. Schiffman) is 300 ng/ml. Fifty-six % (9/16) patients showed adequate GMT 5 years post vaccination. All 9 patients had minimal change nephrotic syndrome (MCNS). Forty-four % (7/16) children had a GMT less than 300 ng/ml. Three of these patients had focal sclerosis, 3 had membrano proliferative glomerulo nephritis (MPGN) and 1 patient had IgM nephropathy. Of these 7 patients one with the lowest GMT (23 ng/ml) developed pneumococcal peritonitis. During this same period, in 20 other unvaccinated nephrotic patients followed continuously from 76-81, 7 cases of peritonitis occurred ($p < .05$). Additionally, 1 unvaccinated child died of pneumococcal sepsis. We conclude that pneumococcal vaccination provides long lasting immunity in MCNS patients and that vaccinated nephrotic patients with diseases other than MCNS should be evaluated annually for presence of adequate antibody.

1044 TOXIC SHOCK SYNDROME: CLINICAL EFFECT OF STEROID TREATMENT. James K. Todd, Marilyn Ressman, Sharon A. Caston, Andrew M. Wiesenthal. C. Henry Kempe Center for Investigative Pediatrics; Departments of Pediatrics and Pathology, The Children's Hospital; Denver.

Toxic shock syndrome (TSS), in its most severe form, can cause shock; pulmonary, cardiac, and renal failure; and death. Corticosteroid (CS) therapy is often empirically used in such situations. We retrospectively compared the outcome of 38 patients with TSS, 20 having received CS and 18 not (NCS). All patients met the Center for Disease Control strict definition, were hospitalized, had a proven or potential focus of Staphylococcus aureus infection, received appropriate antistaphylococcal antimicrobial therapy, and had shock or postural hypotension. Groups were compared by the Mann-Whitney U test for nonparametric, unpaired data. There were no significant differences between the CS and NCS groups when analyzed (mean ± S.D.) for age (18.8 ± 18.1), sex, month and year of admission, day of illness admitted (3 ± 1.2), maximum severity of illness, maximum fever, or weight. Patients with TSS of this initial severity not treated with corticosteroids had fever for 5.8 ± 2.9 days and required supportive therapy until 7.6 ± 3.2 days. Patients in the CS group received a total dose of 36 ± 25 mg/kg CS (prednisone equivalent) for 6.4 ± 3.7 days. CS therapy reduced duration of fever ($p < 0.05$) if given within 3 days of TSS onset, however, a concomitant reduction in severity of illness could not be documented. A prospective, randomized, placebo-controlled trial of CS therapy in early severe TSS is recommended.

1045 CLINICAL & PHARMACOKINETIC EVALUATION OF CEFOTAXIME (CTX) IN INFANTS & CHILDREN. M. Varghese, A.J. Khan, K. Kumar, H.E. Evans. Dept. of Ped. Jewish Hosp Med Ctr/SUNY Downstate Med. Ctr. Brooklyn, NY

CTX, a new cephalosporin with expanded spectrum of activity has not been studied in infants & children. 26 patients (mean age 4 yrs), including 10 with Pneumonia, 11 soft tissue infections and 3 with urinary tract infections (UTI) were treated with average doses of 60 mg/Kg per day given parenterally in 4 divided doses. Etiological organisms isolated from 16 patients (H. influenzae, S. Pneumoniae, S. aureus, S. Pyogenes and E. Coli.) were sensitive to CTX (zone size ≥ 23mm). The MICs ranged from 0.06 to 2.0 mcg/mL (mean 0.69). All patients improved clinically by 5th day of therapy. Primary pathogens in each case were eradicated. None developed clinical side effect(s). CBC, liver & renal function monitored serially remained normal except transient elevation of SGOT & alk. phosphatase in 1 case each. Pharmacokinetics were determined following the last dose in 11 patients. Mean (± 1SD) levels (mcg/mL) with a dose of 50 mg/Kg are presented in the table. The peak levels were more than 100

mg/Kg	N	½h	½h	1h	2h	4h	8h	t½(min)
50 IV	5	115	59	30	13.4	2.6	1	64.93
		(22.36)	(23.02)	(11.18)	(6.98)	(0.89)	(0)	(16.89)
50 IM	6	125	58.33	29.1	14.1	4.5	1	72.81
		(41.8)	(18.63)	(10.2)	(5.3)	(3.67)	(0)	(3.1)

times higher than the mean MICs of the organisms. The t½ with IM dose was slightly longer than with IV ($P > 0.05$). CTX appears to be a safe, effective antibiotic for children. Its efficacy in meningitis reported in adults needs further evaluation in children

1046 QUANTITATIVE CULTURES AND GRAM STAINS OF MIDDLE EAR EFFUSIONS IN ACUTE OTITIS MEDIA. Ellen Wald, Dale Rohn, Univ. of Pittsburgh Sch of Med., Children's Hosp. of Pittsburgh, Dept. of Peds., Pgh., PA (Spons. by Richard Michaels).

The antibiotic susceptibility of certain bacteria is markedly affected by inoculum size. In patients with acute otitis media (AOM), clinical response to antibiotic treatment and persistence of middle ear effusion (MEE) may conceivably be influenced by initial MEE colony counts. To determine the usual bacterial burden in patients with AOM quantitative bacterial colony counts were performed on 46 samples of MEE recovered by tympanocentesis. On 25 of the samples Gram stains were performed and read independently. Significant bacterial isolates were recovered in 30 (65%) instances. In 3 samples the colony counts were $<10^2$ colony forming units (cfu)/cc while in 27 samples the colony counts ranged from 10^2 to $\geq 10^4$ cfu/cc.

ORGANISMS	Total	$<10^2$	10^2	10^3	$\geq 10^4$ cfu/cc
S. pneumoniae	19	3	3	5	8
H. influenzae	6	0	2	1	3
B. catarrhalis	1	0	0	1	0
Non-hemolytic strep	1	0	1	0	0
P. aeruginosa	3	0	0	1	2
	30	3	6	8	13

Organisms were seen on Gram stain in 8/10 instances when the colony count was $\geq 10^4$ cfu/cc, but in only 3/15 instances when the colony count was $<10^4$ cfu/cc. We conclude that (1) bacterial colony counts in MEE of patients with AOM is $\geq 10^4$ cfu/cc in 50% of cases, and (2) as in other body fluids, positive Gram stains in MEE are helpful in predicting high bacterial colony counts.

1047 USE OF A LATEX AGGLUTINATION TEST TO DETECT STAPHYLOCOCCAL AUREUS PROTEIN A AND COAGULASE IN PLASMA FROM INFECTED ANIMALS. Daiming Wang and Robert Bortolussi. (Spon. by Richard B. Goldbloom) Dalhousie University, Izaak Walton Killam Hospital for Children, Halifax, Canada.

A S. aureus latex agglutination (SALA) test has been developed using latex particles coated with fibrinogen and IgG. The test can be read in 3 minutes and detects coagulase (binding to fibrinogen) and Protein A (binding to IgG) which are produced by S. aureus. Purified protein A (1 µg/ml) or crude coagulase were detected equally well when suspended in saline or plasma at 37°C, thus suggesting that these 2 bacterial products were not neutralized under these conditions. We wondered, therefore, if the test might also detect these extracellular products in vivo and developed animal models for S. aureus bacteremia, osteomyelitis, empyema and peritonitis to examine this possibility. Before S. aureus infection, plasma obtained from all 54 animals were negative by the SALA test. After I.P. or I.V. injection with S. aureus, 76% (22/29) of bacteremic animals had positive tests compared to only 21% (3/14) nonbacteremic animals ($p<0.05$). The 11 animals with osteomyelitis, empyema or peritonitis with culture confirmed deep tissue infection but sterile blood cultures all had positive SALA tests when their plasmas were tested (but not their serum). In the 3 animals with osteomyelitis the SALA test remained positive until the animals died or their infection was cleared by antibiotics (confirmed at necropsy). Control animals infected with S. epidermidis, E. coli or streptococci all had negative SALA tests. The test appears to detect protein A and coagulase of S. aureus in vivo and may have useful clinical applications.

1048 VARICELLA ZOSTER VIRUS(VZV) ANTIBODY LEVELS (Ab) IN NEONATES AFTER ZOSTER IMMUNE GLOBULIN(ZIG). Elaine E L. Wang, Charles G Prober, Ann M Arvin (Spon. by R. Gold). University of Toronto, The Hospital for Sick Children, Toronto, Ontario, and Stanford University Medical School, Stanford, California.

Infants in our Nursery received 1 ml of ZIG,(approx. 0.59 cc/kg) intramuscularly for chickenpox prophylaxis within 72 hr of exposure to a nurse with herpes zoster. A serum specimen was obtained from 32 infants <2 mos old prior to ZIG. Repeat specimens were obtained from 13 and 27 patients at 72 hr and 6 wk resp. after ZIG. Ab to VZV were measured by radio-immunoassay and expressed in $\log_{10}$ units. VZV Ab for different birthweights were:

BW	<1000 GM	1001-2000	>2001
No. of Patients	5	11	16
Mean Ab(± SEM)	3.84(± 0.7)	5.24(± 0.4)	4.76(± 0.28)

No significant difference in Ab was found between the 3 BW groups. Compared to nontransfused babies, there was no difference in Ab in 6 babies after multiple packed red cells nor in 5 babies after fresh frozen plasma. One baby in each BW group had low initial Ab(<3.6). One of these babies and one additional 6 mos old had no detectable Ab. A 4-fold rise in Ab was demonstrated in 5 of 13(38%) and 8 of 19(42%) patients at 72 hr and 6 wk resp. after ZIG. These babies were indistinguishable from the others in BW, gestational age, postnatal age, pre-ZIG Ab, weight when ZIG given, illness severity, and transfusion histories. A stable or higher level of VZV Ab was found at the 6-wk followup in 18 of 29(62%) infants. This study confirms the transplacental passage of VZV Ab even to preterm infants < 1000 gm.

1049 NATURALLY ACQUIRED HEMOPHILUS INFLUENZAE TYPE b (HIB) CAPSULAR POLYSACCHARIDE (CP) ANTIBODY (Ab) IN A HIGH RISK POPULATION. Joel I. Ward, Milton K. Lum, Kelly Burkart, Richard A. Insel, Thomas R. Bender. (Spon. by B. Anthony) Dept. of Pediatrics: Harbor-UCLA Med. Ctr., UCLA; Univ. Rochester NY; CDC, Anchorage, AK.

Alaskan Eskimos have the highest known incidence of HIB disease. The disease risk is concentrated during infancy (3%) in first year. In Eskimo children older than 2 years, levels of Ab to CP are significantly greater (3-fold) than in U.S. controls. To characterize Ab to HIB CP in Eskimos, we used RIA and ELISA and determined the proportion of Ab inhibited by E. coli K100 CP.

Age	(Mean Conc.(ng/ml) RIA	ELISA	Mean Percent IgG	IgM	IgA
1 yr (N=5)	449	356	7%	88%	5%
2 yr (N=11)	567	824	8%	85%	7%
3 yr (N=10)	573	1160	9%	81%	10%
4 yr (N=21)	897	1256	15%	78%	8%
Adult (N=23)	2018	1470	21%	72%	7%

In children <5 yrs., 86% had >25% Ab inhibitable by E. coli K100 CP. In spite of high maternal Ab (RIA: mean 0.47 µg/ml) varied from 1% to 99% of the maternal level. IgM is the predominant Ab to HIB CP in this population, which results in reduced transplacental Ab. The large proportion of children with Ab inhibited by K100 CP suggests that cross-reacting bacterial antigens contribute to natural levels of HIB Ab. A means to increase levels of passive IgG in young infants or to hasten the acquisition of IgM antibody might provide a means to prevent disease in this and other populations.

1050 RESPONSE TO PNEUMOCOCCAL VACCINE (PV) IN CHILDHOOD ACUTE LYMPHOCYTIC LEUKEMIA (ALL). Leonard B. Weiner Ernest M. Post, Judith B. Allen, Harry A. Feldman and Gerald Schiffman. SUNY Upstate Medical Center, Depts. of Pediatrics and Preventive Medicine, Syracuse and SUNY Downstate Medical Center, Depts. of Microbiology and Immunology, Brooklyn.

In a prospective study of dodecavalent PV, 28 children with ALL, 2.6 to 16.8 years old, had antibody concentrations measured pre-immunization (PRE) and 30 days post-immunization (POST). We found that the geometric mean titers (GMT) of antibody to 7 of the 12 serotypes were > 200 ng/ml POST, but that 3 (serotypes 1, 8, and 12) had also been > 200 ng/ml PRE. There was at least a 2-fold rise in GMT for 8 of the 12 serotypes. The numbers of patients with antibody concentrations > 200 ng/ml were:

Serotype	1	3	4	6A	7	8	9	12	14	18	19F	23
PRE	23	8	5	3	4	24	2	18	5	9	0	17
POST	26	23	12	10	15	25	16	23	14	18	8	19

For 8 of the 12 serotypes, POST levels were correlated to the PRE levels for each patient ($r > 0.5$, each $p < 0.01$). The patients' treatment status at the time of immunization affected the grand GMTs (all 12 serotypes combined) as follows:

	On Chemotherapy	Off Chemotherapy	t	p
PRE	49 (N=20)	109 (N=8)	1.83	NS
POST	168	548	2.07	$p < 0.05$

Only 2 of the patients on chemotherapy were in relapse.

The data indicate that antibody concentrations considered to be protective against infection are not achieved by the administration of pneumococcal vaccine to children with ALL receiving chemotherapy.

1051 LOW RISK OF INFECTION WITH VENTRICULOSTOMY CATHETERS (VC) USED FOR INTRACRANIAL PRESSURE (ICP) MONITORING. Leonard B. Weiner, Robert K. Kanter, Anne Marie Patti, Elisabeth M. Post and Michael P. Owen. (Spon. by Frank A. Oski) SUNY Upstate Medical Center, Depts. of Pediatrics and Neurosurgery, Syracuse, New York.

VC are useful in monitoring ICP in the critically ill brain injured pt. but may cause ventriculitis. We reviewed the charts of 40 pts. with VC from 1977-81 to determine the incidence of infectious complications. Diagnoses included: head trauma (8), Reyes Syndrome (20), CNS infections (3), post-anoxic encephalopathy (5), intracranial hemorrhage (2), CNS neoplasm (1) malfunctioning shunt (1). VC were tunnelled subcutaneously for 5-6 cm proximal to the burr hole site. Oxacillin prophylaxis (200 mg/kg/day) was given IV to all pts. and periodic cultures of the VC drainage system were obtained.

Two pts. with pre-existing bacterial meningitis had VC placed to monitor ICP, and were successfully treated with the VC in place. Six pts. had colonization of the VC system (VC tip:4, VC drainage:2) in the absence of any evidence of systemic or CNS infection. Only one patient had catheter related ventriculitis (enterococcus) which occured on the 6th day of ICP monitoring. In our pts. VC remained in place for 3-28 (mean 10.1) days. The mean duration of monitoring was not greater in the 6 pts. who became colonized. Colonization was detected between 2 and 21 (mean 8.9) days following VC placement. VC are a safe method for monitoring ICP; catheter related infection occurred in only 2.5% of pts.

1052 THE DEVELOPMENT OF PARAINFLUENZA (PV)-SPECIFIC IGE IN NASOPHARYNGEAL SECRETIONS (NPS) FOLLOWING INFECTION: POSSIBLE ROLE IN PATHOGENESIS OF CROUP AND WHEEZING. Robert C. Welliver, David T. Wong, Elliott Middleton, Martha S. Sun, Pearay L. Ogra. State University of N.Y. and Children's Hospital of Buffalo, Department of Pediatrics, Buffalo, N.Y.

A group of 25 infants and children with acute PV infection were tested for the presence of PV-specific IgE in samples of NPS taken at various intervals after the onset of illness. IgE antibody to PV types I-III in NPS was determined by an enzyme-linked immunosorbent assay (ELISA), using purified PV strains and monospecific goat antisera to human IgE. During the acute phase of illness, antibody against the infecting serotype was detectable in NPS specimens taken from 60% of patients with wheezing and 42% of patients with croup without wheezing. None of 8 patients with upper respiratory illness (URI) alone manifested PV-specific IgE. PV-specific IgE was detectable during convalescence in some patients with all forms of illness, but was observed more commonly and in higher titer ($p<0.05$) in patients with croup or wheezing than in patients with URI alone. These observations suggest a possible role for the development of virus-specific IgE in the pathogenesis of both croup and wheezing due to PV, in a manner similar to respiratory syncytial virus as described previously.

1053 TOXIC SHOCK SYNDROME IN A NEWBORN INFANT. Chester B. Whitley, Linda R. Thompson, Michael T. Osterholm, Patrick M. Schlievert, Greg R. Elliott and Barbara A. Burke (Spon by William Krivit) University of Minnesota, Department of Pediatrics, Microbiology, Laboratory Medicine & Pathology and Minnesota Department of Health, Minneapolis. Toxic shock syndrome (TSS) is a recently described illness characterized by (a) fever, (b) mild or profound hypotension, (c) multisystem dysfunction, (d) skin desquamation 8-12 days after onset, and has been associated with a specific Staphylococcus aureus pyrogenic exotoxin. TSS has been described predominantly in previously healthy, menstruating women in whom the association with tampon use and cervicovaginal colonization by S. aureus has been recognized. However, affected non-menstruating patients have also been observed among whom wound infection by S. aureus has frequently been implicated. We describe the fatal course of a 3-week infant with staphylococcal abscess related to previous heel puncture in the nursery. After three days of marked clinical improvement on IV nafcillin, the patient suddenly deteriorated with rapid progression from lethargy and diaphoresis to ileus, oliguria, cardiomegaly, profound shock and respiratory failure. Post mortem exam confirmed the impression of multisystem involvement including the visceral and cutaneous histopathology characteristic of fatal TSS cases. Multiple ante and post mortem cultures of blood and CSF were sterile, however, wound aspiration cultures grew penicillin-resistant, nafcillin-sensitive S. aureus productive of pyrogenic exotoxin type C. This case, the youngest reported patient with TSS, illustrates another clinical presentation of neonatal staphylococcal disease. Furthermore, it reiterates that TSS is a disease not limited to menstruating women but may also occur in patients with focal S. aureus infection.

1054 ROLE OF BREAST-FEEDING ON THE OUTCOME OF RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION IN THE NEONATE. David T. Wong, Carol L. Parker, Shaheen M. Al-Nakeeb, Pearay L. Ogra. State University of New York at Buffalo, Children's Hospital, Department of Pediatrics, Buffalo, N.Y.

Groups of neonatal cotton rats seronegative for RSV antibody were breast fed immediately after birth, either by their own seronegative mothers, or foster-fed by lactating females who had been infected with live RSV 3-5 weeks prior to delivery of their own litters. The neonates foster-fed by seropositive mothers elicited appreciable levels of RSV-specific IgG antibody in the serum after initiation of breast feeding. However, such reactivity was not observed in the serum of infants breast-fed by their own seronegative mothers. All neonatal animals were infected intranasally with RSV 3 days after beginning of breast feeding. The animals were sacrificed at frequent intervals to determine the degree of RSV shedding and development of antibody response in the serum. Neonates breast-fed by their own seronegative mothers exhibited significantly more virus shedding in their respiratory tract, and earlier and higher degree of RSV-specific serum antibody response than observed in infected infants who were foster-fed by RSV-seropositive animals. These results support the observations that breast feeding may protect infants from serious RSV infection and the immunologic reactivity transferred via breast-milk may be important in regulating specific immune responses in infected neonates.

● **1055** ABSENCE OF HISTORY OF GENITAL HERPES SIMPLEX VIRUS (HSV) INFECTIONS IN MOTHERS OF INFECTED INFANTS: SOURCE- ASYMPTOMATIC SHEDDING VS. PRIMARY INFECTION Anne S. Yeager, Ann M. Arvin, M. Carol Sweeney, Dept. Pediatrics Stanford University School of Medicine, Stanford, CA.

At least 50% of mothers of infants with acquired HSV infections deny symptoms of recurrent genital HSV in the past. It has been inferred that asymptomatic (Sx-) shedding at the time of birth is the usual source of infection in these infants. The purpose of this study was to evaluate the incidence of Sx- shedding in pregnant women who had had HSV isolated (HSV +) from genital lesions during pregnancy and to make an immunological and clinical assessment of the time of onset of HSV infection in mothers of infected infants. Of 58 pregnant women with HSV + perineal lesions who had a cervical culture performed on the same day, 2 (3.4%) shed HSV from the cervix. Of 326 cultures taken to detect Sx- shedding from 139 pregnant women who were previously HSV +, 2 (0.6%) were positive; therefore, 1.4% of these women had Sx- shedding. None of 27 delivery cultures were HSV +. Of 21 mothers of infected infants, 5 had a history of recurrent genital HSV and 16 did not. Of the latter, 7 mothers had clinical findings compatible with a primary infection. All of these mothers and their infants had neutralization titers of $\leq$ 1:10 to HSV 1 and 2. Of the infants of the other 9 mothers who denied a history of HSV, 7 had neutralization titers of $\leq$ 1:10. Only 2% of 41 normal infants of mothers with recurrent HSV infections during pregnancy had titers at this level. The rate of Sx- shedding in women with recurrent HSV is similar to that of normal women. Primary maternal infections at term are an important source of neonatal HSV infection.

● 1056 ENTERIC TYPE ADENOVIRUS: AN IMPORTANT CAUSE OF GASTROINTESTINAL AND RESPIRATORY DISEASE IN HOSPITALIZED INFANTS. Robert H. Yolken, Faye Lawrence, Flora Leister, Howard E. Takiff, Stephen E. Straus. Johns Hopkins Hospital, Department of Pediatrics, Baltimore, Maryland and The National Institutes of Health, Bethesda, Maryland.

An enteric type of adenovirus (ET Ad) has recently been identified as a causative agent of infantile gastroenteritis. We utilized enzyme immunoassay and tissue culture techniques to prospectively evaluate the role of ET Ad in diarrhea occurring in hospitalized infants. We found that ET Ad was associated with 14 of 27 cases of diarrhea occurring during a twelve week study period in the late autumn and early winter months. On the other hand, ET Ad was found in the stool of only 1 child without diarrhea (P<.001). While adenoviruses other than ET Ad were found in the stools of 2 children with diarrhea, such viruses were also found in the stools of 5 of 72 children without diarrhea.

Children infected with ET Ad had diarrhea for a mean of 8.0 days, a period that was longer than that observed in the children with gastroenteritis not associated with ET Ad. Also noteworthy was the high rate of respiratory symptoms noted in the children with ET Ad gastroenteritis. Thirteen of the 14 children with ET Ad gastroenteritis had respiratory symptoms such as cough, rhinorrhea or wheezing and 6 had roentgenographic evidence of pneumonia. In some cases ET Ad was also isolated from the respiratory tract of infants with ET Ad gastroenteritis. This study documents that ET Ad can be an important cause of acute gastrointestinal disease in hospitalized infants and young children.

1057 IMMUNOGENICITY AND REACTOGENICITY IN CHILDREN FOLLOWING IMMUNIZATION WITH HEPATITIS B VACCINE. John M. Zahradnik and F. Blaine Hollinger (Spon. by William P. Glezen), Baylor College of Medicine, Depts. of Microbiology and Immunology and Virology/Epidemiology, Houston, Texas.

Children living in families where at least one member is a carrier of hepatitis B virus (HBV) are at risk for infection with virus. While passive immunity via immune globulin is helpful, it is neither totally effective nor practical in such a situation. Active immunization with HBV vaccine in adults has been shown to be safe and efficacious. One hundred and twenty high risk children, ages 18 mos. to 16 years were screened for any serologic evidence of previous HBV infection. Seventy-one who had no evidence of previous infection were enrolled in a double-blind, randomized trial. The subjects received either two doses of 16 µg of formalin-inactivated, alum-adsorbed hepatitis B surface antigen (HBsAg) or an alum-formalin diluent in 0.4 ml administered I.M. one month apart. Both preparations were prepared by the NIAID. Systemic and local side effects have been remarkably absent as compared to adults reactions which were limited to occasional mild discomfort at the injection site. Anti-HBs, as measured by radioimmunoassay developed in approximately 65% of the subjects within the first two weeks, and 75% within a month, a seroconversion rate that was comparable to that seen in adults.

This vaccine appears to be significantly free of systemic or local reactions and equal in immunogenicity to responses seen in adults. It appears to be of potential benefit to children who are at risk.

METABOLISM

●1058 HORMONE-SENSITIVE LIPASE IN CULTURED HUMAN ADIPOCYTES. Festus O. Adebonojo, Paul M. Coates and Jean A. Cortner. Jos. Stokes, Jr. Research Inst., Children's Hospital of Philadelphia, Philadelphia, PA

Hormone-sensitive lipase (HSL) is responsible for mobilization of triglycerides from adipose tissue (AT). Characterization of this enzyme from human adipose tissue has been hampered by the large tissue requirements for such studies. We adapted methods for culturing adipocytes, derived from small amounts of AT from children, for study of HSL under defined conditions. Cultured adipose cells (CAC) were grown in the presence or absence of conditions which promote lipid accumulation (fat-enriched (FE) or regular (R) medium, respectively). HSL activity was measured in the aqueous fraction of CAC, and in the original AT, before (basal) or after (stimulated) 30 min exposure to 5µM epinephrine.

		HSL activity $\bar{x}$ ±SD		
Enzyme source	(n)	basal	stimulated	p (paired t)
CAC + FE medium	(6)	6.1±1.5	10.4±3.7	<.03
CAC + R medium	(10)	2.8±0.9	4.6±1.4	<.01
Original AT	(10)	5.4±2.8	19.4±7.3	<.01

Results (nmol glycerol released/min/mg protein) indicate that: 1) CAC retain HSL activity; 2) this activity can be stimulated by epinephrine; 3) HSL activity in CAC is enhanced under conditions which favor lipid accumulation (FE vs R, p <0.01 both basal and stimulated). The availability of CAC, which retain the metabolic properties of the original tissue, may permit the characterization of HSL and its response to effectors, and provide a system for evaluating potential genetic variants of this enzyme.

● 1059 LDL METABOLISM DURING PREGNANCY AND LACTATION. John M. Andersen and Charles R. Rosenfeld, University of Texas Health Science Center, Department of Pediatrics, Dallas.

We have shown that in the ewe low density lipoprotein cholesterol(LDL-C)levels increase 50% in late pregnancy and fall rapidly to less than nonpregnant values during lactation. The mechanisms responsible for these changes were examined by studying the turnover of plasma LDL and high density lipoproteins(HDL)by following the plasma decay of injected homologous ^{125}I-LDL and ^{131}I-HDL simultaneously (n=12). Parameters of LDL metabolism included: a) LDL cholesterol level(mg/dl), b) LDL fractional catabolic rate (fraction of plasma pool/day), and c) LDL protein synthetic rate (mg/day). The mean (±SE) values for these parameters in 4 physiologic states studied were: I. Nonpregnant:a) 20±2.7, b) .316±.028, c) 60±8; II.Pregnant (130-140d): a)31±2.4, b).810±.130,c)303±68; III.Postpartum Lactating (5d): a)15±2.1, b)1.10±.096, c)127±15; IV.Postpartum Nonlactating (5d): a)30±3.4, b).545±.015, c)159±11. HDL metabolism was unaltered. From these data it is apparent that increased LDL catabolism occurs in pregnancy in concert with increased plasma LDL levels(p<.05); thus, the hypercholesterolemia of pregnancy must be due to greater LDL synthesis than LDL catabolism. The increased LDL catabolism seen with lactation (p<.05 comparing pregnant and nonpregnant) is incompletely compensated by LDL synthesis; thus, plasma LDL falls. At least a portion of the increased LDL catabolism of pregnancy may reflect transfer of LDL-C to the fetus and its increased conversion to steroid hormones; whereas the increased LDL catabolism in lactation may reflect secretion of LDL-C into milk.

1060 THE EWE AS A MODEL FOR THE STUDY OF MECHANISMS CAUSING PREGNANCY INDUCED HYPERCHOLESTEROLEMIA. John M. Andersen and Charles R. Rosenfeld, University of Texas Health Science Center, Department of Pediatrics, Dallas.

The mechanisms responsible for elevations in very low density lipoproteins(VLDL)and low density lipoproteins(LDL)and for hypercholesterolemia in normal, pregnant women in the 3rd trimester are unknown. An animal model is needed to investigate these mechanisms in detail;thus, we sought to ascertain if the pregnant ewe could be used. Sheep plasma lipoproteins were isolated quantitatively by ultracentrifugation and the cholesterol(C) content of each fraction quantitated. Plasma total C in nonpregnant,pregnant(130-140d), postpartum lactating(5d) and postpartum nonlactating(5d) sheep were 55±7.6($\bar{X}$±SE), 74±3.2, 56±2.6 and 67±1.4 mg/dl, respectively. The changes in total plasma C were largely a result of alterations in the LDL-C fraction(d=1.020-1.063 g/ml), which averaged 20±2.3 mg/dl in the nonpregnant animals, increased to 31±2.4 mg/dl in the third trimester, decreased to 15±2.1 mg/dl during lactation, but remained elevated at 30±3.4 mg/dl in the nonlactating postpartum animals. LDL-C levels in nonpregnant, pregnant and lactating ewes were significantly different(p<0.05). There were no significant changes in the high density lipoproteins(HDL)-C and VLDL-C levels. We conclude that the ewe is a reasonable model in which to study the hypercholesterolemia of pregnancy. In addition, the results are consistent with the view that LDL-C provides at least a portion of C secreted in the milk of the ewe. Finally, we hypothesize that these alterations in plasma LDL-C levels are the result of purturbations in the rate of catabolism of LDL while the catabolism of HDL and VLDL are relatively constant.

1061 FURTHER CLINICAL STUDIES OF SODIUM BENZOATE (SB) AND PHENYLACETATE (PA) IN N-ACCUMULATION DISEASES (NAD). Mark L. Batshaw, Stephen L. Newman and Saul W. Brusilow Dept. Ped., and The John F. Kennedy Inst., Baltimore, Md.

Amino acid acylation (AAA) via SB or PA can serve as a means of excretion of waste-N in NAD. The role of these drugs in long-term therapy of urea cycle enzymopathies (UCE) and their effect on hyperammonemia (HA) from other causes were studied. Twenty-five patients with neonatal onset UCE were treated for 3-44m. with protein restriction, SB (250-400 mg/kg/d), PA (250mg/kg/d) and arg. (1-4mmol/kg): CPS 2, OTC 7, AS 6, AL 10. Alternative pathways accounted for a significant percentage of total effective waste N excretion: hippurate-N 26±3, phenylacetylglutamine-N 34±3, citrulline-N 16±2, argininosuccinate-N 56. Three OTC deficient patients died; all others are alive. Four symptomatic OTC heterozygotes were similarly treated. HA episodes decreased, behavior improved and intellectual performances increased. 48 HA episodes were treated with SB (250-500mg/kg) plus arg. (1-4mmol/kg); NH^+_4 decreased from 250±20 to 82±7uM in 4 hr. One propionic acidemic child received SB; NH^+_4 fell from 89 to 36uM. Two hepatic failure children received PA. In one NH^+_4 fell from 290 to 50uM in 24hr. and increased to 900uM after PA was stopped. In the second, NH^+_4 was 220uM before, 196uM 12 hr. and 290uM 24 hr. later. 5 Reye syndrome (RS) patients received SB; NH^+_4 did not fall significantly, 443±69 → 374±54uM. One RS patient received PA (250mg/kg); NH^+_4 fell from 316 to 130uM in 4 hr. No side effects resulted from SB or PA. AAA therapy is beneficial in UCE and possibly in other NAD.

1062 ELECTROPHORESIS OF SOLUBLE PROTEINS OF MUSCLE FROM MALIGNANT HYPERTHERMIC PATIENTS. T.J.J. Blanck and M.Thompson(Spon.Mark C. Rogers)Dept.of Anesthesia/ Critical Care, Johns Hopkins University, Baltimore, MD. 21205

Malignant Hyperthermia (MH) is a disastrous metabolic disorder of muscle triggered by anesthetics and muscle relaxants which commonly presents in children without previous warning.Currently there is no definitive screening procedure to determine which patients might be susceptible to MH.This paper presents electrophoretic data of soluble proteins from the muscles of 2 patients who had previously experienced MH and from 8 control patients. The soluble fraction from biopsy specimens of the vastus lateralus of 2 MH patients demonstrates an increase in a low molecular weight protein (mw 13080 ± 470). We have also observed an increase of this low molecular protein in the muscle of individuals related to MH patients(#11&12). This data is summarized in the table below:

No.	A*	B†	B/A	No.	A*	B†	B/A
1.	20.9	0.75	0.04	7.	44.6	7.4	0.16
2.	36.4	2.8	0.08	8.	19.2	4	0.21
3.	19.5	0.54	0.03	9.	30.5	28.7	0.94
4.	29.6	4.2	0.14	10.	18.2	29.8	1.64
5.	28.1	3.8	0.14	11.	19.1	41.7	2.18
6.	22.9	9.2	0.40	12.	31.0	49.0	1.58

*Relative amount of a 16480 mw protein present in large amounts in all samples. †Relative amount of a 13080 mw protein (increased in MH patients # 9 & 10).

Electrophoresis of muscle from a larger number of MH patients and their relatives could indicate the utility of this methodology.

1063 ELEVATED PLASMA CATECHOLAMINES IN CLINICALLY STABLE AND IN STRESSED MAGNESIUM (Mg) DEFICIENT WEANLING RATS. Joan L. Caddell and Deborah L. Proxmire (Spon. Thomas Aceto, Jr.), St. Louis U. Sch. Med., Dept. Pediat./Adol. Med., St. Louis, MO; NICHD, Bethesda, MD; and Upjohn Diagnostics,Kalamazoo.

We are exploring the hypothesis that Mg deficiency contributes to the pathogenesis of some crib deaths (SIDS). Since many clinical and pathological features of SIDS might be explained by persistent elevation of blood catecholamines, we are investigating catecholamines in Mg deficiency. Weanling male Sprague-Dawley rats weighing 35.0±0.35 g were fed purified diets containing no added Mg (0-Mg) or 150 mg of added Mg (150-Mg) for one week. Plasma and bone Mg were measured by atomic absorption spectrophotometry, and plasma catecholamines, by radioenzymatic assay using ^{3}H. Of 16 rats fed 0-Mg, 5 died, 5 inadvertently suffered stress (fits, etc), and 6 appeared stable. Eight 150-Mg rats were studied. Plasma Mg of 0-20 rats was 0.47±0.07 mg/dl, 23% of control, 2.05±0.09, despite slight elevations in stressed rats. Bone Mg from 0-Mg rats was 967.5± 33 mg/kg dry wt., 30% of control, 3,219± 85 mg/kg dry wt. Catecholamines were expressed as pg/ml plasma.

Experimental	Norepinephrine	Epinephrine	Dopamine
150-Mg, stable	414± 34*,**	103± 26*	41± 5*
0-Mg, stable	1,161± 184	596± 156	128± 25
0-Mg, stress	8,979±2,519	11,403±3,752	1,450±632

*Analysis of variance testing showed P<0.001.** Mean ± SEM.

We conclude that apparently stable weanling rats with dietary Mg deficiency have elevated plasma catecholamines. The epinephrine fraction showed the greatest increase during stress in the Mg-deficient animals. (Support: Upjohn Diagnostics, Upjohn Co.,and the Life Seekers, St. Louis, MO).

1064 DIABETIC OSTEOPATHY IN ADOLESCENT DIABETICS: IMPROVEMENT WITH BETTER CONTROL OF HYPERGLYCEMIA. S.Castells, C.Colbert, M.Noval, R.S.Bachtell, and H.Copur, SUNY, Downstate Med Ctr, Dept of Ped, Brooklyn, New York and Miami Valley Hospital, Clin Rad Testing Lab, Yellow Springs, Ohio

There is a decrease in bone mass in insulin dependent diabetics and frequent periarticular changes in poorly controlled diabetics. Twenty-four adolescent diabetics taking insulin once a day and on poor control of blood glucose, were admitted to the Hospital and placed on good blood glucose control by administering insulin bi-daily. Serum Ca, P, and alkaline phosphatase levels and radiographic bone density were obtained before and at 3 month intervals of good diabetic control. Bone density was determined by the method of radiographic photodensitometry of Colbert et al. (Clin Orthop 65:39,69) and compared to normal subjects of both sexes. Two quantitative indexes of diabetic control, M-value and serum Hb A_{1C} significantly improved in bi-daily injections. At 3 months, M-value decreased from 108.4±20 in 1 injection to 37.5±4.2 on bi-daily, p<0.01 and Hb A_{1C} from 12.1%±0.6 to 9.2%±0.6, p<0.01. Serum Ca, P and alkaline phosphatase were not significantly different in diabetics on poor and good control from normals. Two patients on poorly controlled diabetes had bone density one SD below normal for age and sex. After 6 months of improved glucose control with bi-daily injections, bone density in the 2 patients increased to normal values. These findings suggest normalization of bone density in poorly controlled diabetics with improvement in glucose control.

1065 KINETIC STUDIES OF COPPER METABOLISM IN WILSON'S DISEASE FIBROBLAST CULTURE. Wai-Yee Chan, Le Ann Tease, and Owen M. Rennert. University of Oklahoma Health Sciences Center, Department of Pediatrics, Oklahoma City.

Wilson's Disease (WD) is an autosomal recessive inherited metabolic disorder of copper caused by excessive deposition of the element in various organ systems resulting in copper toxicosis. The abnormal gene was shown to be expressed in cultured skin fibroblasts derived from the patients. WD cultured fibroblasts showed an increased accumulation of copper (threefold of that of normal cells) especially when the cultures were grown in Eagle's minimum essential medium supplemented with 20% fetal bovine serum. In spite of this, WD cultured fibroblasts demonstrated normal response towards cytotoxic effect of copper. Kinetic studies of uptake indicated that WD cells incorporated less copper than control cells initially;

Uptake Time (Hours)	1	2	3	4
WD (n=2)	0.33±0.03*	0.93±0.26	1.07±0.03	1.55±0.50
Normal (n=3)	1.23±0.23	1.57±0.36	2.30±0.67	1.63±0.56

*Cu-64 cpm X 10^2/mg cell protein (mean ± S.D.)

however, with normal fibroblasts copper uptake plateaued and declined by the third hour of incubation, whereas uptake in WD fibroblasts continued to increase linearly beyond the fourth hour of incubation. Cellular efflux of copper was normal in WD fibroblasts. These observations further support the thesis that the abnormal gene of WD is expressed in cultured skin fibroblasts.

1066 NEONATAL HYPOCALCEMIA IN TWINS AND TRIPLETS. David A. Clark, William H. Bernstrom, Dept. of Pediatrics, SUNY, Upstate Med. Ctr., Syracuse, New York.

While studying hypocalcemia in low birth weight (LBW) infants we found that multiple births (MB) had lower serum calcium (CaS) at 24 hr than preterm single births (PSB) of equal BW and GA. We compared cord and 24 hr CaS in 25 full term infants (FT), 27 PSB and 32 MB. In PSB, CaS at 24 hr correlated with BW (R=.67, p<.01). In PSB >1500 gm, cord CaS was lower than in FT but the decrease from cord to 24 hr CaS (Δ) was similar. In PSB <1500 gm, a larger Δaccounted for the lower 24 hr CaS. In MB, cord CaS was equal to that of PSB >1500 gm, but a large Δled to a low 24 hr CaS, as in PSB <1500 gm. MB CaS at 24 hr was not correlated with BW or GA.

Fetal calcium accretion and the adaptive increase in maternal parathyroid function are maximal during the third trimester; our PSB and MB subjects were born when only half of this period had elapsed. Since individual MB infants weighed as much as PSB infants >1500 gm, the total fetal mass requiring mineralization was twice as great (3x in triplets). The data suggest that MB infants were insufficiently endowed with calcium in utero to sustain CaS in early neonatal life, resembling more immature PSB < 1500 gm.

CaS	Fullterm	Preterm		Multiple Birth
mg/dl(S.E.)	n=25	>1500 gm n=14	<1500 gm n=13	n=32
Cord	10.4(.09)	9.2(.17)	8.8(.19)	9.4(.14)
24 hr	9.9(.3)	7.9(.17)	6.5(.27)	6.9(.08)
	1.4	1.3	2.3	2.5
GA(wks)	38-40	34.2(.2)	30.1(.5)	33.4(.4)
Wt(gm)		1856(91)	1227(50)	1844(92)

●1067 PHENYLALANINE HYDROXYLASE ACTIVITY IN MAN MEASURED IN VIVO BY TRACER INFUSIONS OF STABLE ISOTOPE-LABELED PHENYLALANINE AND TYROSINE. Joe T. R. Clarke and Dennis M. Bier, Dalhousie Univ., Dept. of Peds., Halifax, N.S., and Wash. Univ. Schl. of Med., Div. of Metab., St. Louis, MO.

Steady state phenylalanine (phe) and tyrosine (tyr) turnover rates and phe hydroxylase activity in vivo were determined in 6 healthy adult males. Continuous infusions of tracer amounts of L-[ring-$^2H_5$]phenylalanine ([$^2H_5$]phe) were administered for 14 h at 3.11 ± 0.51 μmol·kg^{-1}·h^{-1}. After 10 h, a priming dose (approx. 2.7 μmol·kg^{-1}) followed by a continuous infusion of L-[1-^{13}C]tyrosine ([^{13}C]tyr; 2.32 ± 0.36 μmol·kg^{-1}·h^{-1}) was added and maintained, along with the [$^2H_5$]phe infusion, for 4 h. Venous plasma samples were obtained before the initiation of each infusion and every 30 min during the combined [$^2H_5$]phe and [^{13}C] tyr infusion. Isotopic enrichments of [$^2H_5$]phe, [^{13}C]tyr and [$^2H_4$]tyr were determined by gas chromatograph-mass spectrometric analysis of the trifluoroacetyl-, methyl ester derivatives of the amino acids. Free phe and tyr turnover rates, calculated from the observed enrichments, were 36.1 ± 5.1 μmol·kg^{-1}·h^{-1} and 39.8 ± 3.5 μmol·kg^{-1}·h^{-1}, respectively. Phe hydroxylase activity was estimated to be 5.83 ± 0.50 μmol·kg^{-1}·h^{-1}, accounting for 15-20% of the total phe or tyr fluxes. Basal steady state phe hydroxylase activity in vivo in man is significantly lower than that estimated by phe loading studies. The use of continuous simultaneous infusions of tracer amounts of stable isotope-labeled phe and tyr provides a safe and direct means for studying physiological regulation of phe hydroxylase activity in vivo.

1068 SUPPRESSION OF UREA SYNTHESIS, INCREASED NITROGEN RETENTION, AND UNCHANGED GLUCOSE TURNOVER AFTER GROWTH HORMONE ADMINISTRATION TO GROWTH HORMONE DEFICIENT CHILDREN. William T. Dahms, Ruth P. Owens, Satish C. Kalhan, Douglas S. Kerr, and Robert K. Danish. Case Western Reserve University, Rainbow Babies & Childrens and Cleveland Metropolitan General Hospital, Department of Pediatrics, Cleveland, Ohio

We measured the effect of growth hormone(GH) on urea synthesis glucose turnover, and nitrogen retention in 10 euthyroid GH deficient children before and after 6 daily injections of GH (0.1 U/kg·day). The patients consumed an isocaloric diet with 11% of calories derived from protein. Urea synthesis and glucose turnover were determined after an overnight fast using a 5-hour constant infusion of [6,6-$^2H_2$]glucose and [$^{15}N_2$]urea. Results were:

	Pre Rx	Post Rx	p value
Urea Synthesis(mg/kg·hr)	6.1±0.5	4.3±0.6	.002
Glucose Turnover(mg/kg·min)	4.7±0.4	4.3±0.6	.43
BUN(mg/dl)	13.1±2.4	7.4±2.5	<.001
Nitrogen Retention(mg/kg·day)	67±14	130±13	<.001
Glucose(mg/dl)	82±6.8	91±6.9	.025
Growth Velocity(% expected)	53±13	153±12	<.001

Urea synthesis and BUN were correlated before(r=0.85, p<.01) and after(r=0.79, p<.01) GH treatment. The decrease in urea synthesis in each patient was not significantly correlated with growth rate after 6 months of GH(0.1 U/kg tiw). We conclude that in GH deficient children given GH: 1)The increase in nitrogen retention and decrease in BUN is due to decreased urea synthesis; 2) Fasting glucose turnover is not changed; and 3) Acute metabolic changes in response to GH are poor predictors of subsequent growth rate.

1069 DIURNAL GLUCOSE-DEPENDENT FLUCTUATIONS IN GLYCOSYLATED HEMOGLOBIN LEVELS IN INSULIN-DEPENDENT DIABETES: D. Daneman,N. Luley and D. Becker, Univ. of Pittsburgh, Children's Hosp. of Pittsburgh,Dept. of Pediatrics,Pittsburgh,Pa.

To evaluate the relationship between short-term glycemic control & both stable & labile fractions of GHb,we measured blood glucose(BG)hourly for 24h on 31 occasions in 13 IDD children(age: 8-24yr;duration:0-14½yr).GHb was measured 6 times/24h both in whole blood(WB-/Total GHb)& after 48h incubation at 4°C in normal saline (SI-/stable GHb)to remove the labile fraction(WB-minus SI-GHb).SI-GHb(mean±SD 10.3±1.5%)was always lower than WB-GHb(11.5±1.6%;p<0.0001).To compare the variability of these 2 methods of GHb measurement,the standard deviations,coefficients of variation & ranges for each day were analysed.All 3 measures were much smaller in SI compared to WB specimens(p<0.005).Mean blood glucose (MBG)correlated more closely with mean WB- than SI-GHb(r=0.58,p<0.001 & r=0.45,p<0.05 respectively).The mean labile fraction correlated closely with the mean amplitude of glycemic excursions (MAGE)a measure of diabetic instability(r=0.62,p<0.001).There was also a significant correlation between the labile fraction & both a simultaneous BG(r=0.37,p<0.001)& MBG over the previous 6h(r=0.60 p<0.001).In 1 subject WB-GHb decreased 4.4% & SI-GHb 3.1% over 7wk of good glycemic control.These results(a)confirm the presence of both labile & stable forms of GHb;(b)show a closer correlation of short-term glycemia with WB-than SI-GHb;(c)highlight the possible relationship of the labile fraction to diabetic instability(MAGE), &(d)confirm the relatively rapid decline of both fractions with improved metabolic control.We recommend routine measurement of stable(SI)GHb when assessing control in children with IDD.

1070 PHYSIOLOGICAL SIGNIFICANCE OF REDUCED HEPATIC GLUCAGON RECEPTORS IN THE FETUS (F). Sherin Devaskar, David Styer, Supriya Ganguli, Mark Sperling. Univ. of Cincinnati, Depts. of Peds. and Maths. Child. Hosp. Med. Ctr. Cin.

Glucagon receptors (GR) of F liver membranes are lower in number and poorly coupled to adenylate cyclase when compared to adult. To investigate the physiological significance of these observations, we measured the effect of infused glucagon at 5 or 50 ng/kg/min on glucose turnover (GT), net glucose production (Ra) and net utilization (Rd), with an appropriate compartmental model via double isotopic dilution techniques. Results in 5 F at 129±3d gestation weighing 2.5±3 kg were compared to 5 non-pregnant adults. Glucose (G), glucagon (IRG) and insulin (IRI) also were measured. Peak responses are shown in the table.

Sheep	Glucose	IRG	IRI	GT	Ra	Rd
Fetus	mg/dl	pg/ml	μU/ml	mg/min	mg/min	mg/min
Basal	12±3	168±27	16±3	15±2	0	9±2
5 ng/kg/min	13±4	863±305*	16±4	22±9	0	12±3
50 ng/kg/min	25±3*	2100±470*	25±2*	39±13*	48±12*	39±12*
Adult Basal	59±4	93±10	15±1	108±9	108±9	108±9
5 ng/kg/min	96±20*	600±100*	18±1*	295±62*	295±62*	210±50*

* p< 0.05 from corresponding basal.

Despite a 5-fold increase in F IRG, F glucose, IRI, and Ra remained unchanged; no net F glucose production was evident. In contrast, similar IRG levels in adult significantly increased Ra and other parameters. A 10-15 fold (pharmacological) increase in IRG was necessary to induce F Ra; F GT was now derived from endogenous sources, not by placental transfer. Conclusion: decreased sensitivity of F liver to IRG in-vivo is consistent with the observed decrease of functionally linked GR in vitro.

1071 PLASMA AND RBC COBALAMINS IN B_{12} DEFECT DISORDER. S. Bruce Dowton, John C. Linnell,Fred D. Ledley and Harvey L. Levy, Harvard Medical School, Children's Hospital Medical Center, Boston; Westminster Hospital, London.

B_{12} (Cbl) defect with methylmalonic aciduria and sulfur amino acid abnormalities is an inborn error affecting the B_{12} dependent metabolic systems (N5-methylTHF-homocysteine methyltransferase and methylmalonyl-CoA mutase). Two coenzymatically active B_{12} forms are involved, respectively methyl-Cbl (MeCbl) and deoxyadenosyl-Cbl (AdoCbl). The basic defect in B_{12} is unclear.

In a 3 month old affected male with intrauterine growth retardation, megaloblastic anemia, and characteristic biochemical abnormalities, we measured Cbl distribution in blood.

	(pg/ml)				
Plasma	Total Cbl	MeCbl	AdoCbl	OHCbl	CNCbl
Basal	1160	93	835	128	104
Post-OHCbl	11,760	353	235	11,172	-
Controls	185-935	130-600	35-185	20-90	0-50
RBC					
Basal	84	42	17	25	-
Post-OHCbl	3,260	1,467	65	1,565	163
Controls	125-525	10-50	60-315	30-250	0-30

The increased basal state plasma AdoCbl level and the large post-OHCbl increment in MeCbl suggest that a B_{12} metabolic defect is unlikely. The low RBC AdoCbl even after treatment suggests that intracellular retention of AdoCbl might be inadequate. This might secondarily alter the tissue distribution of MeCbl. The result would be insufficient cobalamin for metabolic homeostasis.

1072 GLUTAMINE TRANSPORT INTO ISOLATED RENAL MEMBRANE VESICLES FROM NORMAL AND ACIDOTIC RATS. John W. Foreman, Robert A. Reynolds, Louise M. Pepe and Stanton Segal. Department of Pediatrics, Children's Hospital of Philadelphia, PA.

During acidosis, there is an increased glutamine extraction by the kidney with a concomitant increase in ammoniagenesis. The factors regulating this increased uptake are incompletely understood. To examine glutamine transport independent of mitochondrial metabolism, we examined glutamine uptake into isolated brush-border membrane (BBMV) and basolateral membrane (BLMV) vesicles obtained from normal and acidotic rats. In normal BLMV,glutamine is transported by two saturable systems with Km_1=0.04mM, $Vmax_1$= 0.09nmoles/mg per min and Km_2=3.2, $Vmax_2$=2.2. These kinetic parameters did not change when the BLMV were made from acidotic rats. Glutamine uptake into BBMV from normal rats was also mediated by two systems with Km_1=0.3mM, $Vmax_1$=1.7nmoles/mg per 15 sec. and Km_2=1.1, $Vmax_2$=4.8. In BBMV from rats made acidotic with NH_4Cl, glutamine was also mediated by two transport systems with Km_1=0.3mM, $Vmax_1$=2.2nmoles/mg per 15 sec and Km_2=1.7, $Vmax_2$=9.1. The major effect of acidosis on glutamine transport in BBMV was to increase the Vmax of the high capacity, low affinity system by 1.9 times. There was no effect of acidosis on initial rate of glutamine uptake by BLMV. Metabolic acidosis increased the brush-border membrane transport of glutamine. However, such an occurrence in vivo cannot account for the marked increase in renal extraction during acidosis since 99% of the filtered glutamine is reabsorbed during normal acid-base conditions. The data suggest that changes in membrane transport parameters per se do not account for increased renal glutamine uptake during acidosis.

1073 CHEMICAL DIAGNOSIS OF REYE'S SYNDROME-DETERMINATION OF α-AMINOBUTYRIC ACID AND LYSINE. Michael J. Germer, Guy E. Griesmann, Robert Garrison, Wai-Yee Chan and Owen M. Rennert. University of Oklahoma Health Sciences Center, Department of Pediatrics, Oklahoma City.

Hyperaminoacidemia is one of the classical observations in Reye's Syndrome (RS). Serum amino acid profiles were studied on a daily basis in 11 patients with RS throughout their clinical course. A characteristic variation in levels of α-aminobutyric acid (ABA) and lysine (LYS) correlating with the clinical outcome of the patients was observed.

	LYS (μmoles/dl)	ABA (μmoles/dl)
Survivors (8)	64.0 ± 13.1	9.1 ± 2.9
Nonsurvivors (3)	113.5 ± 12.0	22.0 ± 2.2
Normal	11 - 27	1 - 3

Serum LYS and ABA concentrations were significantly elevated in all patients. However, values of these amino acid concentration in patients who eventually died (nonsurvivor) were twice that found in patients who survived (survivors). A plot of LYS vs ABA concentration segregated the survivors and nonsurvivors into two distinct groups. Linear regression analysis of data from each group gave the following: Survivors: y = 6.83x + 3.34, r = 0.87; Nonsurvivors: y = 0.07x + 20.17, r = 0.20. Survivors demonstrated a decrease in the values as symptoms subsided, while nonsurvivors remained constantly high. This elevation of ABA in RS appears to be specific. It is proposed that LYS and ABA concentrations can be used to confirm the diagnosis and severity of the disease, predict the prognosis and aid in assessing the value of therapeutic efforts.

1074 INFECTION AND THE DEVELOPMENT OF TYPE I DIABETES MELLITUS. Fredda Ginsberg-Fellner, George Petrossian, Mary E Witt, Edward Bottone, Eugene Ainbender and Pablo Rubinstein, Mt.Sinai School of Medicine, Depts. of Pediatrics and Microbiology and Lab. of Immunogenetics, N.Y. Blood Center, N.Y.C.

Etiologic factors in the development of insulin-dependent diabetes mellitus, IDDM, in genetically susceptible individuals are still uncertain. In our continuing efforts to identify such factors, cross-sectional and longitudinal studies in families of IDDM patients are in progress. Serum immunoglobulin levels, antibody titers to adeno, rubeola, rubella, mumps and Coxsackie B1-B5 viruses are measured. Historical data on infections, antibiotic use and immunizations are obtained. All family members are typed for HLA antigens A,B,C and DR. Data from 72 families have been evaluated. IgG, IgA and IgM levels of the IDDM patients were increased in comparison to their non-diabetic sibs: 805, 155, 141 vs. 786, 126, 118 mg/dl, even though the mean age of the sibs was greater, 17.5 vs. 15.4 years. In addition, IgM levels of the diabetics were equal to those, 138 mg/dl, of their older parents. No significant differences in antiviral antibody titers were found comparing the subgroups of diabetics, sibs and parents. However, subjects with HLA DR 3 and DR4 displayed increased titers to measles, mumps and rubella viruses as well as increased IgM levels. Sibs and diabetics had similar immunization histories and birthweights. However, the use of antibiotics and documented febrile illnesses were significantly increased in the diabetics compared with their non-diabetic sibs.

The data add support for a role for infections in the development of Type I diabetes in genetically at-risk subjects.

● 1075 PERINATAL GLUCOSE AND INSULIN HOMEOSTASIS IN RELATION TO PREPARTUM MATERNAL GLUCOSE INFUSION. Lawrence J. Grylack, Stephen S. Chu, John W. Scanlon, Columbia Hosp. for Women, Divs. of Neonatology and Anesthesiology, Georgetown Univ. Sch. of Med., Dept. of Pediatrics, Washington, D.C.

Perinatal glucose (G) and insulin (I) homeostasis and the risk of neonatal hypoglycemia (NHG) were assessed in relation to prepartum i.v. infusions given to 59 mothers undergoing C-section at term without labor under epidural anesthesia. Group A (n=20) received 1000 cc of Ringer's lactate without dextrose for one hour; group B (n=20), 1000 cc of 5% Dextrose for one hour (50g/hr); and group C (n=19), 1000 cc of 5% Dextrose for 2½ hours (20g/hr). Blood was sampled from the mother (M) and umbilical vein (UV) at birth, and from the newborn at one (N_1) and 2 (N_2) hours.

Mean ± S.D. Plasma Glucose (mg/dl), Plasma Insulin (μU/ml)

	MG	UVG	UVI	N_1G	N_2G
Grp A	70.3±13.7	58.7±11.3	8.6±6.5	58.8±10.9	70.0±9.6
Grp B	234.4±74.6	207.8±59.7	50.8±31.6	66.3±23.2	60.8±11.0
Grp C	153.4±59.4	128.6±42.7	25.2±13.6	51.2±20.0	63.0±18.8

Mean MG, UVG and UVI differed among all groups ($p<.01$). N_1G differed between groups A and C ($p<.05$). N_2G differed between A and B ($p<.01$), and A and C ($p<.02$). NHG (≤30mg/dl) occurred at one hour in 0/20 in group A, 3/20 in B, and 4/19 in C. The incidence of NHG correlated with the use of a glucose solution ($p<.05$), and with MG≥117mg/dl ($p<.02$), UVG≥105mg/dl ($p<.01$), and UVI≥26μU/ml ($p<.001$). These results indicate that prepartum glucose infusions can produce maternal and fetal hyperglycemia and hyperinsulinemia, and early neonatal hypoglycemia in the normal term pregnancy.

1076 HUMAN GROWTH HORMONE (hGH) THERAPY SPECIFICALLY INCREASES BILE ACID POOL SIZE. James E. Heubi, Deborah J. Gregg, Stephen Burstein, Mark A. Sperling, M.T. Ravi Subbiah, Dwight E. Matthews, Depts. Pediatrics and Metabolism, Univ. Cincinnati, Cinti., OH and Washington Univ., St. Louis, MO.

Although abnormalities of lipid and bile acid (BA) metabolism are described in patients with hGH deficiency, the contribution of cholesterol (C) and BA synthesis and BA pool sizes to these disorders has not been investigated. Therefore, we studied 7 children (mean age 9.8 yrs) with isolated hGH deficiency (n=5) or multiple trophic hormone deficiencies (n=2) before and after 6 months hGH therapy (height velocity during hGH 9.3 ± 1.2 cm/yr, mean ± SE). C and BA synthesis were calculated by sterol balance and BA pool size measured by isotopic dilution techniques using a stable isotope (chenodeoxycholic 11,12 d_2 acid). Plasma total C (200 ± 15 mg/dl), HDL-C (44 ± 4 mg/dl), LDL-C (135 ± 12 mg/dl) and triglycerides (114 ± 16 mg/dl) were higher than age-matched controls and not changed after hGH. There was no change in either C synthesis (164 ± 34 mg/day before vs. 231 ± 43 mg/day after hGH) or BA synthesis (49 ± 9 mg/day before vs. 82 ± 19 mg/day after hGH). Biliary lipid composition and C saturation were similar to controls and unchanged with hGH. However, chenodeoxycholic acid pools which were reduced prior to hGH (399 ± 93 mg/m^2) compared to 7 controls (617 ± 45 mg/m^2, $p < .05$) increased significantly ($p < .05$) to 506 ± 51 mg/m^2 after hGH. Therefore, hGH may play a specific role in bile acid metabolism through an effect on pool size regulation.

1077 COMPARISON OF VITAMIN D, 25-HYDROXY-VITAMIN D (25 HCC), AND CALCIUM-PHOSPHORUS SUPPLEMENTS IN PREMATURE INFANTS. L. Hillman, L. Martin, S. Salmons, B. Fiore, and W. McAllster. Wash. U. Med. Sch., St. Louis Children's Hospital, Dept. of Ped., St. Louis

Both insufficient minerals and vitamin D metabolites contribute to the hypomineralization of extremely premature infants. Thus, 58 infants, 30.3 ± 1.8 weeks and 1192 ± 167 gms, were assigned to one of four prevention groups; 400 I.U. D + standard formula (C) (14), 800 I.U. vitamin D + standard formula (D) (15), 2 μg/kg/d 25-HCC + standard formula (OHD) (15), and 400 I.U. D + high calcium-phosphorus formula (CaP) (14). Baseline (0) and weekly samples plus L wrist x-rays were taken during the study and at 9 and 12 weeks of age on 400 IU D + standard formula. Only D and OHD groups increased serum 25-OHD; however, both serum calcium and bone mineralization were improved by D and CaP but not OHD. Thus, both increased mineral availability and increased vitamin D improves mineralization. Failure of 25 HCC to duplicate the effect of increased vitamin D is unexplained.

	25-OHD ng/ml				serum calcium mg/dl				% mod.-sev. hypomin.			
Wk	C	D	OHD	CaP	C	D	OHD	CaP	C	D	OHD	CaP
0	14	17	17	14	9.2	9.4	9.4	9.7	--	--	--	--
1	12	21*	23*	13	9.2	9.5	9.0	9.3	31	33	47	42
2	13	21*	24*	14	9.0	9.6*	9.3	9.7*	--	--	--	--
3	13	24*	25*	18	9.2	9.5	9.2	9.5	--	--	--	--
4	17	20	25*	20	9.3	9.4	9.8	9.8	43	10	54	18
9	17	25*	24	15	9.1	9.5	9.3	9.8	40	0*	36	0*
12	14	26*	24	18	9.8	10.3	10.0	9.8	13	0	13	17

* Different from C by t-test or chi squared $p < .05$

1078 METABOLISM OF SIALOGLYCOCONJUGATES IN SIALIC ACID STORAGE DISEASE. Allen L. Horwitz, Larry Hancock, M.M. Thaler, and G. Dawson. (Spon. by A. Dorfman). University of Chicago Medical Center, Depts. of Ped. and Biochem., Chicago, IL and University of Calif. Med. Center, Dept. of Ped., San Francisco, CA.

Sialic acid storage disease has been defined in a patient with neurovisceral storage of the monosaccharide N-Acetylneuraminic acid (sialic acid) in lysosomes. Tissues and skin fibroblasts contain more than 200 times more sialic acid than normal. Studies have been undertaken to determine if the accumulation is due to excessive synthesis or defective degradation. Sialic acid lyase, the enzyme believed responsible for sialic acid degradation was normal in activity in liver extracts, although it could not be detected in normal or affected fibroblasts. The lyase activity was detected by the formation of $^{14}C_3$N-acetylmannosamine from ^{14}C-sialic acid. Incorporation of ^{3}H-mannosamine into sialic acid-containing glycolipids and glycoproteins was slightly elevated. The pool of sialic acid available for synthesis is thus not increased despite excessive cellular sialic acid. This suggests enhanced de novo synthesis of sialic acid and a failure in reutilization of sialic acid derived from sialoglycoconjugate degradation. Sialic acid storage disease probably involves a defect in translocation of sialic acid from lysosomes to the site of biosynthesis. Supported by N.I.H. grants HD-09402, HD-04583, and N.I.H. fellowship CA-06884.

● 1079 CORRELATION OF PANCREATIC ENDOCRINE AND EXOCRINE FUNCTION IN CYSTIC FIBROSIS. Mitchell E. Geffner, Robert M. Itami, Barbara M. Lippe, Solomon A. Kaplan Baiba K. Gillard, Seymour R. Levin, UCLA School of Medicine, UCLA Hospital & Clinics, Department of Pediatrics, and Wadsworth V.A. Hospital, Department of Medicine, Los Angeles.

Impaired carbohydrate (CHO) tolerance is a known complication of cystic fibrosis (CF). Proposed mechanisms include disorganized β-cell function 2° to pancreatic fibrosis and/or impairment of the enteroinsular axis (EIA) signaling system for insulin release. The former may correlate with pancreatic exocrine (PEX) function; the latter may reflect non-pancreatic GI involvement. Five thin CF patients (mean±SEM: age 23.6±3.5 yrs.; body weight (BW) 49±7.0 kg.; ideal BW (IBW) 55.3±4.7 kg.) received 5 insulinotropic stimuli: oral glucose (OG), intravenous glucose (IVG), IV tolbutamide (IVT), IV secretin, and IV isoproterenol (IVI). Serum pancreatic iso-amylase (PIA) was used as an index of PEX function. All 5 patients showed a significant positive correlation between PIA and insulin secretion after indirect stimulation of the EIA by OG ($r=0.97, p<0.01$) and after the IV secretagogues IVG ($r=1.00, p<0.001$), IVT ($r=0.92, p<0.05$) and IVI ($r=0.94, p<0.02$). Basal glucagon also positively correlated with PIA. A sixth patient who was obese (18 yrs.; BW 75.3 kg.; IBW 60.9 kg.) had abnormal CHO tolerance with marked hyperinsulinemia basally and in response to all secretagogues; his PIA indicated normal PEX function.

Thus, in CF, insulin reserve directly correlates with PEX function, whether insulin is stimulated orally via the EIA or directly IV. Obesity, coexisting with normal PEX function, may result in hyperinsulinemia and insulin resistance in CF, as it does in normal individuals.

1080 CEREBROTENDINOUS XANTHOMATOSIS PRESENTING AS BILIARY ATRESIA. William G. Johnson, Gerald Salen, Phyllis Taterka, and John F. Nicholson, College of Physicians and Physicians and Surgeons of Columbia University and the College of Medicine and Dentistry of New Jersey.

Two siblings, male and female, developed obstructive cholangiopathy by six weeks of age. At surgery at 3 and 5 months of age respectively, each was found to have correctable extrahepatic biliary atresia. Following surgery, clinical hepatic disease resolved, but both children developed cataracts, and a slowly progressive neurologic disorder characterized by mild mental deficiency, seizures, ataxia, and hyperreflexia. In the third decade of life, the male has a xanthoma of the achilles tendon. Both siblings have normal plasma cholesterol, but elevated plasma cholestanol (10.2 and 18.0 mg/dl; normal 0.6 +/- 0.2) and erythrocyte cholestanol (8.1 and 12 mg/dl). Cholestanol accounts for 5.0 and 8.1% of total plasma sterols (normal 0.2 +/- 0.2) and for 5.4 and 9.0% of total erythrocyte sterols (normal 0.2 +/- 0.2).

These findings are diagnostic of cerebrotendinous xanthomatosis, an inherited disorder of sterol metabolism, and suggest that abnormal bile acid metabolism in early life resulted in correctable extrahepatic biliary atresia.

1081 THE EFFECT OF CHRONIC METABOLIC ACIDOSIS ON GROWTH AND BONE COMPOSITION. B.A. Kaiser, H. Leitz, E.S. Moore. Michael Reese Med. Ctr., Univ. Chicago, Pritzker Sch. Med., Dept. Ped. Chicago, IL.

Chronic metabolic acidosis (CMA) usually results in growth inhibition, hypercalciuria and bone abnormalities. To evaluate the possible relationship between growth inhibition, increased urine calcium (Ca) loss and bone composition during CMA, we studied ammonium chloride (NH_4CL) induced CMA in the rapidly growing weanling rat. For a period of 30 days, rats were fed ad-lib on normal rat chow (1.2% Ca), with acid group A (n=7) receiving increasing amounts of NH_4Cl (1.5 to 2.0%) added to the drinking water, while control group C (n=8) received distilled water. Group A developed a moderate metabolic acidosis compared to C: pH, 7.30±.09 vs 7.49±.02 units, p<.001; HCO_3^-, 16.3±3.9 vs 26.2±1.4 mM, p<.001. Group A excreted a greater amount of urine Ca compared to C (132±56 vs 96±12 μEq/day, p<.05). Group A grew poorly when compared to C; the weight gain of A was only 61% of C (117.3±4.6 vs 188.1±6.1 gms, p<.001), the increase in body length of A was 81% of C (7.1±0.3 vs 8.8±0.1 cms, p<.001). Although the femurs of A weighed less (0.458±0.042 vs 0.606±0.051 gms, p<.001) and were shorter(1.240±0.025 vs 1.149±0.040 in., p<.001) than C, their bone Ca (6.690±0.263 vs 6.431±0.476 mEq/gm wet wt., p=ns)and collagen(hydroxyproline)(14.450±1.051 vs 14.577 ±0.736 gms/mg wet wt., p=ns) content per unit wt. of long bone were identical. Therefore a change in the chemical composition of rat cortical bone does not accompany the growth inhibition and the hypercalciuria caused by the CMA induced by NH_4Cl.

●1082 INSULIN RECEPTORS IN THE FETAL CENTRAL NERVOUS SYSTEM, Michael S. Kappy and Mohan K. Raizada, University of Florida College of Medicine; Departments of Pediatrics and Physiology; Gainesville.

Recent studies have demonstrated specific insulin receptors in the central nervous system (CNS) of adult rats. In addition, evidence obtained in vitro suggests that macromolecular biosynthesis in the CNS may be insulin-sensitive.

We measured specific insulin binding to plasma membranes prepared from five 18-21 day fetal rat brains and compared it to the binding present in similar preparations from 5 adult rats to substantiate the possible role of insulin as a brain growth-promoting peptide during fetal development.

Mean specific insulin binding was 4.0 ± 0.8% (SEM) and 1.7 ± 0.2% of total radioactivity present per 75 ug protein in the membranes prepared from fetuses and adults, resp. (p<.02). Maximum insulin binding capacity (Ro) was greater in membranes prepared from fetal brains (580 ± 170 pg) than from adult brains (200 ± 60 pg/75 ug protein) (p<0.05).

Thus both insulin binding and binding capacity (receptor concentration) in fetal rat brains were greater than in adults. Since the onset of rapid brain growth occurs late in the gestation of the rat, the presence of insulin receptors in the rat brain at that time is consistent with the theory that insulin has an important role during fetal development as a regulator of metabolic events, including the growth of the brain.

1083 VARIATION IN GLYCEMIC EFFECT OF INSULIN IN DIABETIC CHILDREN. Kirk M. Kerensky, Dorothy J. Becker, and Allan L. Drash, University of Pittsburgh, Department of Pediatrics, Pittsburgh, PA

We examined, using intravenous (IV) and subcutaneous (SQ) insulin tolerance tests (ITT) (0.3 u/kg of soluble insulin) the onset (10% decrease in plasma glucose from baseline) and lowest plasma glucose (PG) in 18 pts. ($\bar{x}$ age 14.9±1.7 yrs.) with insulin-deficient diabetes (IDD) of $\bar{x}$ duration 9.0±3.6 yrs. These were compared to IVITT's (0.1 u/kg) in 15 endocrinologically normal patients age 14.7±1.6 yrs. admitted for evaluation of short stature. IV insulin induced a fall of PG with a slope (Kt) similar in IDD and controls. However, $\bar{x}$ time to nadir of this drop with IV insulin was significantly prolonged (p<0.001) in IDD vs controls (58.9±29.6 vs 25.3±5.2 min., respectively) and unrelated to basal PG or serum insulin antibody binding capacity (ABC). The PG rebound from the nadir in IDD (17.4 mg/dl at 90 min. and 32.0 mg/dl at 150 min.) was less (p<0.001) than that of controls at 90 min (47.5 mg/dl). The degree of this rebound did not correlate with ABC and was associated with normal growth hormone (GH), cortisol (F), and glucagon (G) responses. We conclude that counter-regulatory hormones and ABC are minimal factors in the variability of insulin glycemic effect.

The range of time of onset of SQ insulin action was very variable (20-90 min.) and was unrelated to basal PG, G, GH, F, or ABC. Because of insulin action variability, the timing of insulin injections plays a major role in the control of IDD. Consequently, ITT may be helpful in determining the timing of routine insulin administration.

● 1084 KETONE BODY OXIDATION BY DEVELOPING RAT LUNG. Robert E. Kimura, Gunilla E. Thulin, Joseph B. Warshaw. Yale Univ. Sch. of Med., Dept. of Peds., New Haven, CT

We have reported that glucose oxidation to CO_2 is decreased in suckling rat lung compared to adult rates. We have now determined the rate of β hydroxybutyrate oxidation to CO_2 in developing rat lung and determined the effect of β hydroxybutyrate on glucose oxidation in lung. Maximal rate of β hydroxybutyrate oxidation by developing rat lung slices decreases from 0.60 ± 0.05 (S.E.) n moles/mg wet wt/hr at 6 days of age to 0.42 ± 0.02 by 16 days of age. (p<0.005). Adult rates are also 0.42. Glucose oxidation to CO_2 in developing rat lung increased from a suckling rate of 0.20 n moles/mg wet wt/hr to an adult rate of 0.44. In the presence of β hydroxybutyrate glucose oxidation in lung decreased by 25% in suckling and adult animals. Though the maximal rate of β hydroxybutyrate oxidation in rat lung only decreased 33% from 6 days of age to adult, the concentration of β hydroxybutyrate available during the suckling period is 6 fold greater than in the adult. This data suggest that ketones are a significant oxidative substrate in lung during a period when glucose oxidation is suppressed.

●1085 REGULATION OF THE PENTOSE PHOSPHATE PATHWAY BY AN NADP-BINDING PROTEIN: A NEW FORM OF METABOLIC REGULATION. Henry N. Kirkman. Univ. of N. Carolina Sch. Medicine, Dept. of Pediatrics, Chapel Hill.

NADPH is required for the reductive biosynthesis of numerous substances. In many species, the principal source of NADPH is the pentose phosphate pathway, for which glucose-6-phosphate dehydrogenase (G6PD) is the initial and rate-limiting step. Earlier reports from this laboratory indicated that G6PD of normal and G6PD-deficient red cells is inhibited 5-fold to 200-fold by an unknown macro-molecular substance. The combination of this factor and G6PD deficiency, not G6PD deficiency alone, accounts for the clinical problems in many of the 100 million people with defects of G6PD. The factor has now been identified as a protein which regulates G6PD by holding most of the red cell NADP ($NADP^+$ and NADPH) in a bound form. The protein appears to be distinct from both Fx protein and the Eggleston-Krebs factor. It causes half of the red cell NADP to remain with the proteins during P-10 chromatography of 1:10 stroma-free hemolysates and subsequent ultrafiltration on Amicon CF-25 cones. With this protein concentrate a sigmoid curve is obtained when the observed $NADP^+/NADP$ ratio of unbound dinucleotide is plotted against various fixed $NADP^+/NADP$ ratios of total (bound and unbound) dinucleotide. This finding accounts for the previously noted inhibition and sigmoid kinetics of intracellular G6PD. Part, if not most, of the NADP binding is attributable to a protein of about 26,000 daltons that is obtained largely as a single band after chromatography on ion-exchange and S-200 Sephacryl columns.

1086 INTRAUTERINE GROWTH AND FASTING METABOLISM IN THE INFANTS OF OBESE MOTHERS. R.Kliegman, T.Gross, S.Morton, R.Dunnington. (Spon.by A.A.Fanaroff) Case Western Reserve Univ., Depts. Pediatrics and OB/GYN, Cleveland, Ohio

To determine the effect of maternal obesity(MO) on fetal growth and neonatal metabolism, 12 MO term pregnancies(P) were compared to 10 controls. Pre P weight (239.1±9.8 vs 120.3±4.3 lbs)*was ↑ while P weight gain (16.4±6.3 vs 30.1±2.5) was ↓ in MO. Maternal height, parity, delivery glucose(GLU) infusion and abnormal GLU tolerance were equivalent. Infants of MO(IOM) were heavier (3.9±0.1 vs 3.2±0.1 kg) as were their placenta (687±65 vs 572±43g) while ponderal index was ↓ (12.7±0.1 vs 13.5±0.1). Scapula (4.7±0.2 vs 3.7±0.2cm) and tricep (4.9±0.2 vs 3.6±0.3) skin folds were ↑ in the IOM as was the percent of LGA infants (41 vs 0); length, head circumference and cord blood GLU were unaltered. Neonatal GLU was stable in controls while IOM had ↓ GLU at 60 (26.3±2.7 vs 63.1±8.2mg%), 90(40.9±4.5 vs 63.7±7.8), 120(54.7±6.7 vs 71.4±6.7) and 180(50.7±5.6 vs 79.1±10.2) min. All IOM were asymptomatic. Insulin levels were equivalent at each time period. Triglycerides(T) ↑ after birth in controls. Cord vein (64±20 vs 13±2) and artery (24±5 vs 9±1) T were ↑ in IOM. After birth IOM T increased further remaining higher at 30(72±15 vs 32±6) and 60(78±18 vs 29±5) min. Glycerol increased after birth in both groups but was ↑ in IOM between 60 and 240 min, while IOM β-hydroxybutyrate(BHBA) was ↑ at 90 and 240 min. Conclusion: MO may result in ↑ fetal adipose tissue growth. Postnatal metabolism is characterized by transient asymptomatic fasting hypoglycemia. Augmented availability of alternate fuels in IOM may spare GLU utilization and ↑ circulating GLU levels. *Mean ± SE

1087 CHANGES IN IONIZED CALCIUM WITH PARENTERAL CALCIUM ADMINISTRATION. Anne Koons, Anita Baldomero, Shyan Sun, Minerva Castillo.(Spon. F. Behrle)New Jersey Med School. Div. Neonatology, Newark, New Jersey

The use of intravenous calcium (Ca) in sick infants has been recommended to maintain Ca homeostasis. We compared bolus and continuous infusions to determine which method better maintained levels of ionized Ca (iCa). The new Radiometer I CAL1 Ionized Calcium Analyzer was used for simultaneous determinations of iCa in mmol/L & pH. The instrument also corrects for iCa at pH 7.4 (ciCa). By random selection, 10 pts were treated by continuous (group A) and 8 pts by intermittent bolus (group B) infusions. 250 mg/kg of Ca gluconate was given over 24 hours to group A and in 4 divided doses at 6 hr intervals to group B. iCa determinations were carried out at hours 0-3, 4-6, 8-12, 18-24. Changes in iCa (Δ iCa) compared with pre-infusion iCa levels were measured. Although unpredictable variations in Δ iCa and Δ ciCa were observed, iCa consistently increased in both groups A & B.

	Mean Δ ciCa mmol/L			
Time (hrs)	0-3	4-6	8-12	18-24
Group A	0.045	0.032	0.017	0.157
Group B	0.084	0.205	0.155	0.270
p (t one tail)	NS	.03	.03	NS

In each time period the mean Δ iCa was greater in group B than A. This data supports the conclusion that intermittent bolus Ca is more effective in increasing iCa than continuous Ca infusion. The intermittent method can also minimize the risk of extravasation and tissue necrosis commonly seen with continuous infusions.

● **1088** RETINOPATHY RISK FACTORS FOR CHILDREN WITH DIABETES. John I. Malone, W. Sanderson Grizzard, Thomas C. Van Cader, & Luis R. Espinoza. U. of So. Florida Col. of Medicine, Dept. of Pediatrics,Ophthalmology & Medicine, Tampa, FL.

Seventy-eight youths with insulin dependent diabetes (IDD) were followed for 4 or more yrs. with annual fluorescein angiography (FA). FA was graded: 0-10 microaneurysms=no significant abnormalities (NSA), 10 or more microaneurysms plus fluorescein leakage= significant abnormalities (SA), neovascularization=proliferative retinopathy (PR). Glycemic control was evaluated with HbAlc. The IDD were grouped as (1) No progression in FA for 4 yrs.=NP or (2) Progression from NSA to SA or PR during 4 yrs.=P. The results:

	Age	Duration	Sex M	Sex F	Insulin 1	Insulin 2	HbAlc
NP	15.5±.31	7.7±.48	24	14	18	20	10.5±.32
P	17.2±.43	9.4±.53	15	25	19	21	10.7±.32
p<	.01	.025	.01		NS		NS

HLA typing performed on 30 of the IDD's showed an increase in B8 in both groups when compared to 100 non-diabetic controls (ND) p <.01. Similarly DR3 and DR4 were each significantly increased in IDD when compared to 495 ND. The combination of DR3, DR4 was present (13/17) 77% of IDD with P of retinopathy, (5/13) 39% with NP (p<.02) and 3% of NP controls. PR was noted in 10 of 40 with P; DR3, DR4 was present in 90% (9/10). Control as indicated by HbAlc and frequency of insulin injections (1 or 2 per day) did not influence P of retinopathy. Increasing duration of IDD in females with HLA DR3,DR4 are significant risk factors for the development of proliferative diabetic retinopathy in youth.

1089 LOW PLASMA CALCITRIOL LEVELS AND RESPONSE TO CALCITRIOL SUPPLEMENTATION IN IDIOPATHIC JUVENILE OSTEOPOROSIS (IJO), Harold K. Marder, Reginald C. Tsang, George Hug, Alvin C. Crawford. Univ. of Cincinnati College of Medicine, Children's Hospital Medical Center, Depts. of Pediatrics and Orthopedics, Cincinnati.

The cause of IJO is unknown and abnormalities in calcitropic hormones have not been previously sought in this condition. Low plasma calcitriol (1,25-dihydroxyvitamin D) levels ($\bar{x}$ = 4 pg/ml) and normal serum calcifediol (25-hydroxyvitamin D) and parathyroid hormone levels were noted during the evaluation of an 11-1/2 year old female with osteoporosis of recent onset characterized by metaphyseal "neo-osseous" porosis and compression fractures pathognomonic of IJO. Bone mineral content was markedly abnormal (0.322 gm/cm^2; normal range, 0.390-0.902 gm/cm^2) and one fracture occurred monthly during the 6 month pre-treatment observation period. Treatment with calcitriol, 1.0 ug daily, resulted in bone mineral accretion with eventual normalization of bone mineral content. Only 5 fractures, 2 associated with significant trauma, occurred during 24 treatment months. A calcitriol level 5 months after menarche and 3 weeks after stopping calcitriol supplements was 70 pg/ml. The observed response suggests a relationship between calcitriol deficiency and the pathogenesis of IJO. Furthermore, the similarities between the findings in this child and those in women with postmenopausal osteoporosis implicate sex steroid deficiency as a possible cause of IJO which would explain the spontaneous remissions invariably experienced by these patients after puberty.

● **1090** LACTIC ACIDOSIS DUE TO LIPOAMIDE DEHYDROGENASE (LAD) DEFICIENCY: IMPROVEMENT AFTER ORAL LIPOIC ACID. R. Matalon, K. Michals, R. Hart, D. Stumpf, S. Goodman, and J. Parks. Univ. of Ill. Chicago and Univ. of Colorado, Denver.

A male born at term weighing 2.9 kg, had neonatal hypothermia and persistent failure to gain, vomiting, and metabolic acidosis. At 8 months he weighed only 4.1 kg, was hypotonic, unable to support his head, and had very little muscle mass. CT scan showed moderate cortical atrophy. Lab investigation revealed acidosis (pH 7.0-7.2), hyperalaninemia (3x normal), lactic-pyruvic acidemia (4x normal), and increased excretion of lactic, 3-OH-isovaleric, 2-OH-glutaric 2-keto-glutaric, 2-OH-isocaproic, malic and fumaric. Clinical and biochemical features were not changed by thiamine (600 mg/day), biotin (10 mg/day), bicarbonate (1.5 g/day) or protein restriction. Studies on cultured fibroblasts showed reduced activity of pyruvate and 2-keto-glutarate dehydrogenase complexes. LAD was 20% of control mean (n=27). Apparent Kms for LAD substrates were normal in forward and reverse directions. Lipoic acid, 400 mg orally per day, produced almost complete clearing of the abnormal organic aciduria, lactic and pyruvic acidemia dropped to 2x normal. Ten months later, he weighs 8 kg, muscle tone has improved, and he can sit and say a few words. Oral treatment with lipoic acid may help correct clinical and biochemical abnormalities due to LAD deficiency, usually a fatal disease.

1091 IDM MODEL: EFFECTS OF FETAL HYPERINSULINISM ON RAT HEPATIC INTERMEDIARY METABOLISM. Kenneth McCormick, Elizabeth Donlon, and Paul Davis. (Spon. by Gilbert B. Forbes), University of Rochester Medical Center, Rochester, New York.

To determine the direct effects of hyperinsulinism on fetal hepatic metabolism, 1 mm^3 liver explants were prepared from 19 day rat fetuses. For 48 hours the explants grew on nylon screens in petri dishes under 95:5 O_2/CO_2, nourished in artificial medium (BGJb) supplemented to a final conc. of zero,250, or 500 mU porcine insulin/ml for the duration of tissue culture. After several rinsings of the explants with buffered saline, rates of ketogenesis, lipogenesis, and gluconeogenesis were measured using 1 mM oleate, 250μCi/ml of ^3H_2O, and ^{14}C(U)-lactate (.035μCi/μmole), respectively. Acetoacetate (acet) and β-OH butyrate (βOHB) production rates were determined in the ketogenesis experiments. Reactions took place at 37°C and were linear for 2 hours. Results are expressed as mean ± SE (N); units are nmol/min/mg DNA.

Insulin mU/ml	Lipogenesis: fatty acids	Ketogenesis: acet	Ketogenesis: βOHB	Gluconeogenesis: glucose equiv.
0	1.0±.1 (6)	26±2 (13)	18±1 (14)	14±2 (14)
250	2.0±.8 (3)	18±1 (8)	12±1 (8)	-
500	1.8±.1 (5)	11±1 (9)	9±1 (10)	6±1 (14)

The metabolic rates for cells exposed to insulin, either 250 or 500 mU/ml, were significantly different from controls (p<.05). Chronic hyperinsulinism attenuates fetal hepatic glucose and ketone production, accounting in part for hypoglycemia in the IDM; and it augments lipid synthesis. The latter may contribute to the corpulence of these infants.

1092 AUTOSOMAL DOMINANT VITAMIN D DEPENDENT RICKETS (VDRR). Paul T. McEnery (Sponsored by Clark D. West). University of Cincinnati, College of Medicine, Children's Hospital Medical Center, Cincinnati, Ohio

VDRR, an autosomal recessive inborn error involves defective conversion of liver metabolized 25 hydroxycholecalciferol in the kidney to 1,25 dihydroxyvitamin D_3 (1,25 $[OH]_2$ D_3) with resultant low serum levels of 1,25 $[OH]_2$ D_3.

Children in three distantly related families have been followed for VDRR. Family pedigree shows seven generations dating to 1865 when the original parents immigrated from Bavaria to southern Ohio. Individuals of generation III and beyond have a varying history of recurrent bone pain, generalized muscle weakness or multiple cortical bone fractures as adults and rickets, bowed legs and failure to thrive as children. Two adult females in generation V had virtually absent serum 1,25 $[OH]_2$ D_3 levels, hypocalcemia, hyperparathyroidism, and mild osteomalacia. High dose vitamin D_2 normalized serum 1,25 $(OH)_2$ D_3 and resolved symptoms. Children receiving vitamin D_2 have low serum values of 1,25 $(OH)_2$ D_3 for age. Fifteen of 26 children with rickets are males. Fifteen of 21 adult onset osteomalacia are females, and on vitamin D_2 have normal levels of 1,25 $(OH)_2$ D_3 and resolution of disease. Adult males treated as children for rickets, no longer on therapy have normal values of 1,25 $(OH)_2$ D_3.

VDRR appears in this pedigree autosomal dominant with variable degrees of expression. The basic defect is hypothesized as a high Km for renal tissue enzyme 1 hydroxylase conversion of 25 hydroxycholecalciferol.

1093 METABOLIC RESPONSES TO CONSECUTIVE INJECTIONS OF ALANINE AND FAT IN HYPO- AND NORMOGLYCEMIC SMALL-FOR-GESTATIONAL-AGE (SGA) BABIES. Mats Mellander, Karl G Sabel, Aimon Niklasson, Ragnar Olegard, (Sponsored by Mildred T. Stahlman). Univ. of Goteborg, Dept. of Pediatrics, Sweden.

The purpose of this study was to examine the roles of gluconeogenic substrate (GS) availability and fatty acid oxidation in glucose homeostasis of newborn SGA infants. At 4 hrs of age, as their first caloric intake, 5 hypoglycemic (HG) ($\leq$30 mg/dl) and 5 normoglycemic (NG) SGA infants were given injections of L-alanine, 150 mg/kg, and 1 hr later Intralipid 0.5 g fat/kg. Plasma concentrations (conc.) of glucose, alanine, pyruvate, lactate, triglycerides, free fatty acids (FFA), glycerol, β-OH-butyrate (BOHB) and acetoacetate were followed for 5 hrs. After alanine injection glucose conc. did not change in the HG but decreased in the NG ($p < 0.05$). The Δ alanine at 60 min. was greater in the HG than in the NG ($p < 0.05$). The sum of alanine, lactate and pyruvate remained high in the HG but decreased rapidly in the NG ($p < 0.005$). FFA and BOHB decreased in all 10 infants. After fat injection, in the two groups, the glucose, FFA and BOHB concs. increased significantly and the subsequent decreases in GS concs. were similar.

The results of this study indicate that: 1) GS deficiency is not a significant etiologic factor in the early hypoglycemia of SGA infants, 2) HG, as compared to NG, SGA infants have a slower elimination of GS suggesting impaired gluconeogenesis, 3) in most HG SGA infants an artifical increase of fatty acid oxidation augments GS elimination which, with the concomitant increase in blood glucose conc., suggests improved gluconeogenesis. This might be secondary to increased intramitochondrial concs. of acetylCoA, a necessary co-factor for pyruvate carboxylase.

1094 LOCAL CEREBRAL GLUCOSE UTILIZATION IN THE BEAGLE PUP MODEL OF INTRAVENTRICULAR HEMORRHAGE. Laura R. Ment, Charles C. Duncan and William B. Stewart (Spon. by Bennett A. Shaywitz), Yale Univ. Sch. of Med., Dept. of Pediatrics, Neurology and Neurosurgery, New Haven, Connecticut, 06510.

Although intraventricular hemorrhage (IVH) is thought to be a manifestation of alteration in blood flow to the germinal matrix, the metabolic consequences of this lesion are unknown, and neonates with IVH often have long lasting hypoglycorrhachia, which may imply profound alterations in cerebral metabolism. We have used the 14C 2-deoxyglucose (2DG) method to study local cerebral glucose utilization (LCGU) in the beagle pup model of IVH. 12 pups (12-48 hrs, 300-425 g wt) were anesthetized, tracheotomized, paralyzed, and ventilated. Arterial blood gases and blood pressure were obtained through a femoral artery cannula. IVH was induced in 6 by removal of 20-25% of their total blood volume via a femoral venous catheter followed by rapid venous reinfusion 5 minutes later. 6 additional pups served as controls. In the hemorrhage pups, MABP was 80 mm Hg prior to the withdrawal of the blood, 65 mm Hg during the hypotensive phase and 93 mm Hg following reperfusion. Control pups had MABP 82 mm Hg throughout. 50 minutes following the induction of IVH, LCGU was measured. 14C 2DG concentrations were 24, 16, 22 and 18 μC_i for the cortex, white matter, caudate nucleus and germinal matrix respectively of the controls. For the experimental group 2DG concentrations included cortex 22, white matter 21, caudate nucleus 22 and germinal matrix 21 μC_i. Although cerebral blood flow changes are known to occur in specific brain regions in this model of IVH, there may be uncoupling of blood flow and metabolism throughout the brain.

1095 GUT TRANSPORT OF $^{45}Ca^{2+}$ IN FETAL LAMBS (FL). E.S. Moore, C.B. Langman, M. Loghman, M.J. Favus, F.L. Coe. Pritzker Sch. Med., Univ. Chicago, Michael Reese Med. Ctr., Depts. Ped. and Med., Chicago, IL

Studies were done in 11 FL age 100-150 days gestation (term= 150 d). 8 control (C) FL had sham bilateral nephrectomy (Nx) and 3 FL were made chronically hypocalcemic by Nx. Blood was drawn at surgery and on post op day (D) 10 for pH, ionized Ca (Ca^{2+}) and total Ca. On D 10, FL were sacrificed and portions of duodenum (Duo), jejunum (je), ileum (Il), and ascending (CoA), transverse (CoT), and descending (CoD) colon used to measure $^{45}Ca^{2+}$ transport by everted gut sacs. Adjacent segments were used to measure CaATPase. On D 10, Ca and Ca^{2+} were signficantly less ($p<.001$; $p<.001$) and Pi signficantly greater ($p<.001$) than for C. Values are mean and ±SEM:

		Duo	Je	Il	CoA	CoT	CoD
^{45}Ca Uptake	C	23.2	27.5	28.5	34.3	65.4	23.5
μm Ca/mg prot/30"		±5.5	±4.2	±5.2	±6.4	±17.5	±3.4
$x10^{-3}$	Nx	--	21.5	31.7	33.6	78.3	29.8
		--	±7.6	±13.6	±13.4	±32.2	±10.0
CaATPase	C	59.3	73.7	24.2	12.2	25.5	22.9
μm Pi/mg prot/5"		±16.9	±15.9	±7.1	±4.9	±7.8	±4.9
$x10^{-2}$	Nx	66.9	101.8	30.0	--	27.3	20.6
		±28.3	±9.3	±4.4	--	±12.2	±4.7

There was no difference between gut segments from C and Nx for ^{45}Ca uptake and CaATPase and $^{45}Ca^{2+}$ uptake did not correlate with FL serum Ca, Ca^{2+} or gestational age. These data suggest that in utero, gut $^{45}Ca^{2+}$ transport is not dependent on $1,25(OH)_2D_3$.

1096 TESTOSTERONE, ESTRADIOL, AND RELATIVE PONDEROSITY: RELATIONSHIP TO HIGH AND LOW DENSITY LIPOPROTEIN CHOLESTEROL IN ADOLESCENT BOYS. J.A.Morrison, J.Gutai, P.M.Laskarzewski, T.J.Orchard, P.R.Khoury, C.J.Glueck. U.Cincinnati Col.Med. Cin.Gen.Hosp., Dept Med., Ped., Cincinnati, Ohio.

The fall in high density lipoprotein cholesterol (HDLC) during male adolescence has been postulated to result from increasing testosterone(T). In adults, exogenous T lowers HDLC while endogenous T correlates positively with HDLC. We measured plasma estradiol (E2) and T in 42 boys, ages 14-17 yrs. By multiple regression analysis with HDLC as a function of E2, E2*T, T, E2*Quetelet(Q), and race, the multiple R^2 was .46, $p=.008$. With low density lipoprotein cholesterol (LDLC) as a function of E2, $E2^2$*Q, Q, Q^2, T*Q, E2*T, and $E2^2$*T, the multiple R^2 was 66%, $p=.001$. With the ratio of LDLC/HDLC as a function of E2, E2*T, Q, Q^2, $E2^2$, $E2^2$*T, T*Q, and race, the multiple R^2 was .77, $p=.0001$. In boys with high E2, as T rose, HDLC fell; with median E2, there was a flat horizontal relationship between T and HDLC; at low E2, there was a small positive relationship between T and HDLC. The relationship between HDLC and T was shifted progressively downward in a vertical axis as subjects' Q went from low to mid to high. LDLC/HDLC rose as T rose in boys with highest Q and highest E2. For boys with mid-low Q and mid-low E2, LDLC/HDLC:T relationships were respectively horizontal, and negative. This cross sectional data reveals complex relationships between T, E2, Q, their interactions, and HDLC, LDLC, and LDLC/HDLC. In aggregate, changes in T, E2, and Q in boys during adolescence can account for a significant proportion of the decrements in HDLC and increments in LDLC, changes, which relative to girls, are atherogenic.

1097 GALACTOSE ENHANCED NEONATAL MURINE HEPATIC GLYCOGEN SYNTHESIS. S.Morton & R.Kliegman. (Spon.by A.Fanaroff) Case Western Reserve Univ., Dept.Peds., Cleveland, OH

Neonatal glucose(GLU) homeostasis is imprecisely controlled as evident by fasting hypoglycemia and alimented hyperglycemia. Galactose(GAL) alimentation has recently been suggested to help regulate carbohydrate assimilation. To better define the mechanism of GAL enhanced GLU homeostasis, 5 day old newborn rats were fasted overnight and fed 0.6g/kg of GLU or GAL by oro-gastric tube. Blood GLU and GAL and hepatic glycogen(GLYC) content were determined at 0 and 15 and then at 30 min intervals. Fasting GAL levels were 0.5±0.1mg%.* After GAL feeding, blood GAL ↑ rapidly, achieving peak values at 15 min (84.9±21.3). Thereafter GAL levels ↓ to 39.8±11.6 and 19.4±5.6 at 30 and 60 min. By 240 min GAL returned to fasting values. Fasting GLU was 55.5±4.2%. After GAL feeding, blood GLU ↑ at 15 min (91.7±6.5) achieving peak values at 60 min (102.1±14.6). Between 60 and 240 min GLU remained elevated declining at 300 min to 54.7±6.6. After GLU feeding blood GLU ↑ at 15 min (125.3±13.4) achieving peak values at 30 min (250.3±43.4). GLU ↓ until 300 min (83.7±9.9). The glycemic response following enteric GLU was greater than that following GAL at 15,30,60,120 and 300 min. Hepatic GLYC ↑ minimally between 15-180 min after GLU, but later ↑ at 240 (52.9±12.1μmol/g) and 300 (81.2±14.7) min compared to the 0 time (15.4±2.3). In contrast after GAL, GLYC ↑ at 60 min (34.2±6.1) and ↑ further to 300 min (76.2±7.6). GLYC was consistently ↑ after GAL compared to GLU feeding from 60-180 min. Conclusion: Neonatal enteric murine GAL alimentation may result in augmented control of blood GLU levels due to enhanced early hepatic GLYC synthesis. *Mean ± SE

● 1098 CARNITINE DEFICIENCY AND RENAL FANCONI SYNDROME. Michael L. Netzloff, Arthur F. Kohrman, Margaret Z. Jones, Ronald K. Emaus, Loran L. Bieber, Salvatore DiMauro. Michigan State University College of Human Medicine, Department of Pediatrics/Human Development, East Lansing, MI and Columbia University, New York City, N.Y.

Tissue carnitine levels and renal loss of carnitine were studied in a 5 3/12 year old child with muscle weakness, mental retardation, and Fanconi syndrome. Muscle weakness became more apparent when the patient was learning to walk. A muscle biopsy showed lipid excess in type 1 muscle fiber in a pattern consistent with carnitine deficiency. Free carnitine was determined in muscle and liver (means ± standard errors): muscle, 2.29±0.05, control 17.1±1.3 nmol/mg noncollagen protein (ncp); liver, 1.86, control 8.24±1.22 nmol/mg ncp. Three subsequent 24 hour urine collections and midpoint serum determinations of total, free and short chain acylcarnitine were done: total carnitine, urine, 120±22.4, control 86 µmol/24 hours; serum, 9.58±0.67, control 46.1±1.8 µM. Levels of total carnitine in the blood were extremely low, approximately 20% of normals. The levels of muscle and liver carnitine were similarly decreased. In contrast the urinary levels of carnitine were elevated when compared to normals, and particularly in view of the low serum, muscle, and liver values. An L-carnitine loading test resulted in transient retention of carnitine. In this patient, the data suggest that systemic carnitine deficiency and related muscle weakness can be induced by excessive renal loss of carnitine, and may possibly be another manifestation of renal Fanconi syndrome. Furthermore, the condition may be treated with supplemental oral carnitine.

1099 3,5 DIMETHYL 3' ISOPROPYL THYRONINE (DIMIT) TREATMENT IN DIABETIC PREGNANCY: GLYCOGENOLYTIC EFFECTS ON FETAL TISSUES. N. Neufeld, S. Melmed, (Intr. by B. Kagan). Departments of Pediatrics and Medicine, Cedars-Sinai Medical Center, UCLA School of Medicine, Los Angeles, CA.

DIMIT, a nonhalogenated thyroid analog, crosses the placenta and exhibits metabolic effects in the fetus. We have shown (J. Clin. Invest., Dec. 1981) that DIMIT administration (0.5 mg/kg on d. 25 and 26) to alloxan diabetic pregnant rabbits promoted fetal lung maturity and increased lung phospholipids. This was associated with reduction in fetal lung glycogen.

Therefore, the effect of DIMIT on fetal heart and liver glycogen content were examined. Fetuses of diabetics (D) had significant elevations in cardiac (6.3±0.9 vs 2.4±0.5* µg/mg protein) and liver glycogen (19.4±1.4 vs 6.6±1.5** µg/mg protein) compared to controls (C). DIMIT depleted cardiac glycogen in D fetuses (1.3±0.4** µg/mg vs D); liver glycogen was indetectable in both DIMIT treated C and D groups. D blood glucose was significantly elevated (274±48 vs 48±4 mg/dl* vs C); and lowered to normal with DIMIT treatment (64±6 mg/dl***, vs D).

Conclusion: DIMIT, a maternally-administered fetal-active thyromimetic agent caused glycogen depeletion in fetal tissues in diabetic pregnancy, and amelioration of maternal diabetes. Potential beneficial effects in diabetic pregnancy include maturation of fetal lung, improvement of myocardial function and hepatic enzyme induction. These beneficial effects further support a therapeutic role for DIMIT in the treatment of diabetic pregnancy.

(m±SEM, for n=12-20 fetuses per group; *p<0.01, **p<0.001)

(Supported by a grant from the United Cerebral Palsy Foundation)

●1100 EFFECTS OF NOCTURNAL FEEDING ON GROWTH RATE, [^{15}N]-GLYCINE TURNOVER AND TOTAL BODY PROTEIN SYNTHESIS IN TYPE III GLYCOGEN STORAGE DISEASE. Itzhak Nissim, Marc Yudkoff, Charles Stanley, Lester Baker and Stanton Segal. The Children's Hospital of Philadelphia, Department of Pediatrics, Philadelphia, PA.

[^{15}N]glycine kinetics and whole body synthesis were measured in a patient with debrancher deficiency whose growth rate increased from 4 to 15 cm/yr after treatment with nocturnal intragastric feeding. The study was done on three separate occasions: (a) in the fasted state; (b) during an intragastric glucose infusions at 150% of the estimated glucose production rate; and (c) while the patient received this glucose infusion plus an amino acid supplement (Vivonex). The results were as follows:

	K Gly (h^{-1})	Pool Size (µmol/100g)	Flux (µmole/100g/hr)	Prot. Synth. (g/kg/d)
Fasted	4.5	18.5	83.0	0.6
Glucose	2.68	25.0	67.0	1.2
Glucose + AA	1.53	41.4	63.0	2.2
Normal adult(3)	3.3-4	5.5-8.1	23-36	3.4-4.3

We conclude that growth failure in type III glycogen storage disease is referable to accentuated catabolism of endogenous protein to provide gluconeogenic amino acids. Treatment with exogenous glucose promotes growth by reducing this process. Inclusion of amino acids in the treatment regimen further stimulated the rate of total body protein synthesis.

● 1101 EFFECT OF NUTRITIONAL REHABILITATION ON THE PROTEIN METABOLISM OF MALNOURISHED CF ADOLESCENTS. P.Pencharz, E.Archibald. (Spon: T.Heim) Research Institue, Hospital for Sick Children, Toronto, Canada.

Rates of whole body amino nitrogen flux (Q) were measured in 6 malnourished adolescent and young adult CF patients-3 male & 3 female. The subjects underwent nutrition rehabilitation utilizing a continuous naso-gastric infusion of an elemental diet (Vivonex) at 70-80ml/kg/d for 10-12d. Turnover rates (Q) were measured using a ^{15}N-glycine tracer administered as a single dose (20mg ^{15}N) at 0800 Urine was collected for 24h and Q calculated from the cumulative excretion of ^{15}N in urinary ammonia. Studies were repeated 3 times in each subject as shown below.

Vivonex Intake		Weight Gain	Amino Nitrogen Flux (Q) (mgN/kg/d)		
Protein (g/kg/d)	Energy (kcal/kg/d)	(kg)	Control	Day 4	Day 8-11
1.5±0.4	79±18	3.2±0.3	696±13*	631±154	357±86*

* $p < 0.05$

On the Vivonex infusion, net absorbed energy intake was improved by 20% and was associated with a significant weight gain. Initially there was no detectable change in the rate of whole body protein turnover (Q). However by day 8-11 Q was approximately 50% of control values. We interpret these results as indicating that the changes in whole body protein metabolism in response to refeeding occur promptly and may be largely complete by 8-11d. We and other investigators have noted that malnourished subjects have high initial protein turnover rates. By the use of the single dose approach used in this study we have been able to determine the rate of response for protein metabolism during refeeding.

● 1102 SUSTAINED NORMOGLYCEMIA IN NEWLY-DIAGNOSED TYPE I DIABETICS: SHORT-TERM EFFECTS AND 1 YEAR FOLLOW-UP. Kusiel Perlman, Robert M. Ehrlich, Annette Girling, Robert M. Filler, A. Michael Albisser, (Spon. by Don Fraser) Hosp. for Sick Child., Depts. of Paed. & Surg., Toronto, Canada.

With informed consent, we studied 12 non-obese newly-diagnosed ketosis prone diabetics aged 10-16 years 5 of whom began insulin therapy by a portable preprogrammed system of central venous infusion 16-48h following diagnosis. The infusions were maintained for 28-62d. In this group the mean ac plasma glucose was 86±3 mg/dl with normal meal excursions (peak glucose rise of 29±3 mg/dl at 41±4 min) throughout the infusion periods. Following an initial 1-2d period of stabilization the mean 24h urinary glucose excretion in the infused subjects was 0.2±0.06g. Mean HbA_1 dropped significantly from 14.5±1.2% before to 9.2±0.9% after infusion. In 3 patients the value fell into the normal range (6.5-8.5%). Exogenous insulin requirements decreased from 1.4±0.22 U/kg/d to 0.37±0.07 U/kg/d during the infusion period. In the 7 conventionally treated prospective controls the mean fasting plasma glucose was 231±12 mg/dl, the mean 24h glucose excretion was 30.8±8.2g, and the mean HbA_1 dropped from 15.8±0.9 to 11.2± 0.5%. The peak daily insulin requirements were 0.65±0.12 U/kg. 17-100d following diagnosis the requirements decreased to 0.29 ±0.15 U/kg/d. No patient was able to totally discontinue insulin therapy. 350±35 days following diagnosis the daily exogenous insulin requirements for the infused patients was 0.63± 0.06 U/kg and the HbA_1 was 12.9±1%, not significantly different from the control patients who required 0.74±0.12 U/kg and had a HbA_1 of 12.7± 0.8%. We conclude that in adolescents a 1-2 month period of glycemic normalization at diagnosis of Type I diabetes only results in a partial transient remission and does not in itself effect improved metabolic control one year later.

●1103 TREATMENT OF HYPERARGININEMIA WITH ARGININE (ARG) - RESTRICTED DIET AND SODIUM BENZOATE (SB). Ijaz A. Qureshi, Jacques Letarte, René Ouellet, Mark L. Batshaw and Saul W.Brusilow. Dept.of Pediatrics, Université de Montreal, Montreal, and John Hopkins School of Medicine, Baltimore.

Hyperargininemia is a chronic disorder of the urea cycle, in which high levels of plasma ARG may be responsible for neuromuscular weakness and psychomotor retardation. We have treated a 16-year old anorexic girl, homozygote for arginase deficiency, with ARG-restricted diet in conjunction with SB therapy. SB at 250-375 mg/kg/d was initially given with a normal diet furnishing 0.5g prot/kg/d. This brought plasma ARG down to 319 ± 13 µmol/l (mean ± SEM), from a control level of 625 ± 3 µmol/l (normal 75 ± 17). Plasma NH3 and glutamine became normal. SB therapy shifted the pattern of excretion of urinary N from urea to hippurate. Urea N was reduced to 12.7 ± 0.7 % of total N from control values of 35.1 ± 2.1 %, while hippurate N increased to 35.4 ± 1.9 % from 1.5 ± 0.1. Urinary ARG decreased to 1449 ± 60 µmol/d from 2492 ± 170. Orotate excretion became normal.

The isonitrogenous ARG-restricted diet given subsequently was partly based on an ARG-free essential amino acid mixture and contained 0.5g of ARG/d as compared to the normal values of 2.0 g/d. This diet alongwith SB therapy further reduced plasma ARG to 161 ± 14, whereas ARG excretion decreased to 460 ± 25 µmol/d. The biochemical data indicate that SB therapy reduces the endogenous synthesis of ARG by removal of NH_3N through hippurate formation, while ARG-restricted diet controls the exogenous input of ARG. This approach has enabled the patient to gain 3 kg in weight over 1 year, with a net improvement of neurological status.

● 1104 OXIDATION OF [1-^{14}C]PALMITOYL-COA (PC) AND [1-^{14}C] ISOVALERIC ACID (IVA) BY FIBROBLAST MITOCHONDRIA FROM INDIVIDUALS WITH GLUTARIC ACIDURIA TYPE II (GA II) AND ETHYLMALONIC-ADIPIC ACIDURIA (EMA). William J. Rhead and Brad A. Amendt (Spons. by J. Robillard), U. of Iowa Sch. of Med., U. of Iowa Hosp. and Clinics, Dept. of Peds., Iowa City, IA

GA II and EMA are clinically and biochemically related inborn errors of metabolism, characterized by hypoglycemia, acidosis and complex organic acidurias. Clinically, EMA appears to be a milder variant of GA II. The oxidation of PC and IVA was studied in fibroblast mitochondria from 4 normal individuals, and 3 individuals each with EMA/mild GA II and severe GA II. Mitochondria from GA II cells showed greatly decreased oxidation of PC (0.02 ± 0.017 nmol/mg/hr; 3.9% of control; N=5); oxidation of IVA was also deficient in these mitochondria (0.58 ± 0.25 nmol/mg/hr; 33% of control; N=3). Mitochondria from the patient with mild GA II revealed milder impairment of PC and IVA oxidation (0.08 ± 0.08 and 1.03 ± 0.83 nmol/mg/hr, 16% and 58% of control, respectively; N=2). Mitochondria from 2 EMA cell lines showed normal oxidation of PC and IVA (0.48 ± 0.18 and 1.56 ± 0.51 nmole/mg/hr, 94% and 88% of control, respectively; N=4). [1,6-^{14}C]succinate oxidation was normal in all EMA/mild GA II mitochondria and was 63% of control in one GA II cell line. Mitochondrial oxidation of electron transferring protein-linked substrates is severely impaired in severe cases of GA II and less so in mild cases; oxidation of these substrates is normal in EMA, representing the first in vitro, subcellular demonstration of biochemical and genetic heterogeneity in this group of phenotypically similar disorders.

1105 THE EFFECT OF L-CARNITINE (CN) ON THE OXIDATION OF ^{14}C-LEUCINE (LEU) AND ^{3}H-ACYL-COA'S BY RAT TISSUES AND HUMAN SKIN FIBROBLASTS. William J. Rhead and Richard Entz (Spon. by J. Robillard), U. of Iowa Sch. of Med., U. of Iowa Hosp. and Clinics, Dept. of Peds., Iowa City, IA

The addition of CN to rat tissue and mitochondrial preparations is said to increase the production of ^{14}CO2 from [1-^{14}C]LEU by stimulating the activity of the branched chain ketoacid dehydrogenase (BCKAD). In our laboratory, CN increased the oxidation of [1-^{14}C]LEU in rat muscle homogenates to 174 ± 12% of control levels (N=3); in contrast, CN decreased the oxidation of [2-^{14}C]LEU to 73 ± 19% of control levels in the same homogenates (N=3). Similarly, addition of CN did not increase the oxidation of [1-^{14}C]LEU by suspensions of human skin fibroblasts derived from either normal controls or patients with classical maple syrup urine disease. CN did not increase the dehydrogenation of [2,3-^{3}H]isovaleryl-CoA (^{3}H-IVA-CoA) or [2,3-^{3}H]butyryl CoA (^{3}H-BUT-CoA) in intact rat liver mitochondria (80 ± 30% and 111 ± 115% of control values, respectively; N=7). However CN did enhance dehydrogenation of ^{3}H-BUT-CoA by rat muscle mitochondria (RMM) to 1025 ± 279% of control levels (N=7) while not increasing the oxidation of ^{3}H-IVA-CoA by RMM (149 ± 85% of control; N=8; P>0.1). The CN-dependent increase in ^{3}H-BUT-CoA dehydrogenation was completely blocked by octylsulfobetaine, an inhibitor of acyl-CN translocase. CN does not seem to stimulate the overall rate of degradation of the branched chain amino acids (BCAA) in either human skin fibroblasts or rat tissues, and BCKAD does not appear to be the rate limiting enzyme in the catabolism of the BCAA.

1106 INSULIN-MEDIATED CELL GROWTH AND [^{125}I]-IODOINSULIN BINDING IN THE HL-60 CELLS. Alan D. Rogol and Michael L. Johnson. Departments of Pediatrics and Pharmacology, University of Virginia School of Medicine, Charlottesville, Virginia.

Insulin mediates rapid (transport) as well as delayed (e.g. cell growth) effects on cellular metabolism. Since the HL-60 cell, a human promyelocytic cell, can be cultured in defined medium plus insulin, we studied the effect of insulin concentration on cell duplication and [^{125}I]-iodoinsulin binding parameters. The HL-60 cell line was grown in RPMI 1640 medium plus 10% heat inactivated fetal bovine serum (FBS) or in medium plus insulin (0-5 ug/ml; 0-8.3x10^{-7}M). The insulin binding studies were performed with [^{125}I]-monoiodoinsulin. The binding isotherms and displacement curves were analyzed by least-square fitting to a 2-site model and by the method of Scatchard. Cellular doubling times ranged from 1.85 days in 10% FBS and 2.08 days in insulin (8.3x10^{-7}M) to greater than 3.5 days at insulin concentrations below (1.67x10^{-8}M). There was net cell death below 1x10^{-10}M. The half maximal doubling rate occurred at 4.0±10^{-9}M insulin ("K_D"=2.5x10^{8}M^{-1}). A high affinity, low capacity insulin binding site was defined with K_A 3.1±0.5x10^{8}M^{-1} for cells cultured in 10% FBS. The site number was approximately 10,000 per cell. There is a trend toward more avid binding to a high affinity site as the insulin concentration is lowered and a sharp decline in cell growth at insulin concentration below 1x10^{-10}M. Whether the effects of insulin on cellular growth are mediated through insulin receptors defined above or through other growth factor binding sites cannot be determined from these data.

● 1107 TEN YEAR PROGNOSIS OF IMPAIRED GLUCOSE TOLERANCE (IGT) IN SIBLINGS OF CHILDREN WITH INSULIN DEPENDENT DIABETES (IDD). Arlan L. Rosenbloom and Sarah S. Hunt. Univ. Fla. Coll. Med., Department of Pediatrics, Gainesville.

140 2 to 25yr old siblings of 67 children with IDD had 2 hr. oral glucose tolerance testing (OGTT) in 1969-71. We traced similar proportions of those classified as abnormal (44/58, 79%) and normal (61/82, 74%) by screening criteria (8.3mmol/l at 1hr or 7.2mmol/l at 2hr). Six sibs developed IDD after 3 months (1), 2yrs (2), 3yrs (1), and 7yrs (2), all from the abnormal screen group (6/44, 13.6% predictability, 100% sensitivity, 61.6% specificity). The National Diabetes Data Group criteria for children (>7.8mmol/l 2nd hr of OGTT) identified 19 sibs including 5 of the 6 who went on to develop IDD (5/19, 26.3% predictability, 83% sensitivity, 86% specificity). 4/6 sibs who later developed IDD were retested with 4hr OGTT; 3 had glucose areas outside normal mean+2SD but so did 8/36 sibs screened abnormal and retested, who did not develop IDD. Ratios of insulin area to glucose area were <mean-1SD for age-group controls in 3 who developed IDD but also in 5/36 others. Thus relative hypoinsulinemia during OGTT is common (75%) in those who develop IDD, but not in those with IGT who do not develop IDD over the subsequent decade (14%).

The 2hr OGTT identified a subset of sibs of IDD at increased risk (14-26%) or at low risk (0-1%). However, without promise of preventative treatment this knowledge is of no value to the individual and may be harmful. This first long term followup study of IDD sibs with IGT indicates that their disorder is already chronic at the time of clinical onset of IDD.

● 1108 INTENSIVE MANAGEMENT ENHANCES GROWTH OF DIABETIC CHILDREN. Mary C.J. Rudolf, Myron Genel, Susan Bates, William V. Tamborlane. Yale Univ. School of Medicine, Department of Pediatrics, New Haven

The relationship between metabolic control of diabetes and linear growth has been difficult to establish. We have recently reported that improved control of diabetes increases somatomedin (Sm) levels. In the present study, we examined whether intensive treatment altered growth in 9 adolescent diabetics aged 13±2 yrs. Growth velocity (GV) was determined before and during treatment with either the insulin pump or multiple injections. Intensive treatment over 6 months resulted in near-normal glucose control as indicated by inpatient 24 hr profiles (IP), home glucose monitoring (HGM) and glycosylated hemoglobin (HbA_1) (nl 5-8%). This required a 50% increase in daily insulin dose (ID).

	IP	HGM	HbA_1	ID	GV	SmC
	mg/dl	mg/dl	%	u/kg	cm/yr	u/ml
before	254±81		12.4±3.0	1.0±0.3	6.0±1.3	1.1±0.7
after	107±48	120±65	8.4±1.5	1.5±0.3	10.3±3.2	2.1±1.3
	p<.005		p<.005	p<.005	p<.005	p<.05

During conventional treatment, all patients had normal growth velocities and somatomedin-C levels. With intensive therapy, growth velocities increased strikingly accompanied by a 2-fold rise in SmC. Skeletal maturation, previously normal or slightly delayed, did not advance excessively. These data demonstrate that the metabolic and hormonal changes accompanying intensive treatment enhance growth velocity even in children with apparently normal growth on conventional therapy.

1109 DECREASED PYRIDOXAL PHOSPHATE (PALP) LEVELS FOLLOWING PHOTOTHERAPY (PHOTORx). Nathan Rudolph, Aruna Parekh, Joan Hittelman. (Spon. by Leonard Glass) Depts. of Pediatrics and Psychiatry, SUNY, Downstate Med. Ctr., Bklyn, N.Y.

Conflicting results have been reported on the effects of PhotoRx on riboflavin (B_2) levels in red blood cells (RBC). B_2 acts as a co-enzyme in the conversion of pyridoxine and pyridoxamine phosphate to PALP, an essential co-factor in the metabolism of tryptophan and other amino acids. As part of an ongoing study of the biochemical, physiological and behavioral responses to different methods of eye protection in term neonates undergoing PhotoRx, we measured RBC and plasma PALP, and RBC B_2 sufficiency, sequentially in 27 neonates on PhotoRx and in 13 control infants, on approximately the 3rd-4th, 5th-6th, & 14th-18th postnatal days.

In control infants, mean RBC PALP declined slightly, but significantly (p<.05), by day 5. Infants on PhotoRx for <48 hrs. showed a similar decrease (p<.025); however, after >48 hrs. PhotoRx, there was a highly significant (p<.001) decline, with values significantly lower than controls (p<.025). By the 3rd week (i.e. ±10-12 days after stopping PhotoRx) RBC PALP in treated infants remained lower than controls (p<.05). Plasma PALP in controls decreased slightly, but not significantly, with time; whereas in PhotoRx infants significant changes occurred similar to those in RBCs. Mean RBC B_2 decreased slightly in controls, but significantly only in PhotoRx infants, especially after >48 hrs. Rx(p<.001).

Our data suggest that the B_2 decline after prolonged PhotoRx may be of metabolic significance and associated with a decrease in PALP. Possible correlations with behavioral changes are currently being studied. (Supported by a grant from March of Dimes)

● 1110 HOMOCYSTINURIA AND MEGALOBLASTIC ANEMIA IN AN INFANT DUE TO SELECTIVE DEFICIENCY OF METHYLCOBALAMIN: Suzanne Schuh, David S. Rosenblatt, Bernard A. Cooper, Maria-Louise Schroeder, Agnes J. Bishop, Lorne E. Seargeant, and James C. Haworth. Departments of Pediatrics and Biochemistry, University of Manitoba, Winnipeg; Departments of Physiology and Pediatrics, McGill University, Montreal, Canada.

A caucasian male infant developed neurological signs at two weeks of age. At fifteen weeks he had megaloblastic anemia and homocystinuria without hypermethioninemia and methylmalonic-aciduria. There was no evidence of deficiency of folate or Vitamin B12. High dose hydroxycobalamin, but not folate, therapy resulted in rapid clinical, hematological and biochemical improvement. Cultured fibroblasts grew well in methionine but not in homocysteine without methionine. Methionine synthetase activity was normal in fibroblasts. Intracellular folate distribution and concentration were normal in fibroblasts, as was total cobalamin accumulated in radioactive Vitamin B12. Intracellular methylcobalamin was below normal (5% compared with 45-70% in controls) without abnormality in adenosylcobalamin concentration. This is the first report of intracellular methylcobalamin deficiency without associated abnormality in adenosylcobalamin. The mechanism is not yet understood.

1111 SURGICAL THERAPY OF HYPERINSULINEMIC HYPOGLYCEMIA. Patricia Simmons, Robert Telander, Morey W. Haymond, Mayo Med. Sch., Depts. of Ped. & Surg., Rochester, MN.

Both medical and surgical management have been advocated in the treatment of hyperinsulinemic hypoglycemia in young children. The present studies were undertaken to evaluate the efficacy of subtotal pancreatectomy in 12 children (median age 3 mos, range 1 d to 12 mos) with sustained hyperinsulinemia. The diagnosis was established by simultaneous plasma glucose (27 ± 3 mg/dl, $\bar{x}\pm SE$) and insulin (30 ± 6 μU/ml) values. When hypoglycemic, 10 patients responded to 0.03 mg/kg iv glucagon (Δglucose 64 ± 6 mg/dl, range 39-100), whereas 2 did not (Δ<8 mg/dl). 8 patients had hepatomegaly (2-7 cm below the RCM). Medical management (frequent feedings, diazoxide, iv glucose) failed to prevent symptomatic hypoglycemia and therefore all 12 underwent subtotal pancreatectomy (85-95% removal). 3 required subsequent pancreatic resection (~99%), two of whom initially failed to respond to iv glucagon. In all cases it was possible to stop iv glucose, discontinue diazoxide and/or decrease frequency of feedings. Hepatomegaly resolved in all 8. In all patients, fasting tolerance increased (by 3 to > 18 hr). One patient was cured of hypoglycemia and one who underwent near-total pancreatectomy developed diabetes. Fasting hypoglycemia can be evoked in the remaining 10 children, necessitating continued medical therapy. In summary, in children with hyperinsulinemia: 1) hepatomegaly is observed frequently; 2) pancreatic resection improves fasting tolerance. In conclusion, subtotal and even near-total pancreatectomy in young children with hyperinsulinemic hypoglycemia improves glucose homeostasis but is rarely curative.

● 1112 HYPOKETOTIC HYPOGLYCEMIA - EVIDENCE FOR A NEW DEFECT IN FATTY ACID OXIDATION Charles A. Stanley, Elisa Gonzales, William Yang, Richard I. Kelley, Lester Baker University of Penna. School of Medicine, Children's Hospital of Phila., Department of Pediatrics, Philadelphia, PA.

Studies of a female infant who developed severe vomiting, coma, hyperammonemia and hypoglycemia following a febrile illness at 1 year of age revealed evidence of a defect in ketogenesis. At the end of an 18 hour fast, which reproduced the signs of her illness (vomiting, lethargy), plasma fatty acids were markedly elevated (2.80 mM/L) while beta-hydroxybutyrate remained low (0.050 mM/L). Urine dicarboxylic acids were elevated at the time of acute illness. Total plasma carnitine was low prior to fasting (10 uM/L) but rose to normal with fasting (50 uM/L). Because treatment with L-carnitine failed to improve fasting ketogenesis, studies of liver tissue were done to identify the site of defect in hepatic ketogenesis. Carnitine palmityl-transferase activity was normal. Liver carnitine content (500 nM/gm) was 50% of normal. However, ketone production by fresh liver homogenate from palmityl-carnitine, octanoyl-carnitine, and octanoate was <10% of human controls (3) while ketogenesis from butyrate and keto-isocaproate was normal.

These results indicate that this patient has a defect in one of the steps in intra-mitochondrial beta-oxidation of fatty acids of 8 or more carbons. It is speculated that the enzyme most likely affected is the medium-chain acyl-CoA dehydrogenase. This previously unrecognized defect in fatty acid oxidation may be present in similar cases of "carnitine deficiency" which fail to respond to carnitine treatment and in other cases of "atypical" Reye's Syndrome.

1113 ^{35}S CYSTINE UPTAKE IN CYSTINOTIC FIBROBLASTS: POSSIBILITY OF AN EXTRA-LYSOSOMAL DEFECT. Beatrice States, Judith Lee, and Stanton Segal. Department of Pediatrics, Children's Hospital of Philadelphia, PA.

Cystinotic cells take up increased levels of exogenous cystine as compared to normal cells. Cystinotic cells, depleted of their cystine pools by pretreatment with cysteamine, show an uptake of ^{35}S in 2 hours well above pretreated normals. The label in intracellular cystine, though less than in untreated cells, is higher in pretreated cells of cystinotics than in normals. Pretreatment of normal cells does not alter the ^{35}S recovered in intracellular cystine. In pretreated cells, there is an elevated incorporation of label into intracellular cysteine. When pretreated cystinotic cells are incubated up to 24 hours in complete media, they differ from pretreated normal cells by accumulating ^{35}S cystine at a rate dependent on the extracellular cystine concentration. Also, pretreated cystinotic cells have attained levels of ^{35}S cystine 3 times greater and have maintained 2 times the ^{35}S cysteine level of normal cells. The amount of ^{35}S cystine present in precipitable protein is 30% greater in cystinotics than normals. The incorporation of label into free cystine or its metabolites is not inhibited by cycloheximide. Pretreated cystinotic cells take up more cystine than normal cells after both short and long term incubations. This property of cystine re-accumulation by cystinotics is not related to prior incorporation of label into protein. Increased uptake of exogenous cystine is a consistent characteristic of cystinotic cells and suggests the possibility of an extra-lysosomal abnormality.

●1114 PICOLINIC ACID (PA) - A FACTOR IN ZINC METABOLISM. Marian Statter and Ingeborg Krieger Wayne State Univ. Department of Pediatrics, Detroit, MI.

PA is a metabolite of tryptophan formed by picolinic carboxylase (PC). Observations in acrodermatitis enteropathica (AE) suggest that it plays a role in zinc metabolism because plasma PA is decreased, kynurenine is increased, and ZnPA lowers the minimum therapeutic zinc dose to 1/3. PA may play a role in zinc absorption, or conservation. We studied 1) the ability to form PA by measuring PC, and 2) the effect of PA and other ligands on zinc transport in human fibroblasts. 1) PC activity was most pronounced in kidney, less in liver and absent in pancreas, brain and leukocytes; PC showed a steady increase from birth to 21 days, when it was higher than in adult rats ($p<0.001$);PC was higher in females than males ($p<0.01$); rats raised for 3 months on a tryptophan free diet had elevated PC (369% in liver,35% in kidney); and, PC was higher in lactating rats than controls (385% in liver, 35% in kidney). 2) Zinc uptake by fibroblasts was rapid during an early phase which showed saturation characteristics. Uptake during a slow second phase was concentration dependent and passive. KCN (1mM) inhibited zinc uptake during the early phase. PA decreased the uptake during both phases and showed stronger inhibitory activity than equimolar concentrations of histidine and citric acid. Inhibition was 50% at a PA/Zn ratio of 0.1/0.01 mM. Conclusion:The rise in liver PC in response to postnatal growth, lactation and PA precursor deficiency (tryptophan), and the high activity of PC in kidney suggest a physiologic function. PA acts in extracellular space as a powerful ligand which prevents cell attachment or entry.

1115 LOW DENSITY LIPOPROTEINS AND TRIGLYCERIDES IN 100 HYPERTENSIVE CHILDREN E.A. Stein, M. Evans., C. Schmidt, C.J. Glueck, J. Loggie, U. Cincinnati College of Medicine, Children's Hospital, Depts. Ped., Path., Med., Cincinnati, OH 45267

To assess associations between plasma low density lipoprotein cholesterol (LDLC), triglycerides (TG), and blood pressure, 100 hypertensive children, 49 receiving antihypertensive medication (Rx) and 51 on diet alone (Diet). In the Rx group there were 28 boys, 21 girls, mean age 17±3 years with 31 whites and 18 blacks; the diet group had 33 boys, 18 girls, mean age 15±3 with 34 whites and 17 blacks. Mean (±SD) TG, LDLC, total cholesterol (TC), high density lipoprotein (HDLC) and the percentage of children having TG and/or LDLC greater than the age-sex-race specific 95th percentile or HDLC less than the 5th percentile were as follows:

	Rx mg/dl	%>95th	Diet mg/dl	%>95th
TG	99±53	28%	88±41	23%
HDLC	49±11	7%	50±10	8%
LDLC	100±32	18%	107±22	14%
TC	169±38		173±27	

A disproportionate number of children both in the Rx group and in the diet group had elevated TG and/or LDLC, $p<.05$. There was no overt difference in the proportion of children with TG and/or LDLC >95th percentile in the Rx group. Nearly 30% of the families of 100 children had myocardial infarction and/or stroke before age 50 years in a first or second degree relative. Elevated TG and/or LDLC levels commonly accompany hypertension in children as does accelerated cardiovascular and cerebrovascular disease. It is important to assess hypertensive children for dyslipoproteinemia.

●1116 FETAL LIVER METABOLISM IN THE UNSTRESSED FETAL LAMB: EXPERIENCE WITH A CHRONIC INDWELLING HEPATIC VENOUS CATHETER. John W. Sparks, William W. Hay, Jr., Giacomo Meschia, and Frederick C. Battaglia, University of Colorado School of Medicine, Division of Perinatal Medicine, Departments of Pediatrics, Ob-Gyn and Physiology, Denver.

Fetal liver metabolism has eluded direct study in vivo, largely for technical reasons. Using a transthoracic approach, we prepared 12 late gestation fetal lambs with catheters in the right hepatic vein (RHV). Catheters were also placed in the fetal umbilical vein (UV), pedal artery (FA), and inferior vena cava (IVC), and in the maternal femoral artery and uterine vein. Catheters were maintained for up to 2 weeks, and position was confirmed at autopsy. After recovery from surgery, whole blood samples were analyzed for concentrations of oxygen, glucose, lactate, ketoacids and acetate. Hepatic venous catheter position was assessed in vivo in 4 animals by injection of glucagon (1 mg/kg), which elevated RHV glucose concentration to levels as high as 3 mM, significantly higher than in the UV, FA, or IVC. RHV glucose normally exceeded the glucose concentrations in the FA and IVC, and RHV glucose correlated with the UV glucose (eq: RHV-glucose = (0.73)(UV-glucose) + 0.12; r = 0.91). In normoglycemic animals (UV glucose $>$ 0.8 mM) UV glucose exceeded RHV glucose ($p < 0.01$ paired) while in spontaneously hypoglycemic animals (UV glucose $<$ 0.55mM) RHV glucose exceeded UV glucose ($p < 0.05$ paired). Lactate averaged 1.4 $\pm$ 0.15 mM in the RHV, significantly lower in the RHV than in the UV, UA or FA (each $p < 0.01$, paired), consistent with net hepatic lactate uptake. We conclude that, under chronic unstressed conditions, the fetal liver 1) normally consumes net lactate and 2) is capable of glucose release in response to hormonal stimulation or spontaneous fetal hypoglycemia.

1117 TOTAL PARENTERAL NUTRITION, AMINOSYN VS FREAMIN III. Shyan Sun, Zanaida Aranda, Kamtorn Vangvanichyakorn, Nora Ruiz, Mark Leveene. (Spon. F. Behrle) New Jersey Medical School, Dept. Neonatology, Newark, New Jersey

Aminosyn (7%) contains twice the amount of titrable acid (37 mEq/L) compared to Freamin III (19 mEq/L). Their 2% TPN solutions also differs in measured pH (2% Aminosyn pH 6.02 vs 2% Freamin III pH 6.442). This study was designed to evaluate if this difference will be evident in newborn infants after infusion. 13 clinically stable preterm infants (BW 710-1800 gm) had baseline studies of pH, PCO_2, HCO_3, BE & anion gap done prior to infusion of 2% FreAmin TPN solution at the rate of 4 ml/kg/hr for 24 hrs. At the 25th hour, same biochemical studies were repeated. On the following day, the same procedures were repeated on the same patient except that TPN solution was changed to 2% Aminosyn. 4 extra infants were studied only with 2% Aminosyn solution. The differences between pre and post infusion biochemical studies were compared:

	Pt	ΔpH	Δ HCO_3	Δ BE	ΔAnion Gap
FreAmin III	13	-0.002	-0.477	-0.8	-0.78
Aminosyn	17	+0.005	+0.053	+0.2	+2.77
P		NS	NS	NS	<0.01

There were no statistical differences in acid base parameters after receiving 2 different solutions. There was a small but significant increase in anion gap after Aminosyn infusion which was not seen after FreAmin III infusion. In conclusion, Aminosyn infusion may result in minimal increase in untitrable acid, but not significant enough to offset acid base balance.

1118 DIABETIC CONTROL AND GROWTH: HORMONAL AND CELLULAR ASPECTS. W.Tamborlane, A.K.Ritchey, P.Davis, M. Rudolf, J.Gertner, Yale U. School Med., New Haven, CT

We have recently shown that insulin pump Rx of diabetes blunts the excessive rise in growth hormone (GH) to exercise while increasing somatomedin C (S) levels. It remains to be determined whether pump Rx a) normalizes spontaneous GH release or the response to α adrenergic stimulation (clonidine) and b) enhances cellular growth. To examine these questions, 10 Type 1 diabetics (15±1 yrs) were studied after 1 wk pump Rx which lowered plasma glucose from 213±19 to 119±8 mg/dl ($P<0.001$). Mean unstimulated GH (UGH) by 24 hr sampling, peak GH after oral clonidine (Clon) and S were determined. Results in diabetics are compared to age-matched normal controls (*$P<0.05$-0.005 vs prepump).

Diabetics	UGH (ng/ml)	GH-Clon (ng/ml)	S (U/ml)
prepump	17±3	48±10	1.1±0.3
postpump	9±1*	28±4*	1.7±0.3*
Normals	10±1*	29±3*	0.9±0.2

To evaluate if the metabolic and hormonal changes induced by pump Rx alters cellular growth, we measured proliferative capacity of erythroid committed stem cells (BFU-E) obtained from peripheral blood in 4 subjects. The assay involved culture with 2IU erythropoietin and is known to be stimulated by GH in vitro. Despite the fall in circulating GH levels, the number of BFUE increased 3-4 fold ($P<0.05$) after only 1 wk of pump Rx.

Conclusions: Improved metabolic control of diabetes rapidly reverses GH hypersecretion to physiologic and pharmacologic stimuli. Despite the fall in GH levels, pump Rx appears to enhance somatomedin generation and cellular growth.

1119 FETAL POLYCYTHEMIA - EFFECTS ON UMBILICAL BLOOD FLOW (UBF), FETAL GLUCOSE UPTAKE (FGU) AND OXYGEN CONSUMPTION (FVO_2). Denis Tenenbaum, Ted Rosenkrantz, George Piasecki, Wayne Cohen, Benjamin Jackson and William Oh. Brown Univ., Dept. of Pediatrics and Surgery, Providence, RI

To determine the effects of polycythemia on fetal glucose homeostasis, we studied 4 chronic sheep preparations at 128±2 (M±SEM) days of gestation. UBF was determined by antipyrine technique and FGU, as well as FVO_2, by Fick's principle. Data were obtained prior to and after exchange transfusion with maternal packed red blood cells to induce polycythemia in the fetus. The data are shown below: (M±SEM)

	Hct(%)	Viscosity@	UBF ml/kg/mn	FGU mg/kg/mn	FVO_2 ml/kg/mn
Control	34±2.6	2.6±.1	232±17	6.5±.9	6.5±.6
Polycythemic	48±2	4.1±.2	173±11	8.0±1.4	7.3±.6
P value*	p<.005	p<.05	p<.01	n.s.	n.s.

*by paired t test @centipoise at shear rate of 90 sec^{-1}

Polycythemia was successfully induced by exchange transfusion and resulted in a significant reduction in UBF. However, no significant change in FGU and FVO_2 was noted. We conclude that fetal polycythemia results in decreased UBF but the fetus compensates by increasing apparent glucose extraction (68±32%) resulting in no alteration in fetal glucose uptake.

1120 INSULIN SUPPRESSION CAUSES ELEVATED GLUCOSE PRODUCTION (Ra) AND DECREASED GLUCOSE DISAPPEARANCE (Rd) IN THE NEONATAL SHEEP. Denis Tenenbaum, John B. Susa, and Richard M. Cowett. Brown Univ., Women & Infants Hospital, Dept. of Pediatrics, Providence, RI.

Hepatic insensitivity for insulin has been postulated as the mechanism for imprecise control of glucose homeostasis in the neonate. Because the insulin effect could not be differentiated from glucagon, somatostatin (SRIF), a suppressor of both, was infused in studies measuring Ra and Rd. Nine term lambs [birthweight 4.1±0.3 kg (M±SEM) and age 4.1±0.5 days] were infused with 0.9% NaCl at 0.06 ml/kg/min plus 25 μCi/kg D-[6-^{3}H] glucose by the prime constant infusion technique to measure Ra and Rd for 150 min (control). After a recovery period of 4 hrs, the study was repeated with SRIF 0.8 μg/kg/min added. Blood was drawn every 15 min for pl. glucose, insulin, glucagon, and glucose specific activity and Ra and Rd were calculated. Pooled data are noted.

Period	Pl.Glu. mg/dl	Pl.Ins. μU/ml	Pl.Glucagon pg/ml	Insulin / Glucagon	Ra mg/kg/min	Rd mg/kg/min
Control	109±5	35±5	219±41	0.18±0.04	6.3±0.4	6.3±0.4
SRIF	119±7	17±2ƒ	150±22*	0.14±0.03ƒ	7.2±0.3†	7.0±0.3*

Paired T - *$p < .05$ †$p < .02$ ƒ$p < .01$

There was a fall in pl. insulin, glucagon, the insulin to glucagon ratio, and elevation of Ra and Rd with SRIF infusion compared to controls. There was no difference between Ra and Rd within the controls, but a fall of Rd relative to Ra within the SRIF series ($p < .001$). We speculate that these results reflect the primary importance of insulin for control of neonatal glucose homeostasis.

●1121 NEAR NORMAL GLUCOSE PRODUCTION IN TYPE 1 GSD. Eva Tsalikian, Patricia Simmons, Campbell Howard, Morey W. Haymond, Mayo Med. Sch., Dept. of Ped., Rochester, MN.

Glycogen storage disease, type 1 (GSD1), results from a defect in hydrolysis of glucose-6-phosphate, blocking glucose (Glu) production (Ra) from either glycogenolysis or gluconeogenesis. However, Glu Ra is 60% of normal in adults with GSD1 in whom hypoglycemia is not a major problem. To determine whether the severe hypoglycemia in GSD1 children results from a relatively greater defect in Glu Ra or accelerated Glu utilization (Rd), Glu flux, using 6,6-dideuteroglucose, was determined in 5 GSD1 and 5 normal children. Plasma Glu and Glu Ra were 85 mg/dl and 6.3 mg/kg·min, respectively, in controls. To establish steady-state conditions, GSD1 children were infused with cold Glu for 2 hr at 6, 3 and 1.5 mg/kg·min at each rate during flux determinations; Glu decreased from 78 to 54 and 45 mg/dl, respectively. Endogenous Glu Ra increased (1.5, 2.0 and 3.1 mg/kg·min, respectively) during decreasing cold Glu infusion. When Glu infusion was stopped in 4 GSD1, endogenous Glu Ra increased to 3.9 mg/kg·min but Rd exceeded Ra, resulting in a decrease in plasma Glu from 50 to 45 mg/dl. In summary: 1) Endogenous Glu Ra in GSD1 children is ~60% of normal, and fails to be completely suppressed during infusion of Glu at 6 mg/kg·min; 2) the fall in plasma Glu associated with discontinuation of cold Glu infusion resulted from higher Glu Rd than Ra, despite an increase in endogenous Glu Ra. In conclusion: Stabilization of Glu homeostasis with age in GSD1 is most likely the result of a relative decrease in Glu utilization, perhaps related to changes in brain weight to body size ratio, and not a proportional increase in Glu production.

1122 EFFECT OF CORTICOSTERONE (B), ESTRADIOL (E) OR PROGESTERONE (P) ON THE METABOLISM OF VITAMIN D IN THE HYPOPHYSECTOMIZED MALE ALBINO RAT. Alfonso Vargas, Carolyn A. Von Zabern, and Allen W. Root, Univ.So.Fla.Coll.Med., All Children's Hosp., Dept.Ped.,Tampa and St. Petersburg.

The effect of B, E or P upon the serum concentrations of 25OHD and $24,25(OH)_2D$ were investigated in male rats hypophysectomized (Hx) at 46 days of life. The animals were divided into 6 groups: G1-intact control; G2-pair fed intact control, G3-Hx,G4-Hx+B,G5-Hx+E and G6-Hx+P.G4,5, and 6 received B,E or P (125,10 or 50 ug/100 g BW respectively) from days 64 to 83 of age. G1,2 and 3 received diluent only. Animals were decapitated 24 hours after last injection. The metabolites of vitamin D were determined by competitive radioassay. Serum values (ng/ml, $\bar{X}\pm$SEM) were:

	25OHD	$24,25(OH)_2D$		25OHD	$24,25(OH)_2D$
G1(12)	18.5±1.8	3.7± .35	G4(21)	6.1±.4	4.6± .37
G2(13)	14.7±1.2	3.8± .25	G5(21)	6.4±.5	3.8± .37
G3(21)	7.7± .6	3.2± .21	G6(18)	7.6±.5	2.9± .20

25OHD values were significantly lower in Hx groups ($p<0.01$ vs G1 and 2). In B treated rats 25OHD values were significantly lower ($p<0.05$) than in control Hx animals. Serum concentrations of $24,25(OH)_2D$ although not significantly altered by hypophysectomy were increased by administration of B(G4 vs G3 $p<0.01$.).

Conclusions: 1) Hypophysectomy lowers serum concentrations of 25OHD, independent of vitamin D intake; 2) Corticosterone may have a specific stimulatory effect on 24-hydroxylase activity.

●1123 ENHANCED FATTY ACID SYNTHESIS IN HYPERINSULINEMIC RAT FETUSES. Rita A. Vileisis and William Oh, Brown Univ., Women & Infants Hosp., Dept. of Ped., Providence, RI

The effect of chronic fetal hyperinsulinemia on fetal fatty acid synthesis was evaluated using the tritiated water technique in 9 pregnant rats. At 19 and 21 days of gestation, alternate fetus in each litter was injected with either 5 units long acting insulin or an equal volume of saline. Insulin injection resulted in significant growth enhancement at term (22 days), 6.2±0.3gm vs 5.5±0.2gm (M±SEM) for controls. Insulin injected fetal lung (190±10 vs 150±10mg), liver (370±20 vs 320±20mg) and carcass (4.52±0.13 vs 4.01±0.13 grams) were significantly heavier than control. Fetal glucose and insulin levels in the insulin injected group were 60±12mg/dl and 7760±1721 µU/ml respectively; in controls, 85±10mg/dl and 153±46 µU/ml, respectively. Fatty acid synthesis and content in the liver and carcass were elevated significantly in the hyperinsulinemic fetuses. (Data below)

	Liver		Carcass	
	Insulin R_x	Control	Insulin R_x	Control
^3H incorp. (cpm/organ)	690±124*	400±92	2136±172*	1139±122
Specific Act. (cpm/µM)	44.5±8.6*	33.0±7.5	34.5±4.8*	21.9±4.4
Fatty Acid Cont. (µM/organ)	16.0±1.3*	12.3±1.0	68.1±7.3*	59.4±6.4

*Significantly higher than control ($p<.05$), M± SEM

No differences were observed for the above parameters in the lung, brain, and placenta between the two groups. The data indicate that hyperinsulinemia produced macrosomia and enhanced fatty acid synthesis particularly in the fetal liver and carcass, suggesting a preferential organ effect of insulin on fetal growth with respect to fat deposition.

● 1124 IMPROVED FATTY ACID (FA) SYNTHESIS IN THE GROWTH RETARDED (IUGR) FETUS WITH INCREASED SUBSTRATE. Rita A. Vileisis and William Oh. Brown Univ., Women and Infants Hospital, Dept. of Pediatrics, Providence, RI.

The effect of increased substrate (glucose) delivery on FA synthesis in IUGR fetal rats was investigated. At 17 days' gestation, 15 time-dated pregnant rats had a jugular catheter implanted and one uterine artery ligated, resulting in IUGR fetuses while those in the unligated horn were appropriately grown (AGA) controls. At 21 days' gestation the animals were infused with either saline or 20% dextrose via catheter for 4 hrs. Fetal organ FA synthesis was measured by maternal ^3H_2O injection and is expressed as ^3H specific activity (SA) (M±SEM).

INFUSION GROUP:	SALINE (n = 7)		DEXTROSE (n = 8)	
	AGA	IUGR	AGA	IUGR
Plasma Glucose (mg/dl)	35±6	24±3	148±10	138±9
Plasma Insulin (µU/ml)	299±49	126±43	381±48	194±27
^3H SA Liver (cpm/µM)	41.6±3.4	28.4±4.0	62.4±6.7	49.4±8.0
^3H SA Lung (cpm/µM)	39.5±7.5	24.5±3.3	44.8±4.5	52.0±9.1
^3H SA Carcass (cpm/µM)	28.9±1.8	21.7±2.2	33.0±2.7	25.0±2.3

The data show that IUGR fetuses had lower plasma insulin levels than AGA, which may account for lower FA synthesis in organs listed above ($p<.05$). Dextrose infusion produced significant increases in plasma glucose for both IUGR and AGA fetuses despite unchanged plasma insulin concentrations. Both IUGR and AGA enhanced FA synthesis during dextrose infusion so that the IUGR fetuses synthesized FA as rapidly as the saline-infused AGA fetus. The data suggest an abundance of glucose improved FA synthesis in the IUGR fetus, independent of insulin activity.

● 1125 A DEFECT IN THE TUBULAR REABSORPTION OF CARNITINE(C) AS A CAUSE OF SYSTEMIC C DEFICIENCY. Lewis J. Waber, David L. Valle, Catherine A. Neill, Saul W. Brusilow, and Austin L. Shug. Johns Hopkins Univ. & Hosp., Dept. of Peds., Baltimore, and William S. Middelton V.A. Hosp., Madison, Wisc.

Systemic C deficiency is a heterogeneous disorder of unknown etiology(s). We have studied a family in which two male siblings have had muscle weakness and cardiomyopathy. One has died. The survivor had low plasma (4.2µM) and muscle (0.35nMol/mg noncollagen protein) C, lipid myopathy, and an exaggerated ketogenic response to fasting (ketones 3x normal after 12 hr. fast). All signs and symptoms have resolved with treatment with 175mg/kg/day C. Since C is required for hepatic ketogenesis, we hypothesized that hepatic C was adequate pretreatment and that his hepatic biosynthetic pathways for C were intact. When plasma C was normalized by treatment, C excretion was 20x normal. Fractional clearance of C (FCC = $(U/P)_C/(U/P)_{creat}$) before and after treatment were elevated.

	fasting plasma C	FCC
normal male adult (3)	47.4 + 1.0 µM	0.043 + 0.007
normal female adult (5)	46.1 + 4.7 µM	0.032 + 0.025
patient's mother	33.1 µM	0.110
patient's father	34.0 µM	0.091
patient before Rx	4.2 µM	0.132
after Rx	20 - 53 µM	0.9 - 1.5

We conclude that C is filtered, secreted (since several of the patient's FCC >1), and reabsorbed (since normally FCC<<1). Our patient appears to have a defect in reabsorption. Inhibition of renal C secretion may be an adjunct to therapy.

1126 CHRONIC HYPERGLYCEMIA ATTENUATES MATURATIONAL RISE OF ACTH IN THE OVINE FETUS WITHOUT AFFECTING CORTISOL MATURATION. David Warburton, (Spon. by A. B. Lewis). University of Southern California School of Medicine, Childrens Hospital of Los Angeles, Department of Pediatrics, Neonatal-Respiratory Disease Division, Los Angeles.

Chronic hyperglycemia was induced by infusing glucose (14±2 mg/Kg/min, M±St) into 4 chronically catheterised fetal lambs from 112 through 133, 135, 142, and 145 days gestation respectively. Serum glucose levels (32±2 mg/dl) and serum insulin levels (48 ± 12 µU/ml) in these fetuses were higher than serum glucose levels (18 ± 2 mg/dl, $p<0.001$) and serum insulin levels (12 ± 3 µU/ml, $p<0.001$) in 4 chronically catheterised control fetuses. Glucose infusion to the fetuses did not alter maternal serum glucose (60 ± 3 mg/dl) or insulin (35 ± 4 µU/ml) levels. In the control fetuses, there was a linear increase in serum ACTH levels from 0 to 200 pg/ml from 120 days gestation onwards ($Y = 9.84X - 1118.69$, $r = 0.92$, $p<0.001$), while in the glucose treated fetuses the maturational rise of serum ACTH levels ($Y = 1.96X - 241.61$, $r = 0.69$, $p<0.001$) was significantly attenuated to below 80 pg/ml ($p<0.001$). However, this did not alter the rapid maturation of serum cortisol levels from < 2 mg/dl to >6 mg/dl which occurred after 140 days gestation.

Chronic hyperglycemia attenuates the maturational rise of serum ACTH levels in the ovine fetus without affecting maturation of serum cortisol levels. I speculate that hyperglycemia may have a direct effect on the pituitary or hypothalamus in the ovine fetus.

1127 ONSET OF DIABETIC COMPLICATIONS(DC) DURING CHILDHOOD. Neil H. White, Sherida Tollefsen, Mary F. Witt, Paul Palmberg, David Meltzer, Julio V. Santiago. Washington Univ. School of Med. Depts. of Pediatrics & Ophthalmology, St. Louis Children's Hospital, St. Louis, Missouri.

Although diabetes causes major morbidity and mortality in adults, onset of DC is thought to be uncommon during childhood. To determine the prevalence of DC before age 20, we analyzed 663 inhospital evaluations of 321 insulin dependent subjects(age 5-20 yrs; duration 0-18 yrs) studied in our Diabetes Registry program. Retinopathy(RET) was assessed by fundoscopy, photography and fluorescein angiography, neuropathy(NEURO) by nerve conduction velocity, and nephropathy by measurement of urine protein(UPr) and creatinine clearance(CrCl).

There were no DC in 25 diabetics during the first year of diabetes. Prevalence of RET and NEURO increased with age and duration of disease:

Age (yrs)	% with RET(N)	% with NEURO(N)	Duration (yrs)	% with RET(N)	% with NEURO(N)
5-10	9(45)	21(46)	0-5	11(149)	33(165)
10-15	19(124)	35(137)	5-10	37(123)	37(103)
15-20	38(152)	42(135)	>10	47(32)	53(38)

Four had proliferative RET, 7% had elevated UPr(>0.3 gm/day), and 3% had low CrCl(<100 ml/min/1.73 m^2). Fluorescein angiography had a minimal advantage over photography in detecting RET.

Results show that DC begin to develop before age 20. Angiography may offer little advantage in detecting background RET. Studies measuring the impact of improved control may benefit from understanding the natural history of DC in childhood.

● 1128 INSULIN-LIKE GROWTH FACTOR I AND II LEVELS AND SOMATOMEDIN PEPTIDE CONTENT IN PLASMA THROUGH NORMAL PREGNANCY. Darrell M. Wilson, Ann Bennett, G. David Adamson, Raymond J. Nagashima, Francis Liu, Mary L. DeNatale, Raymond L. Hintz, Ron G. Rosenfeld, Stanford University School of Medicine, Department of Pediatrics, Stanford, CA.

Because of the continuing controversy regarding plasma levels of the somatomedins (SM) during pregnancy, we have measured SM peptide content (SMPC) and insulin-like growth factor I and II in 57 plasma samples from women at various stages of normal pregnancies. SMPC was measured by RRA using human placental membranes. IGF-I was measured by RIA using the antibody of Furlanetto, distributed by the NIH. Both assays used 125-I IGF-I as radioligand. IGF-II was measured by specific RIA using a rabbit-generated antibody to the C-peptide region of IGF-II. 125-I tyrosylated C-peptide of IGF-II was used as radioligand. All samples were chromatographed in 0.25M formic acid to remove the SM binding protein.

	MALE ADULTS	1st TRI	2nd TRI	3rd TRIMESTER	
SMPC	1.30±0.25	0.83±0.18	1.05±0.55	1.29±0.64	unit/ml
IGF-I	184±32	266±25	204±57	334±86	ng/ml(SD)
IGF-II	687±169	679±202	770±187	722±200	ng/ml

SMPC increased with gestational age. IGF-I levels were similar to adult male values in the first two trimesters but rose dramatically in the third. Overall, IGF-I correlated well with gestational age (r=0.56). IGF-II levels remained constant throughout pregnancy and were not significantly different from normal adult levels. We conclude that the gestational rise in SMPC primarily reflects a rise in IGF-I levels, supporting the possible role of this hormone in fetal growth.

● 1129 INCREASED CALCIUM (Ca) ABSORPTION IN TYPE I DIABETIC CHILDREN (IDD). Mary F. Witt, Neil H. White, Julio V. Santiago, Louis V. Avioli. Department of Pediatrics, Washington University School of Medicine, St. Louis Children's Hospital, and The Jewish Hospital, St. Louis, Missouri.

Decreased cortical bone mass has been observed in IDD; associated biochemical alterations include increased 24,25 dihydroxycholecalciferol, decreased 1,25 dihydroxycholecalciferol, and reduced circulating immunoreactive parathyroid hormone (iPTH). In order to investigate the pathogenesis of these alterations, we studied 26 IDD (age 7-18 yrs.) and 17 normals (age 9-18 yrs.) by the method of Pak and Broadus, which relates intestinal Ca absorption to urinary excretion and utilizes urinary cAMP (UcAMP) as an indicator of acute iPTH changes. Following an overnight fast and a 2 hr. baseline urine collection, a 1.0 gm. oral Ca load was given. Urine was then collected in 2 consecutive 2 hr. periods. Glomerular filtrate (GF), UcAMP, and Ca were measured in each sample. Ca absorption following the Ca load (mg Ca/100 ml GF) was increased ($p<0.01$) in IDD's (0.19±0.03; mean ± SEM) as compared to normals (0.06±0.01). Expressed as mg Ca/mg creatinine, Ca absorption was also increased ($p<0.01$) in IDD's (0.29±0.05) compared with normals (0.08±0.02). In normals, the initial decline in UcAMP after Ca ingestion was followed by a return to baseline in the second 2 hr period. In contrast, the post-Ca decline in UcAMP was sustained throughout both periods in IDD's.

Intestinal Ca absorption is increased in IDD. Ca hyperabsorption may result in suppression of iPTH release, and could explain the observed alterations in vitamin D metabolites and decreased bone mass in IDD.

1130 KETONURIA DOES NOT EXCLUDE HYPERINSULINEMIC HYPOGLYCEMIA. Joseph I. Wolfsdorf, Abdollah Sadeghi-Nejad, and Boris Senior. Tufts University School of Medicine, New England Medical Center, Boston.

Ketonuria in the fasting hypoglycemic child is presumptive evidence of ketotic hypoglycemia. By contrast, absence of urinary ketones with fasting hypoglycemia suggests hyperinsulinemia. Because of the benign course of the former and the potentially devastating neurologic sequelae of the latter, it is critical to differentiate promptly between these two entities.

We examined the relationship between serum B-hydroxybutyrate (BOHB) and plasma glucose and between serum free fatty acids (FFA) and glucose in 34 normal children fasted for up to 24 hours. BOHB correlated inversely with glucose ($y=6.53-1.23x$; $r=-0.78$, $P<0.001$) as did FFA ($y=3.93-0.50x$; $r=-0.63$, $P<0.001$). We compared these results with those in six patients with hypoglycemia due to hyperinsulinism. In the hyperinsulinemic children, hypoglycemia was invariably associated with relative hypoketonemia (glucose <40 mg/dl, BOHB <2 mM; >2 SD below the mean). FFA were also unduly low (>2 SD). However, despite being significantly hypoketonemic when hypoglycemic, four of the six hyperinsulinemic patients had ketonuria.

Thus we confirm that hypoketonemia is a hallmark of hyperinsulinism but emphasize that ketonemia must be evaluated quantitatively and in relation to the concomitant level of glucose. Finally, since it does not exclude hyperinsulinemic hypoketonemic hypoglycemia, ketonuria may be a dangerously misleading finding in a hypoglycemic child.

1131 α-OH BUTYRIC ACIDURIA - A DEFECT IN METHIONINE METABOLISM CAUSING CYCLIC VOMITING AND KETOACIDOSIS. William Yang, Peter Jezyk and Karl S. Roth. Departments of Pediatrics, University of Pennsylvania School of Medicine and Medical College of Virginia. Richmond, Virginia.

Two siblings presented with multiple hospitalizations for cyclic vomiting and severe dehydration, beginning at approximately 5 yrs of age and precipitated by intercurrent viral infections. The severity of the syndrome warranted two admissions of the younger sib for Reye's syndrome. Gas-chromatography of urinary organic acids during these episodes showed massive excretion of α-HB(56mg%) and significant ketonuria. Plasma amino acid levels were normal except for excessive α-NH_2-butyrate (67nmol/cc). Minimal, intermittent homocystinuria was occasionally detected by the nitroprusside reaction. The syndrome was reproduced by fasting under controlled conditions: neither sibling developed hypoglycemia; within the first 12 hrs α-HB increased 7.6-fold(1.98mg%), while ß-HB increased only two-fold(0.44mg%). Oral methionine loading(100mg/Kg) resulted in prompt rises in plasma methionine levels and increased α-NH_2-butyrate into the range reported for Reye's syndrome (75nmol/cc). There was a correspondingly high level of urinary α-HB(38mg%) and ketone bodies. Propionic acid-^{14}C conversion to CO_2 was normal in isolated white cell preparations from both sibs. While the enzyme α-ketobutyrate dehydrogenase is absent in control fibroblasts and leucocytes, initial studies in rat liver documented very high rates of $^{14}CO_2$ production from α-NH_2-butyrate-^{14}C. Such studies are, therefore planned in needle biopsy specimens from the patients.

1132 HYPOGLYCEMIC, HYPOKETOTIC DICARBOXYLIC ACIDURIA - A POSSIBLE DEFECT IN FATTY ACID (FA) OXIDATION. William Yang, Karl S. Roth and Paul M. Coates. Dept. of Pediatrics, Univ. of Penn., Phila., PA., and Med. Coll.of Virginia, Richmond.

A 2 mo. old B female presented with a 2-day history of fever, vomiting and lethargy. She was admitted for treatment of presumed neonatal sepsis; blood glucose at that time was 35 mg/dl with urinalysis negative for ketones. Physical exam was unrevealing; there was no hepatomegaly. Rehydration with 5% glucose produced a striking remission of symptoms. All cultures were negative. Gas chromatography (GC) of urine showed elevations of adipate (35 mg/dl), suberate (10.7 mg/dl) and sebacate (7.8 mg/dl); no lactate or ketone bodies were detectable. At 3 mos. a fasting study was performed; blood glucose fell slowly over 23 hours to 38 mg/dl; free FA increased steadily with disproportionately low ketone formation; urinary adipate, suberate and sebacate increased 10-20 fold over baseline; glucagon stimulation at the end of the study failed to elicit a response. Endocrine parameters (insulin, GH and cortisol) were appropriate throughout the fast; serum carnitine levels and ratio (free:esterified) were normal x2. Mononuclear leukocytes oxidized ^{14}C-palmitic acid and ^{14}C-octanoic acid at 13% and 16% of control levels, respectively. Cultured skin fibroblasts also showed impaired oxidation of ^{14}C-palmitic acid (< 50% of control levels). This infant apparently manifests a defect in intramitochondrial medium-chain FA oxidation. That the defect can be demonstrated in cultured cells may allow us to characterize the specific step at which ß-oxidation is impaired in this patient.

1133 TYPE I GLYCOGEN STORAGE DISEASE: EFFECTS OF GLUCOSE INFUSIONS ON [^{15}N]GLYCINE KINETICS AND TOTAL BODY PROTEIN SYNTHESIS. Marc Yudkoff, Itzhak Nissim, Charles Stanley, Lester Baker and Stanton Segal. Children's Hospital of Philadelphia, Department of Pediatrics, Phila., PA.

Nocturnal infusions of glucose improve growth in children with type I GSD. Turnover of [^{15}N]-glycine and body protein was studied in three patients treated with intragastric glucose administered at either 75% or 150% of the estimated glucose production rate. With the lower glucose infusion, the glycine turnover rate constant and metabolic clearance rate were increased by 30-45% relative to values with the higher rate. Glycine pool size was increased 30-50%, so that overall glycine flux remained constant with either infusion rate. Production of [^{15}N]urea was higher with the lower rate, resulting in reduced body protein synthesis, 2.24 g/kg/day vs. 3.5 g/kg/day, (normal =3.4-4.3). The results suggest that enhanced protein breakdown to provide gluconeogenic amino acid precursors is responsible for growth failure of type I GSD. Glucose infusions relieve this demand thus favoring amino acid flux toward protein synthesis. Measurements of protein turnover with stable isotopes also may provide a clinically useful tool to assess the efficacy of glucose or amino acid infusions to enhance rates of growth in these children.

MORPHOGENESIS AND MALFORMATIONS

1134 OBSTRUCTIVE SLEEP APNEA IN TREACHER COLLINS SYNDROME (TCS). Robert C. Beckerman, Joan M. Tonglet, Department of Pediatrics and Constance Kaufman Center for the Study of Breathing Disorders in Infants and Children, Tulane University, New Orleans, Louisiana. Spon. by Emmanuel Shapira.

We studied four children with TCS who were referred for symptoms of severe sleep disturbance (snoring, restlessness, hypersomnolence, hyperactivity, apnea). Our protocol involved non-invasive awake and asleep evaluation of upper airway structure and function by fluoroscopy, airflow, impedance pneumography, ECG, respiratory gas exchange, and echocardiography.

Age (yrs)	Pharyngeal Obstruction	Apnea	$PACO_2$ mm Hg Aw/As*	$PtcO_2$ mm Hg Aw/As*	Cor Pulmonale
8	+	+	40/49	108/80	+
2/12	+	+	43/48	70/54	±
4	+	+	40/53	63/35	+
4 6/12	±	±	37/38	80/80	-

*Awake/Asleep

Three of four of the children demonstrated pathological sleep apnea associated with abnormalities in respiratory gas exchange and cardiac dynamics. Treatment reversed most of the functional abnormalities and consisted of body posturing, tonsilloadenoidectomy and temporomandibular joint release and tracheostomy in one patient. All children with TCS should be evaluated for airway function and sleep apnea and early aggressive therapy instituted to improve the quality of life.

●1135 THIRD TRIMESTER TERATOGENIC EFFECTS OF SODIUM WARFARIN IN THE RAT. David A. Beckman, Howard M. Solomon and Robert L. Brent. Jefferson Medical College, Department of Pediatrics, Philadelphia, PA.

Sodium warfarin (W) exposure during the first trimester of human pregnancy may result in a warfarin syndrome which includes stippled epiphyses and nasal hypoplasia. It ias been suggested that second or third trimester exposure is associated with an increased incidence of central nervous system (CNS) defects. We investigated the teratogenicity of W during the third trimester in the rat by either single injections of 1.0, 1.25, 1.5, 1.75 or 2.0 mg W per kg body weight on day 15 of pregnancy or single daily injections of 0.25, 0.375 or 0.5 mg of W per kg body weight on days 15, 16, 17 and 18. All rats were sacrificed on day 22. The fetuses and placentae were examined, weighed and the fetuses were placed in Bouin's fixative. The usual reproductive parameters involving malformations, growth and mortality, as well as coagulation time in the mothers, were determined. The CNS was examined particularly carefully. The only consistant effects seen were dose-dependent increases in coagulation time and maternal death with increasing total dose of W. As of this time we have not been able to develop an animal model to support the allegation that late gestation exposure to W results in CNS pathology in spite of the fact that the level of administration resulted in significant maternal death. (Supported by NIH)

1136 OFFSPRING OF WOMEN WITH FETAL ALCOHOL SYNDROME (FAS). Nesrin Bingol, M.D., Silvia Iosub, M.D., Magdalena Fuchs, M.D., Donald S. Gromisch, M.D., and Edward Wasserman, M.D., New York Medical College.

In adults, heavy exposure to ethyl alcohol causes supression of testicular function. Ovarian failure has also been reported but poorly documented in humans. Exposure to ethyl alcohol in utero is reported to cause delayed age of menarche in FAS females, but the reproductive histories of FAS adults have not been previously studied. We examined 41 FAS mothers and their 65 offspring. Of them, five were non-drinkers, two stopped drinking after the delivery of an FAS child, and the rest were heavy ethanol abusers. Of the two women who stopped drinking, one had a successful pregnancy outcome, while the other cannot conceive three years after abstinence.

The 58 children born to the drinking FAS mothers exhibited the typical manifestations of FAS; pre and postnatal growth deficiency, dysmorphic features with microcephaly, hyperactivity, behavior problems, mild to moderate retardation and speech problems.

The seven children born to the non-drinking mothers have the following characteristics: 1) No stigmata of FAS including microcephaly; 2) No pre and postnatal growth retardation, except one; 3) All except one had delayed development, three had cerebral palsy (CP); 4) Two school age children have learning disability, speech and language problems.

In conclusion, the pre and postnatal growth deficiency and dysmorphic features of the FAS children are due to the direct effect of fetal ethanol exposure, while the delayed development, CP and the problems relating to speech and learning may be due to the effect of alcohol on the developing female gonad of the FAS mother.

●1137 THE PRODUCTION OF CONGENITAL MALFORMATIONS IN THE RAT USING TISSUE ANTISERA. XVII. THE PREVENTION OF ANTIBODY PRODUCED MALFORMATIONS WITH LARGE QUANTITIES OF AMINO ACID SUPPLEMENTS. Robert L. Brent, Marcela Jensen, Thomas R. Koszalka, David Beckman, Joan Pugarelli, and John B. Lloyd. Jefferson Medical College, Department of Pediatrics, Philadelphia, PA; University of Keele, U.K.

Once it was discovered that all teratogenic antisera localized in the developing yolk sac, we concluded that the yolk sac dysfunction was an interference with the transport of substances to and/or from the embryo. Our studies in vivo and in vitro indicated that the target of teratogenic antibody is on macromolecular pinocytosis with a resulting severe deficiency of amino acids available to the developing embryo. To confirm this hypothesis, pregnant rats were administered a teratogenic dose of antiserum that was equivalent to an embryonic LD/50 and simultaneously treated with a mixture of 16 amino acids to provide at least twice the daily requirement of amino acids. All litters of treated animals were completely normal as well as having no increase in resorptions. This teratogenic model presents a unique and exciting model for studying embryonic nutrition without any effect on the mother. At this time, we are not certain whether the teratogenesis is due to a deficiency in a single amino acid or several amino acids or to an abnormal imbalance in amino acids provided to the embryo. In contradistinction to most teratogenic animal models, we believe this model may be important in explaining some forms of human teratogenesis. (Supported by NICHD; MRC)

1138 PATHOLOGICAL FINDINS IN RAT EMBRYONIC SITES EXPOSED TO TERATOGENIC YOLK SAC ANTISERUM. Robert L. Brent, Marcela Jensen, Thomas Koszalka and Ivan Damjanov. Jefferson Med. Coll., Depts. of Pediat.; Radiol; Anat.; Hahnemann Med. Coll., Dept. of Pathol., Phila., PA.

The present study consisted of light microscope and electromicroscopic evaluation of the developing yolk sac, exposed in vivo, to an LD/50 dose of teratogenic antiserum. Following the administration of teratogenic antiserum, on the morning of the 9th day, embryonic sites were removed at 4-hourly intervals for the first 48 hours and 12-hourly intervals for the next 96 hours. The embryonic sites were serially sectioned and stained with hematoxylin and eosin and selectd material was prepared for electron microscopy. The first evidence of pathology appeared in the embryo. Thus, dead and dying cells, as well as a decrease in the number of dividing cells, appeared in the embryo before the yolk sac manifested any changes. Secondary changes, such as avascularity of vitelline circulation, reduction in height of the visceral yolk sac endodermal cells and accumulation of excess protein in the yolk sac cavity all were present only after pathological changes appeared in the embryo. Thus, the antibodies against visceral yolk sac have little or no direct affect on the viability of the yolk sac and there is little histopathological evidence of the proven reduction in pinocytosis produced by the teratogenic antibody. These studies further support the importance of this model for studying embryonic nutrition, since not only are there minimal changes in the maternal organism but the target organ itself is only functionally affected by the teratogenic antisera. (Supported by NIH)

● 1139 RIGHT HEART HYPOPLASIA IN THE CHICK EMBRYO: AN EXPERIMENTAL STUDY

Kathleen A. Cass and Edward B. Clark, Department of Pediatrics, Division of Pediatric Cardiology, University of Iowa, Iowa City, Iowa 52242

We studied the effect of right atrial exclusion on cardiac morphogenesis. White Leghorn eggs were incubated to stages (St) 23 or 25. Access to the embryo was gained by opening a window in the shell and incising the chorion. A loop of 10-0 nylon was placed around the free portion of the primitive right atrium and tightened, diminishing right atrial volume. The embryos were reincubated, harvested at or beyond St 39, fixed in diastole and microdissected. Areas of the tricuspid, mitral, pulmonic and aortic valves were measured by planimetry from photographs. The ratio of right and left ventricular (RV/LV) size was calculated. Presence and position of VSDs were noted. The study group included 22 St 23, 22 St 25 operated (op), 33 sham-operated and 60 normal control embryos. The experimental group had a 14% incidence of infracristal VSD compared with none in the sham group. Tricuspid valve areas in op St 23 (1.66+.24 mm^2) and op St 25 (1.41+.24 mm^2) embryos were significantly decreased ($p<.05$) compared with sham-operated controls (2.73+1.53 mm^2). The RV/LV size ratio (0.68+.09) was also significantly smaller than controls (0.716+0.078) ($p<.05$). Pulmonic, aortic, and mitral valve areas were similar in experimental and control groups. We conclude right atrial volume reduction results in hypoplasia of the inflow portion of the right ventricle, presumably on the basis of intracardiac blood flow alteration.

● **1140** RESISTANCE OF THE MALE GONAD TO A HIGH GALACTOSE DIET. Y.T. Chen, D.R. Mattison, B.B. Bercu and J.D. Schulman, NICHD, NIH, Bethesda, MD.

The frequent association between human galactosemia and premature ovarian failure is well documented. In an animal model for this disease the offspring of rats fed a high galactose diet during pregnancy have significantly reduced numbers of oocytes (Science 214:1145, 1981). In contrast, testicular failure is uncommon in galactosemia. Rats were fed a 50% galactose diet during pregnancy and nursing, and the testes were later examined and hormone levels determined in offspring. Exposure to galactose for various periods during pregnancy, throughout the entire gestation, or postnatally to nursing mother until pups were 5 weeks of age did not produce significant differences from control body weight, seminiferous tubular diameter, or microscopic appearance of the testes when the offspring were adults (66 or 127 days). Serum LH, FSH, and testosterone (T) levels (mean ± SEM) were determined 127 days postnatally, and no significant differences from controls were observed in any of the treatment groups (prenatal galactose: LH 34.4 ± 7.3 ng/ml, FSH 307 ± 27 ng/ml, T 632 ± 153 ng/dl; postnatal galactose: LH 32.0 ± 10.1, FSH 320 ± 40.1, T 290 ± 40; controls: LH 35.9 ± 13.6, FSH 344 ± 23; T 449 ± 54.4). Blood galactose and galactose-1-phosphate levels in animal receiving the 50% galactose diet were comparable to levels observed in human galactosemia. Our demonstration of a persistent reduction in oocyte number in the rat following prenatal exposure to a high galactose diet contrasts sharply with the apparent lack of corresponding effects by galactose or its metabolites on the male gonad.

● **1141** STUDIES OF THE CRITICAL PERIOD FOR VENTRICULAR SEPTATION AND GREAT VESSEL FORMATION IN THE CHICK EMBRYO. Edward B. Clark, Norman Hu, and Glenn C. Rosenquist, Division of Pediatric Cardiology, University of Iowa Hospitals and Clinics, Iowa City, Iowa and Childrens National Medical Center, Washington, D.C.

We studied the effect of a timed teratogenic intervention on ventricular septation and great vessel formation in stage 18, 21 and 24 chick embryos. A loop of 10-0 nylon suture was tied to constrict the midpoint of the conotruncus. The loop was left in place either permanently for 24 or 4 hours, or placed and removed as a sham control. The shells were sealed with parafilm, and the embryos were incubated and harvested at stages 35 to 40. The hearts were fixed in diastole and microdissected. The study groups included 252 experimental, 82 sham-operated, and 72 normal control embryos. Data were analyzed by chi-square method for proportions. The incidence of infra-cristal ventricular septal defects was directly related to the duration of conotruncal constriction ($p<.001$) with an equal proportion of defects observed in the permanent-loop group of each stage. Ventricular septal defects occurred in stage 18 but not in stage 21 or 24 sham-operated group. The spectrum of great vessel anomalies included aortic arch interruption, hypoplasia, coarctation and double aortic arch. The incidence of great vessel anomalies was directly related to the duration of loop constriction but less than that of ventricular septal defects. Great vessel anomalies were significantly more frequent ($p<.01$) in stage 21 embryos (34%) than in stage 18 (14%) or stage 24 (14%). We conclude the critical period for mechanical interference of ventricular septation includes stages 18 to 24 while that for aortic arch malformation centers around stage 21.

● **1142** PYLORIC STENOSIS: AN ARREST OF PHYLOGENESIS? Gerald Katzman. (Spon. by M. G. Robinson) Medical College of Ohio, The Toledo Hospital, Dept. of Ped., Toledo, Ohio.

Over a period of three years about 30 Great Lakes Whitefish were dissected. The fish weighed between approximately two and five pounds. Each fish was noted to have a smooth firm glistening "tumor" in the pyloric area of the stomach. Histologic examination of cross sections through the whitefish pylorus revealed a leiyomyomatous hyperplasia of the circular muscle layer. The longitudinal muscle was not noticeably enlarged. The histology of pyloric stenosis in the whitefish is not dissimilar from that seen in the human infant with pyloric stenosis.

The appearance of pyloric stenosis as a normal state present in all members of a single species of fish stimulates new thoughts as to the etiology of pyloric stenosis in the human. The human condition may represent a failure of phylogenesis determined by the absence of appropriate genetic influences. Alternatively environmental factors could also be of importance and the whitefish could serve as a model for studying these possibilities.

1143 ARTHROGRYPOSIS MULTIPLEX CONGENITA? CHERIL CLARSON, JACK JUNG, GRAHAM CHANCE. Department of Paediatrics, University of Western Ontario, London, Canada.

We report an infant born with severe deformational anomalies and respiratory insufficiency. An underlying diagnosis of Werdnig-Hoffmann disease was suspected but it was not possible to substantiate this diagnosis during life. At autopsy, there was loss of anterior horn cells in the spinal cord.

A review of the recent literature provides evidence that there is a distinct form of Arthrogryposis Multiplex Congenita, Amyoplasia Congenita, associated with localised lesions of anterior horn cell columns. The clinical and pathological features of this baby are consistent with this form of Arthrogryposis Multiplex Congenita rather than with classical Werdnig-Hoffmann disease.

The autosomal recessive inheritance pattern of classical Werdnig-Hoffmann disease does not occur in Amyoplasia. Differentiation of this syndrome has important implications for genetic counselling.

1144 DYSTROPHIA MYOTONICA. CHERIL CLARSON, GEORGE VILOS GRAHAM W. CHANCE. Department of Paediatrics and Obstetrics, University of Western Ontario, Canada.

A report of two infants with the neonatal form of Dystrophia Myotonica. Both infants presented at birth with apnea and hypotonia considered to be due to "asphyxia". However, cord blood gases were normal and these findings, together with clinical appearances, led us to consider other causes of respiratory failure and hypotonia in the newborn. Evidence for a neuromuscular cause was provided by the presence of polyhydramnios in pregnancy.

Investigation of mother and baby in both cases provided a definitive diagnosis of previously unsuspected maternal Dystrophia Myotonica and involvement of other family members.

These cases stress the importance of investigation of polyhydramnios especially when associated with apparent "asphyxia" which is not confirmed on examination of cord gases.

● **1145** FETAL ALCOHOL SYNDROME: A PROSPECTIVE STUDY OF MATERNAL NUTRITURE. Paul M. Fernhoff[1], Margaret Halminski[1], Phyllis B. Acosta[1], Iris E. Smith[3], K. Michael Hambidge[4], Arthur Falek[2,3], and Louis J. Elsas[1]. Emory Univ. Sch. of Med. Depts. of Pediatrics[1] and Psychiatry[2], Ga. Mental Health Inst.[3], Atlanta and the Univ. of Colorado Medical Center[4], Denver.

Nutrition, primarily a zinc deficiency has been proposed as underlying the production of the fetal alcohol syndrome (FAS). We studied prospectively the nutriture and alcohol intake of 78 age and race matched pregnant women. Their infants were examined by one clinician for features of FAS without prior knowledge of the maternal status. In mothers, significant positive correlations were found between their alcohol intake and their hair zinc plasma zinc and serum albumin. Significant inverse correlations existed between alcohol intake and the infant's gestational age, birth weight and length. Correlations did not exist between alcohol intake and maternal height, weight, triceps skin-fold thickness, hematocrit, serum iron, ferritin, vitamin A or total proteins. Maternal plasma and hair zinc and infant hair zinc were similar between controls and drinkers. Of the 28 controls, 30 moderate (<60ml ETOH/day) and 20 heavy (≥60ml ETOH) drinking mothers, mean palpebral fissure width was 7.0, 6.7 and 6.0 cm, respectively ($p<0.05$). Features of FAS were more frequent in the infants of both maternal drinking groups. We conclude that in this study group, zinc and other parameters of nutriture were similar among drinking and control mothers and their infants. FAS may have a familial component and is quantitatively related to maternal alcohol intake.

●1146 THE PRODUCTION OF CONGENITAL MALFORMATIONS IN THE RAT USING TISSUE ANTISERA. XVI. THE EFFECT OF TERATOGENIC ANTISERUM ON YOLK SAC FUNCTION IN RAT EMBRYOS CULTURED IN VITRO. Stuart J. Freeman, John B. Lloyd, Marcela Jensen, Thomas R. Koszalka and Robert L. Brent. Univ. of Keele, Dept. of Biochem., U.K.; Jefferson Med. Coll., Depts. of Pediat.; Radiol.; Anatomy; Biochem., Phila., PA.

Early studies of teratogenic antiserum concentrated on demonstrating a direct embryotoxic effect or an indirect embryotoxic effect from resulting maternal immunologic disease. Neither of these hypotheses was true, since teratogenic antiserum localized primarily in the developing yolk sac. The nature of the yolk sac dysfunction has been the concern of our laboratory and the following experiments were carried out. Embryos aged 9.5 days were cultured in vitro for 40 hours and were exposed to either teratogenic antisera or normal rabbit serum. Transport studies utilizing ^{125}I-labelled polyvinylpyrrolidine substrate or ^{3}H-leucine-labelled serum proteins were carried out. The presence of the antiserum decreased the protein content of the conceptus when compared to the control embryos. The pinocytotic uptake of the serum proteins was decreased by the antiserum. Quantitative comparison between in vitro and in vivo studies reveal that malformations are not produced in the developing embryos until the antibody concentration produces a reduction in pinocytosis. This substantiates the previous findings that macromolecular pinocytosis is the main if not exclusive source of amino acids to the developing embryo during early organogenesis and that interference with an adequate source of amino acids can result in embryopathology and teratogenesis. (Support MCR; NIH)

● 1147 EXPERIMENTAL FETAL HYDANTOIN SYNDROME: PHENYTOIN TERATOGENICITY OF PRIMARY AND SECONDARY MOUSE PALATE IS INFLUENCED BY THE H-2 HISTOCOMPATIBILITY LOCUS. Allen S. Goldman, Charles L. Fishman, and Mary K. Baker. The Children's Hospital of Philadelphia, Philadelphia, PA

We have studied the production of cleft lip (palate) (CLP) and isolated cleft palate (CP) by phenytoin in H-2 congenic strains [A/J(H-2^a), A/Wy(H-2^a), A.SW(H-2^s), A.BY(H-2^b), B10.A (H-2^a), and B10(H-2^b)]. These congenic strains differ primarily at the H-2 locus on the 17th chromosome, but otherwise have a common genetic background of either the A or B strains. For CLP the A strains were injected with phenytoin 50mg/K or saline at 9 am. on 10 days after the vaginal plug, and the B strains were injected with phenytoin 100mg/K or saline at 9am. on 10 days, 9 and 10 days, or 8,9, and 10 days after the plug. For isolated CP both the A and B strains were injected with phenytoin 50mg/K or saline at 9 am. on the mornings of 11,12, 13, and 14 days after the plug. The congenic strains A.Wy, A.BY, and A.SW had the identical level of spontaneous CLP. A.Wy(H-2^a) mice have a significantly higher rate of induced CLP than either of its congenic partners, A.BY(H-2^b) ($P < 0.05$) or A.SW(H-2^s) ($P < 0.04$), whereas there is no significant difference in the degree of CLP produced by phenytoin in congenic strains with the B background. Isolated CP produced by phenytoin is significantly influenced by H-2 whether the background is A($P < 0.04$) or B($P < 0.04$). Thus, both induced CLP and induced isolated CP are influenced by H-2 with the A background, but only induced isolated CP is influenced by H-2 with either A or B background.

● 1148 THE USE OF SMALL COHORT STUDIES TO EVALUATE PUTATIVE TERATOGENS-Lewis B.Holmes,Beth C.Kleiner, B.Frank Polk Mass. Gen. Hosp. & Brigham & Women's Hosp.Boston, MA

Several human teratogens cause both major and minor congenital malformations (CM's). The typical study of a teratogen focuses only on major CM's,which occur in 2-4% of newborns. We have developed a method in which the prevalence of both major and minor CM's is recorded. In a sample of 7,157 infants, 3.6% had 1 or more major CM's and 46% had 1 or more minor CM's (such as simian crease).

Standard examination of newborn infants who were exposed in the first trimester to putative teratogens demonstrated:

Teratogen	N	Major CM	Minor CM	1 or more CM Major & Minor
Phenytoin	38	7.9%	36.8%	42.1%
Clomiphene	40	0	40.0	40.0
Sex hormones	166	4.2	31.3	34.3
Diabetes mellitus	172	9.3	60.5	62.8
Controls	7,157	3.6	46.0	49.6

By comparing multiple unexposed infants to each exposed infant, a sample of only 38 exposed and 304 unexposed is adequate to identify a 50% increase (significant at 0.05) in both major and minor CM's with 95% confidence. We found a significant increase of both types of anomalies among infants of diabetic mothers, but not among infants exposed to clomiphene, phenytoin or exogenous hormones. The prevalence of major, but not minor anomalies, was increased among infants exposed to phenytoin.

We conclude that the carefully examined small cohort study can be an informative first step in evaluating putative human teratogens.

● 1149 THE VASCULAR PATHOGENESIS OF TRANSVERSE LIMB REDUCTION DEFECTS. H.E. Hoyme, K.L. Jones, M.I. Van Allen, B.S. Saunders, and K. Benirschke (Spon. by R.J. McKay, Jr.). University of California School of Medicine, Departments of Pediatrics and Pathology, La Jolla; and University of Washington School of Medicine, Department of Pediatrics, Seattle.

Evaluation of four patients with unilateral transverse limb reduction defects indicates that some instances of this structural defect are the result of an in utero vascular accident. Three of the four patients were liveborn infants with unilateral absence of the distal forearm. Doppler examination of blood flow to the affected extremity showed lack of pulsation distal to the point of bifurcation of the brachial artery. No evidence of amniotic bands was found in either the infants or placentas. However, microscopic evidence of fetal vascular occlusive disease was present on multiple sections of each placenta. Occlusion of the brachial artery in those three children was presumably secondary to embolization from the placental vascular thrombi.

The fourth patient, a 116 mm CR length fetus, was aborted following three days of massive vaginal bleeding. Dissection of the arm revealed a massive thrombus occluding the brachial artery just proximal to its bifurcation and proximal to the absent distal forearm. Brachial artery occlusion in this case was most likely secondary to hypovolemia and hypoperfusion associated with fetal blood loss during the placental abruption. Recognition of the disruptive vascular pathogenesis of some cases of unilateral terminal transverse limb reduction defects explains the negligible recurrence risk and should focus attention on careful evaluation of the placenta in such cases.

●1150 THE PURIFICATION OF RAT VISCERAL YOLK SAC ANTIGENS WHICH PRODUCE TERATOGENIC ANTISERUM BY MEANS OF ISOELECTRIC FOCUSING. Marcela Jensen, Thomas R. Koszalka, Paz Vega and Robert L. Brent. Jefferson Med. Coll., Depts. of Pediat.; Radiol; Biochem., Phila, Pa.

In order to clarify our understanding about the mechanism of action of teratogenic antisera, our laboratory has attempted to isolate and characterize those antigens which produce the antisera. Preparative flatbed isoelectric focusing (IEF) in granulated gel utilizing pH= 3-10 ampholytes was used to separate proteins from 19th day rat visceral yolk sac (VYS). After IEF the gel bed was divided into 3 equal segments. Antisera produced against segment 1 (pH 3-5) were not teratogenic. Antisera raised against segment 2 (pH 5-7) and 3 (pH 7-9.0) produced severe congenital malformations when injected into 9th day pregnant rats. Fractions 2 and 3 were further refocused, using pH= 7-9 and pH= 5-7 ampholytes and individual protein-containing bands were eluted with PBS. Many of the proteins from fractions 2 and 3 produced teratogenic antisera. When whole VYS homogenate was passed through a Con-A-Sepharose column, most of the proteins were not absorbed to the gel. A fraction containing glycoprotein was eluted with 20 mM-α-methyl mannoside. Both fractions produced potent teratogenic antibodies. These studies show that the VYS contains a multiplicity of antigens which can stimulate the production of teratogenic antibodies. At least one teratogen-stimulating antigen present in the VYS appears to be glycoprotein in nature. Fraction 3 from IEF is the least complex and is being used for the isolation of teratogen-stimulating antigens. (Supported by NIH)

1151 AN ARTIFICIAL CHEST WALL FOR ECTOPIA CORDIS WITH ABSENT STERNUM. T.G. Keens, C.W.Sargent, B.G. Nickerson, T.Y.K. Lawrence, B.W. Meyer, D.L. Leake, and A.C.G. Platzker, (Spon. by G.N.Donnell). Childrens Hospital of Los Angeles and Harbor-UCLA Medical Center, Los Angeles.

An infant with ectopia cordis with absent sternum remained dependent on mechanical assisted ventilation at 4 months of age because of decreased chest wall stability. The anterior chest wall was comprised only of skin, and collapsed inward with each inspiration. An anterior chest wall prosthesis was fabricated from a polyether urethane coated dacron mesh and surgically implanted. Tidal volume (Vt; ml), trans-pulmonary pressure (Ptp; cmH2O), and intraesophageal pressure (Ppl; cmH2O) during spontaneous breathing; maximal Ppl and transdiaphragmatic pressure (Pdi; cmH2O) against an occluded airway; and dynamic pulmonary (Cpul; ml/cmH2O) and chest wall (Ccw; ml/cmH2O) compliance were measured at 3 weeks before and 2 months after surgery.

	Spontaneous Breathing			Maximal			
	Vt	Ptp	Ppl	Pdi	Ppl	Ccw	Cpul
BEFORE	8	3	-1	8	-2	Infinite	0.5
AFTER	37	5	-5	19	-22	7.8	1.3

Tidal volume and all pressures increased following surgery ($P < 0.001$). Ccw fell, indicating increased stability, after surgery. The prosthesis provided ample chest wall stability to permit the infant to be weaned from mechanical assisted ventilation while awake.

●1152 THE HEART OF THE FETUS OF THE DIABETIC MOTHER - ECHO CARDIOGRAPHIC EVALUATION IN UTERO. Charles S. Kleinman, Richard Donnerstein, Diana Lynch, John Hobbins, Norman S. Talner; Yale University School of Medicine, New Haven, CT

Two-dimensional and M-mode echocardiographic (echo) studies were performed during the third trimester of pregnancy in 85 pregnant diabetic women. These studies were performed to determine if fetal echo study could be of use in the prenatal diagnosis of the hypertrophic cardiomyopathy (HCM) which has been described in infants of diabetic mothers (DM's). There were no significant differences in left ventricular wall (LVFW) or interventricular septal (IVS) thickness between fetuses in the five diabetic classes. When fetuses were grouped together according to gestational age (GA), LVFW and IVS thicknesses in the diabetic fetuses (FDM's) did not differ significantly from normal values that had been established in our laboratory. (At GA 19-26 weeks, FDM's had LVFW and IVS thicknesses of 2.6±0.9 mm and 2.8±0.4 mm respectively.) Eighty-four of the 85 mothers were felt to be in adequate diabetic control. One 28-week fetus whose mother was in poor diabetic control, had an IVS thickness of 5 mm. This was in excess of the normal value at this GA (3.1±1.0 mm). After excellent diabetic control was attained, the IVS thickness of this fetus gradually returned to normal (4 mm) at term. These studies suggest that diabetic control is the important factor in the development of the HCM of the FDM. We further suggest that the evaluation of IVS thickness in utero may serve as a sensitive indicator of diabetic control and thus can be of value in the management of pregnancy in the DM.

1153 THE UPTAKE OF α AMINOISOBUTYRIC ACID AND SUCROSE BY RAT 14TH AND 18TH DAY VISCERAL AND PARIETAL YOLK SAC IN VITRO. Thomas R. Koszalka, Carole L. Andrew and Robert L. Brent. Jefferson Medical College, Depts. of Pediat.; Radiol.; Anat.; Biochem., Phila., PA.

Since the yolk sac placentae are the first functioning placentae in the developing rat embryo, they are the significant placentae present during early organogenesis. This study deals with the ability of the parietal yolk sac (PYS) and visceral yolk sac (VYS) to take up a nonmetabolizable amino acid and to perform pinocytosis during midgestation. Individual PYS or VYS obtained from 14-day and/or 18/day pregnant rats were placed in flasks containing medium 199 (Gibco Co.) and heat-inactivated calf serum, gassed with 95% O_2/5% CO_2 and incubated in a shaking waterbath for 0-4 hours at 37°C with ^{14}C-AIB (Tracer dose). The uptake studies revealed an interesting divergency in VYS and PYS function. While the VYS and PYS had functioning transport systems for the uptake of amino acids (AIBS), only the VYS appears to have a system which incorporates macromolecules by pinocytosis. This finding is surprising in view of the fact that the major cellular component of the PYS, i.e. the giant trophoblast cell, is known to be very active phagocytically. Since previous studies have indicated that specific antisera prepared against the VYS are much more teratogenic than antisera prepared against the PYS, we now have a biochemical explanation for this difference, in that macromolecular transport across the PYS is probably not accomplished by pinocytosis. (Supported by NIH)

●1154 SACRAL MENINGOCELE WITH SEVERE CONGENITAL HEART DEFECTS - ? AUTOSOMAL RECESSIVE TRAIT. Boris G. Kousseff and Donald Pearson. Univ. of So. Fl., Tampa, FL, Southern Ill. Univ., Springfield, IL. Departments of Pediatrics and Neurosurgery. (Sponsored by Lewis A. Barness).

Open neural tube defects are considered to be due to a polygenic multifactorial trait; associated abnormalities are encountered in 1 of 6 affected children.

In 3 of 4 term siblings of adequate size at birth, we found small sacral meningoceles with subsequent development of hydrocephaly. One of the patients was diagnosed prenatally based on persistent two-fold increase of alpha-fetoprotein and presence of rapidly adhering cells in the amniotic fluid from amniocentesis at 15 and 17 weeks gestation. Maternal serum alpha-fetoprotein was within normal limits. The other siblings, a male and female expired during the neonatal periods as a result of transposition of the great vessels and Type I truncus arteriosus respectively. The male also had right renal agenesis. Peripheral lymphocyte Giemsa banded karyotypes were normal in all siblings and their parents.

The findings in this sibship suggest autosomal recessive mode of inheritance for this type of meningocele with severe congenital heart defect and imply heterogeneity for the open neural tube defects. Pediatricians should be aware of this variant, particularly in regard to the 25% recurrence risk for subsequent pregnancies instead of the 5% risk given for the polygenic multifactorial type.

●1155 DIFFERENTIATION AND MORPHOGENESIS IN THE EARLY EMBRYONIC HEART. J. W. Lacktis, F. J. Manasek (Spon. by R. A. Arcilla); The University of Chicago Hospitals and Clinics, Departments of Anatomy and Pediatrics and Committee on Developmental Biology, Chicago, Illinois

Since the heart has cellular contributions from both right (R) and left (L) sides of the embryo during development, it has been proposed that pre-existing differences of the R and L cell populations may account for the asymmetry during heart looping. In a recent study we have implicated myocardial cytodifferentiation, specifically contractile protein synthesis, as a requirement for normal heart morphogenesis. To test the hypothesis that unequal rates of cytodifferentiation may be responsible for cardiac asymmetry, we measured the net accumulation of myosin (M) in myocardial cells derived from the R and L sides during tubular heart formation and looping. Total M was measured in cells isolated from R and L hearts of experimentally produced cardiac bifid chick embryos. At least 50 cells from each R and L heart were measured, and a total of 18 halves of 9 primitive hearts were used. M was measured using indirect immunofluorescence labeling and microspectrophotometric measurement of fluorescence. There was no significant difference in rate of M accumulation between cells from R and L hearts ($p = 0.43$). M distribution, measured in frozen sections using fluorescent antibody, was also uniform in both R and L hearts. We conclude that phenotypic expression is highly synchronized throughout the myocardium. Although M synthesis is needed for morphogenesis, changes in cardiac shape during looping are not related to R-L differences in M accumulation.

●1156 TRANSPLACENTAL BROMISM....AN OVERLOOKED PROBLEM? Henry H. Mangurten and Celia I. Kaye, Lutheran General Hospital, Department of Pediatrics, Park Ridge, Illinois.

Bromism was identified in two infants shortly following birth. Differing phenotypic effects were thought to be related to timing and duration of exposure. The first infant, exposed late in gestation by maternal ingestion of triple bromide during four days preceding delivery, presented with profound hypotonia. Elevated serum and urinary levels of bromide were demonstrated, with a serum half-life of 8.5 days. Gradual clinical improvement was noted over two weeks, with clearance of serum bromide by ten weeks. The second infant presented with cyanotic spells in association with profound generalized hypotonia. The mother reported daily exposure to bromide-containing chemicals in a photographic laboratory from conception until five weeks prior to delivery. Maternal and infant serum bromide levels were elevated. In contrast to the first infant, dysmorphic features, including frontal bossing, increased inner canthal distance, broad nasal bridge and prominent gingivae, were observed. Mild developmental delay was noted at ten months of age. Fetal bromism in association with microcephaly, growth retardation and congenital heart disease has been reported in three infants exposed throughout pregnancy. There are no other reported instances of congenital malformations or dysmorphic features in infants exposed to bromide prenatally These infants illustrate the differential neonatal effects of fetal exposure to bromide at different stages of gestation. The importance of environmental and occupational exposure during pregnancy is clear.

1157 RUPTURE OF THE EMBRYONIC DORSAL MESOCARDIUM M. F. Marusich, F. J. Manasek (Spon. by R. A. Arcilla) Pritzker School of Medicine, The University of Chicago Hospitals and Clinics, Departments of Anatomy and Pediatrics, Chicago, Illinois

The early embryonic heart is attached to the embryo by means of the dorsal mesocardium (DM). During normal development, the DM ruptures, enabling the primitive heart to bend and rotate. The mechanism responsible for DM rupture is unknown. We examined the morphologic sequences of DM rupture by scanning electron-microscopy, using 20 dissected chick embryo hearts at varying stages of development. At stage 12- (15 somites), tiny perforations start to appear in the DM at a level slightly rostral to the mid-heart. By stage 13- (18 somites), the entire mid-rostral 1/3 of the heart is freed of dorsal attachment. At later stages, the perforations extend rostrally and caudally until the DM disappears completely, the site of the former DM being marked by a low ridge of myocardial cells. We tested experimentally the hypothesis that the DM ruptures because of applied tension imposed upon it by the adjacent splanchnic mesoderm (SM). Using 17 cultured embryos (stage 11-, 12 somites), tension in the intact DM was relieved by cutting longitudinally the adjacent SM. This resulted in wide separation of the cut edges, thus relieving stress. Despite the relief in SM stress, the DM developed perforations normally and eventually ruptured. Our study suggests that normal DM rupture does not result from applied tension but is rather an intrinsically regulated event.

1158 HEMATOLOGICAL ABNORMALITIES IN NEWBORNS WITH DOWN SYNDROME. Marvin E. Miller and Janice M. Cosgriff (Spon. by Gilbert Forbes) University of Rochester Strong Memorial Hospital, Department of Pediatrics, Rochester, New York.

The purpose of this study was to determine the frequency and natural history of hematological abnormalities in newborns with Down syndrome. 73 newborns with Down syndrome (documented by karyotype) were ascertained from our hospital between 1965-1981, and their newborn records were reviewed. In 20 cases no complete blood count (CBC) was recorded. In 17 cases a CBC was normal. In 36 cases there was a hematological abnormality including 26 cases of polycythemia (peripheral hematocrit greater than 70), three cases of leukocytosis (white blood cell count greater than 34,000), three cases of thrombocytopenia (platelet count less than 100,000), one case of thrombocytosis (platelet count greater than 400,000), and three cases of concomitant polycythemia and thrombocytopenia. While some of these babies were evaluated for neoplasia or sepsis, there was a total resolution of the hematological abnormality within two weeks without evidence of malignancy or infection.

We conclude that hematological abnormalities which show a benign natural history are common in Down syndrome newborns, with a minimum incidence of 50% (36/73). The finding of a hematological abnormality in a newborn suspected of having Down syndrome is further evidence for the diagnosis of Down syndrome.

● 1159 SERUM ALPHA-FETOPROTEIN (AFP) SCREENING IN DIABETIC PREGNANCY. Aubrey Milunsky, Michael F. Greene and M. Donna Younger. Boston University School of Medicine, Harvard Medical School, Joslin Clinic; Departments of Pediatrics, Obstetrics & Gynecology and Medicine; Boston.

Maternal serum AFP screening in routine pregnancy is a valuable method for the prenatal detection of open neural tube defects (NTD) and some other congenital anomalies. Since diabetic pregnancy outcome is known to be associated with an increased incidence of congenital malformations, we assessed the value of AFP screening in these high risk pregnancies. From 1975-81 we studied 396 diabetic pregnancies, obtaining second trimester serum samples in 90%. We confirmed that pregnant diabetics have lower serum AFP. These values, equivalent to those found 2 weeks earlier in gestation in non-diabetics, suggest the use of a separate AFP reference curve. The remarkable observed frequency of NTD was 22.7/1000 (a 10-20-fold increase), while that for all major anomalies was 11.1%. All 9 of the open NTD were probably detectable by AFP screening, but in only 4 were sera obtained. Maternal sera were studied in only 62.9% of the 35 with major non-NTD anomalies, none having high AFP. Data analysis of ultrasound (U/S) detection of the major anomalies is in progress and was potentially useful in 18/44 cases. Examples were encountered in which careful U/S missed NTD which were subsequently detected because of AFP screening. While awaiting further data analysis, early indications are that both second trimester serum AFP screening and U/S are valuable adjuncts for the management of diabetic pregnancy and moreover have complementary roles.

1160 EMBRYONIC AND FETAL COMPRESSION WITH INCOMPLETE DISRUPTION OF AMNIOTIC MEMBRANES. Susan Niermeyer, David K. Manchester (Spon. by F.C. Battaglia) Univ. of Colorado School of Medicine, Department of Pediatrics, Denver.

The spectrum of defects resulting from early amnion rupture is now recognized to include craniofacial defects, limb reductions, body wall deficiency, scoliosis, and growth retardation. Concurrence of craniofacial and limb defects with body wall deficiency has been reported in nearly every series describing deformation abnormalities, but the role of the amniotic membrane in production of this common constellation has not been precisely defined. Alerted by sonographic evidence of fetal abnormalities, we were able to document fetal, membrane, and placental relationships at birth in three cases of membrane disruption. All three had abdominal wall deficiencies through which liver and intestine protruded external to the amnion. All three had club feet. Two had craniofacial defects underlying adherent membrane histologically identified as amnion. The third delivered ensheathed by an essentially intact amniotic membrane covering the entire body except the protruding viscera. Simple puncture of fetal membranes has been reported to produce deformation abnormalities in animals. On the basis of our observations and repeated reports of similar cases, we propose that the concurrence of extra-amniotic evisceration with craniofacial and limb abnormalities can be explained by leakage of amniotic fluid prior to or during migration of the amnion toward the chorionic plate. Multiple deformations result from compression by relatively intact amnion. The frequent association of these defects may point to a period of particular risk during human gestation.

1161 IS MARIHUANA SMOKING FETOTOXIC? Qutub H. Qazi, Evelyn Mariano, Eva Beller, Doris Milman and William Crombleholme. State University of New York, Downstate Medical Center, Departments of Pediatrics and Obstetrics and Gynecology, Brooklyn, New York.

Administration of marihuana extract to pregnant mammals reportedly results in increased fetal resorption, lower birth weight, and higher incidence of abnormalities of central nervous system, skeleton and viscera. The adverse effect of maihuana smoking on the outcome of human pregnancy, however, has not been reported.

We have observed two newborn infants whose young mothers acknowledged smoking marihuana prior to and throughout pregnancy while categorically denying use of alcohol and other psychoactive drugs. The anomalies we observed were reminiscent of those reported in fetal alcohol syndrome. The infants were small for gestational age and tremulous soon after birth. The first infant had numerous dysmorphic features which included webbed neck, short palperbral fissures, highly arched palate, posteriorly rotated ears, hypoplastic nipples, clinodactyly of fifth fingers, presacral sinus and a Sidney line. The second infant had epicanthal folds, posteriorly rotated ears and a long philtrum with indistinct groove.

In the light of experimental evidence for fetotoxicity of marihuana, it is difficult to dismiss the association of steady use of marihuana during pregnancy by two mothers with abnormalities in their offspring, as reported here.

1162 PRIMARY TESTICULAR FAILURE WITH FETAL PROGESTIN EXPOSURE. Robert Rapaport, Brenda Kohn, Maria I. New, Lenore S. Levine, CMDNJ-New Jersey Med. School, Newark, NJ and Cornell Univ. Med. Coll., New York, Dept. Peds.

A 21 y o boy was determined to have primary testicular failure. A small phallus was noted at birth. Right cryptorchidism, first noted at 12 yrs, was corrected at 13 yrs. Because of possible intermittent torsion of the left testis he had orchidopexy and testicular biopsy at 14 yrs. Biopsy showed prominent Sertoli cells, no spermatogonia or spermatocytes, early Leydig cells in the interstitium. At 15 yrs he had normal axillary and pubic hair, some facial hair; right testis measured 15ml, left 12ml; penis 5.5 X 3cm. He had normal libido, erections and ejaculations. Sexual hair and genital size did not advance. At 20½ yrs 100μg LHRH was infused IV over 3 hrs. His karotype was 46 XY t(10p,18q). *ng/ml

AGE (years)	Δ4-A (ng/dl)	DHEA (ng/dl)	DHEA-S (μg/dl)	T (ng/dl)	LH (mIu/ml)	FSH (mIu/ml)
15 1/3	40	367	280	231	*1.0	*2.1
18 1/2	52	404	445	225	*7.4	*5.2
LHRH - 0'	52	272		294	25.3	50.0
180'	76	503		525	130.0	205.0

12 days after the 4th monthly injection of 200mg IM T enanthate, his LH was 5.4 and FSH 6.2mIu/ml and T 293ng/dl. Of note, he was born to a 42 y o woman after 16 yrs of infertility who had taken norethindrone 5mg qod for 21 days during the 2nd trimester. The data is consistent with primary gonadal failure; the hypothalao-pituitary gonadal axis is normally responsive to exogenous testosterone. Exposure to intrauterine progestins may result in primary gonadal failure.

● 1163 GROWTH CHARACTERISTICS OF FIBROBLASTS FROM PATIENTS WITH THE SYNDROME OF INTRAUTERINE GROWTH RETARDATION, BRANCHIAL CLEFT SINUSES, AND PREMATURE AGING (IUGR-BCS-PA), Jonathan D. Root and Theodore A. Tedesco, (Spon. by Allen W. Root), Univ. So. Florida Coll. Med., All Children's Hosp., Dept. Ped., Tampa and St. Petersburg.

The in vitro growth patterns of fibroblasts from a mother (2 specimens, M1,M2) and son (1 specimen, S1) with IUGR-BCS-PA (Lee et al, Am J Med Genet., in press) were compared with those of fibroblasts from 4 age and sex matched control subjects (C). Skin fibroblasts (4 x 10^5 cells/flask) were cultured in quadruplicate in Eagle's minimum essential medium containing 8% neonatal calf serum. Cells were harvested every other day for 12 days; total cell counts and DNA and protein contents were determined. Within 6 days after initial plating the cell number, protein and DNA contents of the patient cultures were significantly ($p<0.01$) less than those of the controls and remained thus through the 12th day.

	Day 6			Day 12		
	Cell#(x10^6)	Protein(ug)	DNA(ug)	Cell#	Protein	DNA
C	1.69	982	52.9	1.95	1349	54.1
M1	.30	432	24.0	.51	575	26.0
M2	.10	265	17.0	.14	272	28.8
S1	.19	292	25.2	.06	330	36.0

Epidermal growth factor (25 ng/ml) enhanced the growth of all control cells and 2/3 patient cell lines.

Conclusion: Skin fibroblasts from patients with IUGR-BCS-PA have a subnormal growth rate in vitro reflecting the abnormal somatic growth of these subjects.

● 1164 ORIGIN AND EARLY MIGRATION OF HEAD PROCESS (NOTOCHORD) IN THE CHICK EMBRYO. Glenn C. Rosenquist, Children's Hospital National Medical Center and the George Washington U. School of Medicine and Health Sciences, Washington, D. C.

Development of the embryonic axis in vertebrates begins with formation of the head process anterior to the primitive streak. In order to learn the origin of these prenotochordal cells, New explanted Leghorn blastoderms were pre-incubated 12-25 hours (to primitive streak to head process stages); tritiated-thymidine-labeled grafts containing approximately 600-1200 cells were implanted into homologous positions in (or near) Hensen's node of homologously staged recipient embryos, which were reincubated to head-fold to early-limb-bud stages, fixed, embedded in paraffin and serially sectioned. The slides were coated with photographic emulsion and exposed for 7-30 days. Labeled cells were found in notochord of the head and/or trunk in 44 embryos, often along its entire length from the head to the streak. In many of these embryos, labeled cells were also found in ventral neural tube, paraxial mesoderm (somites), and gut endoderm, depending upon the location of the graft in the node. This study indicates that at the short-streak stage and thereafter, the dorsal portion of Hensen's node is a center for prospective notochord cells. Anterior and lateral to the node are the epiblast cells destined for ventral neural tube and paraxial mesoderm. Beginning at the early-head-process stage, notochord mesoderm emerges from the notochord center by first migrating ventrally and then anteriorly in the mesoderm layer, to form the head process anterior to the node.

1165 PRENATAL AND POSTNATAL GROWTH IN INFANTS WITH ABDOMINAL WALL DEFECTS. Y. Wang, L. McGill, B. Quissell, and J.A. Hernandez. Department of Perinatology, The Children's Hospital, Denver, Colorado.

We reviewed the records of 89 infants admitted to our Neonatal ICU with the diagnosis of Congenital Abdominal Wall Defect: 45 gastroschisis and 44 omphaloceles.

The purpose of this study was to determine the influence of these anomalies in the prenatal and postnatal growth patterns of these infants. The following table shows some of the characteristics of the intrauterine growth identified in our study:

	No.	F:M	$\bar{X}$B.Wt.	$\bar{X}$G.A.	%AGA	%SGA	%LGA
GASTROSCHISIS	45	1:1.3	2391	37.6	58	40	2
OMPHALOCELE							
INTACT SAC	34	1:1.4	2793	38.3	74	15	11
RUPTURED SAC	10	1:0.3	2064	36.4	70	30	0

The postnatal growth achieved, when adequate caloric intake was provided, was similar in both groups of infants. A catch-up growth was noted in infants with in-utero growth retardation.

In summary, the incidence of in-utero growth retardation for infants with gastroschisis and omphalocele with ruptured sac is significantly high. We postulate that a possible mechanism involved in this in-utero growth retardation is the loss of nutrients and calories into the amniotic fluid. The normal postnatal growth experienced by these infants following the closure of the defect supports this hypothesis.

The role of these abdominal wall defects in producing in-utero growth retardation needs to be recognized.

NEONATOLOGY

1166 A MICRO HEPARIN ASSAY FOR SICK PRETERM INFANTS. S. Abbasi, M. Grous, C. Mielkie, R. Rodvein, L. Johnson U. of P., Med. Sch., Penn. Hosp., Dept. of Peds., Phila., Pa. and Inst. Med. Sci., San Francisco, Calif.

The human preterm newborn is susceptible to both hemorrhagic & thrombotic events but is, on balance, in a hypercoagulagle state. Small sick preterm infants often require indwelling catheters with the attendant risk of thrombus formation about the catheter tip. To prevent this, heparin is often added to parenteral and flush solutions to a final concentration of approximately 1 unit/ml. Because the clearance of heparin varies greatly especially in small sick infants, a microheparin assay is needed. We have developed such an assay. 50 lamda of plasma are rinsed into a buffer solution containing all necessary clotting factors. Excess thrombin is added and the kinetics of clotting are recorded in the Sonoclot Coagulation Analyzer (R) (Sienco Inc.). Presence of heparin slows down the rate of fibrin formation. The concentration of heparin in the infant's plasma is determined from a standard curve calibrated with known heparin standards. A circulating heparin level of 0.04 to 0.1 units/ml is functionally equivalent to a PTT of ~40 to 60 seconds. This is a range which should minimize the likelihood of clotting and yet avoid increasing the risk of bleeding. Heparin levels in 20 sick preterm infants with indwelling catheters were assayed. Only 3 were found to be in ideal range; 7 were too high; 10 were too low. This study demonstrates that many infants are at a greater than necessary risk of both thrombosis and hemorrhage. In addition, misinterpretation of the cause of bleeding (DIC rather than excessive heparin) could lead to inappropriate Rx (plasma) resulting in increased risk of intraventricular hemorrhage.

1167 RETROSPECTIVE COMPARISON OF THE CONTRIBUTION OF THE PDA IN SEVERE RDS IN VERY LOW BIRTH WEIGHT (VLBW) (1200g) VS. NEONATES WEIGHING 1201g-2000g. David H. Adamkin, Larry N. Cook, and Judy A. Mansfield, (Sponsored by Billy F. Andrews), University of Louisville, School of Medicine, University Hospital, Department of Pediatrics, Louisville, Kentucky.

68 VLBW neonates and 109 neonates (1201-2000g) with severe RDS (+CXR, $FiO_2 > .5$, IMV) were evaluated for the presence of a PDA (clinical exam, echocardiography LA/Ao > 1.2, pulse Doppler, flush aortography).

The incidence of documentable PDA with severe RDS was 81% in the VLBW and 68% in the larger group; not statistically different. All of the VLBW neonates with RDS-PDA received indomethacin enterally and/or surgical ligation, and all but eleven in the 1201-2000g group with RDS-PDA were so treated. The table below compares the two groups:

(*p 0.01 **p 0.005)	N	Mean B.W.	*Days Asst Vent	Pneumothorax	**BPD	*Neonatal Survival
VLBW RDS-PDA-TX	55	922.5g	40.4	45%	81%	50%
1201-2000g RDS-PDA-TX	63	1559g	10	29.7%	23.3%	89.2%
VLBW RDS	13	953.9g	*51	59%	**82%	73.3%
1201-2000g RDS	35	1636g	8	28.6%	3.2%	88.6%

The data indicate that: 1) the incidence of PDA with severe RDS is high but not statistically different in the VLBW vs 1201g-2000g neonates; 2) the PDA does not influence the prolonged assisted ventilation requirement or BPD incidence in the VLBW; whereas, the presence of a PDA in the 1201g-2000g neonate significantly increases the incidence of BPD.

1168 CONTRIBUTION OF THE PATENT DUCTUS ARTERIOSUS (PDA) IN SEVERE RESPIRATORY DISTRESS SYNDROME (RDS). David H. Adamkin, Jenna W. Fleischaker, Valorie Taylor, Peter Murphy, Larry N. Cook, (Sponsored by Billy F. Andrews), University of Louisville, School of Medicine, University Hospital, Department of Pediatrics, Louisville, Kentucky.

A retrospective study of 109 premature neonates weighing 1201g-2000g with severe RDS (+CXR, $FiO_2 > .5$, IMV) evaluated the presence of a PDA (clinical exam, echocardiography LA/AO >1.2, pulse Doppler, flush aortography) for its effect on course and outcome of severe RDS.

The incidence of PDA was 67.9%. All but eleven or 85% of neonates with RDS-PDA received enteral indomethacin and/or surgical ligation for the PDA at the discretion of the attending physician.

	N	Mean BW	Days Asst Vent	Pneumothorax	*BPD	Survival
Group I						
RDS-PDA-TX	63	1559g	10.6	33.3%	26.2%	89%
Group II RDS	35	1636g	8.0	29.4%	3%	91.2%

*$p < 0.01$

The data indicate that a documentable PDA occurs in the majority of neonates with severe RDS between 30-34 weeks gestation. Although time on assisted ventilation was not statistically different, radiographic evidence of BPD was significantly increased in those with RDS-PDA-TX. However, neonatal survival was not different. Without a larger group of neonates with RDS-PDA not receiving PDA ligation, we can only speculate that early ligation of the PDA with severe RDS improves survival and equals those without PDA in this weight group.

1169 TRANSPLACENTAL TRANSFER OF BILIRUBIN IN MATERNAL HEPATITIS. David H. Adamkin, Jay D. Schmid, and Carolyn J. Forgey, (Sponsored by Billy F. Andrews), University of Louisville, School of Medicine, University Hospital, Department of Pediatrics, Louisville, Kentucky.

Transplacental passage of indirect bilirubin has been shown in animal studies and suggested in one human case (Lipsitz in 1973). Our report describes a 1400 gram black male, born at 32 weeks gestation to a 22 yo G2P1 with hemoglobin S-C and non-A, non-B chronic active hepatitis. The infant presented with respiratory distress minutes after C section and had marked icterus and hepatomegaly. The maternal and infant bilirubin values are shown below, along with liver functions.

	TOTAL	DIRECT	INDIRECT	SGOT	SGPT
infant	50.0	36.8	13.2	216	8
mother	55.3	42.0	13.2		

The infant was ventilated, cultured, and begun on antibiotics. Two double volume exchanges were performed for rising indirect bilirubin. The infant died at 24 hours of life from respiratory complications and arrhythmias. Autopsy findings included mild adrenal and gastric hemorrhages. The liver demonstrated multinucleated giant cells, intercellular, intercanalicular and interductal cholestasis. The brain showed no kernicterus.

The data suggest a second case of human placental passage or indirect bilirubin without kernicterus. Direct bilirubin has not been shown to cross the placenta in previous studies, and these findings may be due to the neonatal hepatitis, however, the high direct fraction and the similarity with the maternal value suggest the possibility of transplacental transfer of direct bilirubin.

1170 ARTERIAL PRESSURE IN THE FIRST 48 HOURS OF LIFE IN HEALTHY INFANTS WEIGHING UNDER 1500 GRAMS.
M. Abby Adams and Joseph F.Pasternak.
(Spon. by A.G.S. Philip). Northwestern University School of Medicine, Evanston Hospital, Dept. Pediatrics, Evanston, Ill.

Arterial pressure (AP) is a major determinant of cerebral blood flow (CBF) in newborn infants and thus may be critically involved in the pathogenesis of neonatal brain injury. We monitored AP continuously from birth to 5 days of age in 14 infants weighing less than 1500 grams who were free of pulmonary or neurologic disease. Mean AP (MAP) was recorded via an umbilical artery catheter with a pressure transducer and module interfaced with a microcomputer. Continuous recording was initiated during the first hour of life in 4 infants, the second in 6, and by the fifth in 4; 3600 MAP determinations were stored sequentially each hour and subjected to statistical analysis. MAP was found to correlate significantly with gestational age during each of the first 14 hours of postnatal life ($p<.05$). MAP increased as a function of postnatal age in the majority of infants. This increase was greatest (.31-.42 mmHg/Hour for the first 40 hours) for the least mature infants (27-29 weeks gestation). The increase for the most mature infants (31-32 weeks gestation) was low (0-.1 mmHg/hour) and in 3 infants a small negative slope (decrease) was seen. After 24 hours of age, MAP was similar in the least and most mature infants. Variability of MAP and periods of relative hypotension (2 S.D. below mean) and hypertension (2 S.D. above mean) were independent of gestational age.

The steep rise in MAP during the 1st 40 hours of life in the least mature infants may be due to the perfusion requirements of extrauterine life. These pressures may be at or near the threshold for rupture of immature vascular beds such as are found in the subependymal germinal matrix and thus predispose to intraventricular hemorrhage.

1171 A COMPUTER-ASSISTED PHYSIOLOGIC MONITOR FOR NEWBORNS: DESCRIPTION OF THE SYSTEM.
M. Abby Adams, Joseph F. Pasternak, Barry A. Kupfer.
(Spon. by A.G.S. Philip). Northwestern University School of Medicine, Evanston Hospital, Dept. Pediatrics, Evanston, Ill.

Transcutaneous O_2 (tcO_2) and CO_2 ($tcCO_2$), intracranial pressure (ICP) and arterial pressure (AP) are profoundly affected by clinical events in newborn infants (e.g, apnea, pneumothorax); they also play a significant role in the pathogenesis of certain pathological entities (e.g., intraventricular hemorrhage, perinatal hypoxic-ischemic brain injury) and in the determination of ultimate clinical outcome. Study of the relationship between these parameters, clinical events, and outcome has been hampered by the inefficiency of polygraphic techniques of data storage. We have developed a system of data storage which makes possible continuous, simultaneous recording of multiple physiologic parameters. Monitors which measure ICP, tcO_2, $tcCO_2$, and AP are interfaced with a microcomputer with appropriate voltage and analog-to-digital conversions. Data for each parameter is evaluated and stored sequentially once each second on soft discs. Pertinent clinical information can also be coded sequentially within the parameter storage files, thus enabling rapid evaluation of the effect of clinical events on each parameter. Large volumes of data (eg, 48 hours of continuous BP) can be analyzed within seconds yet moment to moment parameter fluctuations are preserved for recall. Examples of analysis of actual data will be presented which illustrate the flexibility and utility of the system. These will include: recall and display of segments of the original physiologic data in second-by-second detail; calculations of statistical parameters (e.g., mean, S.D.) for sequential segments of physiologic data; the relationship of clinical events (e.g., sleep state) on physiologic parameters; and the interrelationships of each parameter with the others.

1172 ASSESSMENT OF DUCTAL PATENCY BY FEMORAL FLOW VELOCITY DETERMINATION.
Dale C. Alverson, Marlowe W. Eldridge, Rochelle L. Burstein, Terrence Dillon, Steven M. Yabek, Marilyn Tomczyk, Sher B. Werner, Pam A. Angelus, William Berman, Jr. University of New Mexico School of Medicine, UNM Affiliated Hospitals, Dept. of Pediatrics, Albuquerque, N.M.

We used a 20 MHz, range gated, pulsed Doppler device to measure non-invasively femoral blood flow velocity patterns and calculate femoral flow (Q_f) in 28 preterm infants with patent ductus arteriosus (PDA). Corrected vessel diameter was determined by Doppler scanning; mean spatial wave forms were recorded by illumination of the entire flow stream. Peak flow velocity (p), mean flow velocity($\bar{v}$), the peak:mean velocity ratio (p/v) and flow (Q_f) were determined serially in each patient. Prior to PDA closure, p/v averaged 8.4 and Q_f 36 ml/min. After closure, mean p/v fell to 4.2 and mean Q_f rose to 74 ml/min. The femoral flow velocity pattern correlated with the estimated size of ductal shunting; large negative flow velocity vectors (high p/v ratios) were associated with large PDA shunts. Seven patients enrolled in an early PDA closure protocol (<48 hrs of life) were studied by a variety of methods to characterize hemodynamic status. Femoral flow velocity waveforms indicated ductal patency in 6 of 7 patients; the velocity pattern correlated with ductal patency and size, determined by contrast aortography. Contrast echocardiography suggested ductal shunts in 5 of 7 patients; LA/AO ratios were high in only 3 of 7 patients, the same number in which the ductus was apparent clinically. The non-invasive femoral Doppler approach detects patency of the ductus early in life and is as accurate as more invasive techniques.

1173 USEFULNESS OF CARDIAC OUTPUT DETERMINATION IN THE MANAGEMENT OF CRITICALLY ILL INFANTS.
Dale C. Alverson, Marlowe W. Eldridge, John D. Johnson, Marilyn Tomczyk, Sher B. Werner, William Berman, Jr. University of New Mexico School of Medicine, UNM Affiliated Hospitals, Department of Pediatrics, Albuquerque, New Mexico.

We measured cardiac output non-invasively with a pulsed Doppler device to help direct management and monitor the effects of clinical interventions on cardiac performance. Ascending aortic blood flow velocity (V) was measured with a 10 MHz transducer. Aortic diameter (d) was determined echocardiographically. Cross sectional area (A), calculated according to the equation $A=\pi d^2/4$, was used in conjunction with mean velocity ($\bar{V}$) to quantitate ascending aortic flow (Q_{Ao}), according to the equation: $Q=A\times\bar{V}$. Seven infants with patent ductus arteriosus (PDA) showed dramatic increases in Q_{Ao} as ductal shunting increased. At a mean age of 6 days, Q_{Ao} averaged 408 ml/kg/min when PDA symptoms emerged. Reduction in mean Q_{Ao} to 226 ml/kg/min was instantaneous after ductal closure. In 6 infants with persistent pulmonary hypertension, Q_{Ao} was used in conjunction with arterial and venous pressures to calculate systemic vascular resistance (SVR). The values of Q_{Ao} and SVR were used to monitor and adjust medical therapy with tolazoline and inotropic agents. Q_{Ao} was also used to titrate inotropic medication in infants with reduced myocardial performance. Lastly, serial Q_{Ao} measurements detected adverse hemodynamic consequences of pneumothorax in 3 of 7 patients studied. Cardiac output measurements quantifiy hemodynamic performance in a variety of settings and are useful for management & monitoring.

1174 PULSED DOPPLER DETERMINATION OF CARDIAC OUTPUT IN NEONATES AND CHILDREN.
Dale C. Alverson, Marlowe W. Eldridge, Steven M. Yabek, Terrence Dillon, Diane M. Rupas, L. Kathleen Bouma, and William Berman, Jr. University of New Mexico School of Medicine, UNM Affiliated Hospitals, Department of Pediatrics, Albuquerque, New Mexico.

Non-invasive measurement of aortic blood flow mean velocity ($\bar{V}$) was made in 33 children, ages 3 days to 17 years, by pulsed Doppler technique at the time of cardiac catheterization. Measurements were made from a suprasternal approach with nonfocused, variable width (0.6 to 8.0 mm), range gated devices of 3 or 10 MHz frequency. The sample volume, 4 mm in width, was varied in range to maximize the recorded signal. Two dimensional echocardiography was used to verify sample volume position in selected patients. An incidence angle of 0^o was assumed; the aortic diameter (d) was determined by M-mode echocardiography. Aortic flow (D_{Ao}) computed from Doppler recordings was calculated according to the equation: D_{Ao} (ml/min)=$\bar{V}$ (cm/sec) x $\pi d^2/4$ (cm^2) x 60 (sec/min). Values were compared with Fick determined systemic outputs (Q_{Ao}), calculated using measured oxygen consumption, oxygen capacity and oxygen saturations. Subjects with aortic valve abnormalities or left ventricular outflow tract obstruction were excluded from study. Agreement between the two methods was excellent (linear regression $r=0.98$, slope=1.14, $S_{y\cdot x}$=218 ml/min, range 403 to 5500 ml/min). The Doppler method is quick, non-invasive and accurate, especially in smaller patients.

1175 SERUM GAMMA GLUTAMYL TRANSPEPTIDASE (GGT) ACTIVITY IN PREMATURE INFANTS RECEIVING PROLONGED HYPERALIMENTATION.
Craig W. Anderson, Nita Seibel, and Leandro Cordero (Spon. by Grant Morrow, III) OSU College of Med., OSU Hospitals, Dept. of Pediatrics, Columbus, Ohio.

Liver dysfunction associated with prolonged hyperalimentation is seen frequently during the neonatal period. It has been postulated that increased GGT activity is a specific reflection of hepatic canalicular dysfunction. Two groups of premature infants were followed for up to four months with weekly GGTs determined by the assay of Szasz. Infants receiving anti-convulsants were excluded from this study. One group of eight premature infants (BW $\bar{x}$ 1310 $\pm$ 271 gms, $\bar{x}$ GA 32 weeks) received glucose infusions and breast milk and/or formula. From this group, the mean GGT level of 148 $\pm$ 100 IU/L (range 41-354 IU/L) was found to be more elevated than previously reported for premature infants. No significant correlation was found between GGT levels and age as determined by Pearson correlations and the Fisher Z transformation method. Nine other infants (BW 1083 $\pm$ 340 gms, GA 30 weeks) received hyperalimentation (glucose and amino acids) for variable periods with a range of 5-144 days and a $\bar{x}$ of 57 days. By the methods reported above, a significant correlation was found between duration of hyperalimentation and GGT levels ($r=+.59$). From these preliminary data, it appears that GGT levels may have clinical significance, that the range of normal levels for premature infants should be reevaluated, and that there is a positive correlation between GGT activity and duration of intravenous hyperalimentation.

1176 KALLIKREIN-LIKE PROTEASE IN PREMATURE INFANTS: INFLUENCE OF POSTNATAL AGE AND CLINICAL STATUS. Maureen Andrew* and Margaret Karpatkin. New York University Medical School, Department of Pediatrics, New York, NY.

We have demonstrated a kallikrein-like protease in unactivated plasma of premature infants that may be bound to α_2-macroglobulin (α_2-M) and is thus able to cleave small peptide substrates. This study reports the influence of postnatal age and clinical status on this protease activity. 55 premature infants (28-36 weeks gestation) were classified as healthy (IV fluid, antibiotics only) or sick (all other support) on days 1, 7 and 28 of life. Using the chromogenic substrate H-D-Phe-Pip-Arg-pNA healthy infants demonstrated increasing protease activity during the first month of life ($P<0.001$), (mean ± SEM, nmoles p-nitroanaline released/ml/min: day 1, 80 ± 18.4, day 7, 154 ± 18.8, day 28, 210 ± 20.0). Infants that were sick on days 1 and 7 did not demonstrate a postnatal rise in activity (day 1, 33 ± 6.4, vs day 7, 47 ± 8.3, $p=0.3$), however, infants that had been sick on day 1 but by day 7 were healthy had increasing protease activity (day 1, 24 ± 7.2 vs day 7, 117 ± 17.0, $P<0.001$). In addition, sick infants had significantly lower levels than healthy infants on all days studied ($P<0.001$). We conclude that there is increasing kallikrein-like activity in unactivated plasma of healthy premature infants during the first month of life. Sickness significantly lowers the activity and prevents the postnatal rise. We speculate that in sick infants either the protease is not generated to the same degree or is largely bound to plasma protease inhibitors other than α_2-M. These other inhibitors bind directly to the active site.

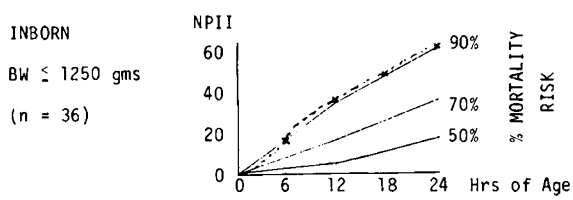
1177 PLASMA PROTEASE INHIBITORS IN PREMATURE INFANTS: INFLUENCE OF GESTATIONAL AGE AND POST-NATAL AGE. Maureen Andrew, Patricia M. Massicotte-Nolan and Margaret Karpatkin. McMaster University Health Sciences Centre, Department of Pediatrics, Hamilton, Ontario, and New York University Medical School, Department of Pediatrics, New York.

This study investigated the influence of gestational age (GA) and postnatal age on the following plasma protease inhibitors: α_2-macroglobulin (α_2-M), C_1-Esterase (C_1E-INH), anti-thrombin III (AT-III) and α_1-antitrypsin (α_1-AT). Premature infants (28-36 weeks gestation) were studied on days 1 (N=31), 7 (N=31) and 28 (N=11) of life. Inhibitors were measured by radial-immunodiffusion and expressed as a percent of normal pooled plasma (mean ± SEM). Infants with disseminated intravascular coagulation (DIC) (fibrinogen <120 mg/dl, or factor VIII: coag <50%, or fibrin related antigen >6.7 µg/ml) were not included. Between 28 and 36 weeks there was no significant correlation with GA for any of the four inhibitors. In contrast, regardless of GA, during the first week of life all four inhibitors increased significantly (α_2-M: 83 ± 6.0 vs 105 ± 6.0, $P<0.02$; C_1E-INH: 61 ± 2.7 vs 105 ± 4.4, $P<0.001$; AT-III: 52 ± 4.3 vs 90 ± 5.7, $P<0.001$; α_1-AT: 89 ± 6 vs 118 ± 5.5, $P<0.001$). At day 28, only α_2-M continued to increase (143 ± 14.3, $P<0.01$). Thus, at birth C_1E-INH and AT-III are low, while by day 7 all four plasma protease inhibitors are in the normal adult range (70-130%). Since premature infants have very low levels for most coagulation factors we speculate that there is an imbalance between the coagulation cascade and its inhibition. This may contribute to the increased risk for abnormal bleeding in premature infants.

1178 MORTALITY RISK GRAPHS FOR NEONATES WITH RESPIRATORY DISTRESS(RD) Alice F. Andrews, Robert H. Bartlett, Dietrich W. Roloff, (Spon. by Robert P. Kelch), Univ. of Michigan Hospitals, Depts. of Pediatrics and Surgery, Ann Arbor, Michigan

Mortality risk graphs for babies with RD can be constructed for any given population by using PROBIT analysis of Neonatal Pulmonary Insufficiency Index (NPII) scores. The NPII plots F_iO_2 and pH against time for the first 24 hours of life.

132 neonates with severe RD had NPIIs calculated and the scores evaluated by PROBIT. Four subgroups were statistically defined, based on being inborn or outborn and on birth weight. The example below shows the course of a single infant plotted (x) on the appropriate graph (inborn, ≤ 1250 gms birth weight).



Knowing an infant's mortality risk early aids in counseling parents. We propose to also use it in the selection of patients for currently unconventional support methods, e.g., extracorporeal membrane oxygenation, which was used for this infant.

1179 INCREASED PLASMA VITAMIN C LEVELS IN PREMATURE NEWBORNS WITH INTRAVENTRICULAR HEMORRHAGE (I.V.H) Ilan D. Arad and Fabian G. Eyal (Spons. by Gertrude Kohn). The Hebrew University Medical School, Hadassah University Hospital, Mt. Scopus, Pediatric Department, Jerusalem, Israel.

Vitamin C is accumulated in the brain by active transport mechanisms which establish a high brain-plasma gradient of the vitamin A damaging insult to the CNS may result in an efflux of ascorbate into the circulation with a consequent rise of plasma levels. We have determined vitamin C plasma levels by the 2,4-dinitrophenylhydrazine method in premature newborns on days 1, 3 and 5 of life while no supplemental vitamin was given. The infants underwent ultrasonographic examinations to detect PVH/IVH and were grouped according to the following findings: Group I - normal; Group II - periventricular hemorrhage ± minimal IVH; Group III - IVH ± ventricular dilatation ± intracerebral hemorrhage. Plasma levels of ascorbate (mean±SEM) expressed in mg% are presented below:

Group	n	Birth Wt (Kg)	Day 1	Day 3	Day 5
I	18	1.46±0.08	1.68±0.08	1.14±0.06	^.68+^.03
II	17	1.13±0.07	1.94±0.14	1.76±0.17	1.34±0.14
III	17	1.10±0.07	2.36±0.15	2.45±0.20	2.09±0.26

Plasma vitamin C levels were significantly higher in group III than in group I ($p<0.005$) and II ($p<0.025$) at all times and the levels in group II significantly higher than those of group I ($p<0.005$) on days 3 and 5. Regression analysis of plasma ascorbate and both birth Wt and gest. age showed no association to account for our results. The higher plasma ascorbate levels in newborns with IVH suggest an efflux of the vitamin into the circulation. Vitamin C determination may be useful for prediction of IVH.

1180 MOST "APNEA OF PREMATURITY" PROBABLY RESULTS FROM INTRAVENTRICULAR HEMORRHAGE. Henrietta S. Bada, Sheldon B. Korones and Charles W. Fitch (Spon by George A. Burghen), University of Tennessee, Department of Pediatrics, Memphis.

To determine the relationship between recurrent apnea of prematurity and intraventricular hemorrhage (IVH), prospective evaluation of 70 infants with birth weight of 1500 gm or less was carried out. Daily evaluation of each infant for a duration of one week included ultrasound head scan and clinical assessment for signs of IVH and recurrent apnea. Of these 70 infants, the 60 who lived longer than 48 hours, were studied for this report. Twenty-three (38%) developed apnea and 45 (75%) were diagnosed as having IVH. Mean age of onset of IVH, was 1.5 ± 0.5 days, and for apnea was 2.7 ± 1.6 days. In infants having both apnea and IVH, first apneic spell occurred on day of or after IVH in all but one patient. Data comparing infants with and without apnea are presented in the table.

	Apnea (n=23)	No Apnea (n=37)
Birth Weight (gm)	1137 ± 223	1198 ± 276
Gestational Age (weeks)	31 ± 2	31 ± 2
IVH: Incidence	21 (91%)	24 (65%)
Grade I-II	16/21 (76%)	9/24 (38%)
Grade III-IV	5/21 (24%)	15/24 (63%)
Other signs present	5/21 (24%)	15/24 (63%)

Compared to babies with no apnea, those with apnea had higher incidence of IVH ($p<.05$) but the hemorrhages were frequently less severe and clinically silent. We conclude that most "apnea of prematurity" probably results from IVH.

1181 INFLUENCE OF THE MODE OF DELIVERY ON THE OCCURRENCE OF INTRAVENTRICULAR HEMORRHAGE. Henrietta S. Bada, Sheldon B. Korones, Hubert L. Magill, and Garland D. Anderson (Spon. by John F. Griffith), University of Tennessee, Departments of Pediatrics, Radiology and OB-GYN, Memphis.

Seventy consecutive preterm infants with birth weight (BW) of 1500 gm or less were screened daily for intraventricular hemorrhage (IVH) during the first week of life using real time ultrasound scans. Mean BW and gestational age (GA) were 1133 ± 282 gm and 31 ± 2.2 weeks respectively. Mean Apgar Scores at 1 and 5 min were 4 ± 3 and 6 ± 3 respectively. Fifty-five (79%) infants developed IVH, and in 48 (87%), IVH was diagnosed within 24 hours of age. Forty-two (60%) infants were delivered vaginally and 28(40%) by C-section. The following table compares vaginally delivered and C-sectioned infants according to the mean BW, GA, Apgar Scores, the incidence of IVH, and mortality rate.

	Vaginal (n=42)	C-section (n=28)
BW (gm)	1137 ± 283	1126 ± 273
GA (weeks)	31 ± 2	31 ± 2
1 min. Apgar Scores	4 ± 2	4 ± 3
5 min. Apgar Scores	6 ± 2	6 ± 3
IVH: number (%)	32 (76%)	23 (82%)
Deaths: number (%)	12 (29%)	10 (36%)

Chi square analysis showed no statistical significant difference between the incidence of IVH and mortality rate in the vaginally delivered and C-sectioned infants. These data show that there appears to be no association between the incidence of IVH and mode of delivery.

1182 CORTICOID CONCENTRATION IN CORD SERUM AFTER PRENATAL TREATMENT WITH BETAMETHASONE OR HYDROCORTISONE. Philip L. Ballard and Graham C. Liggins. Dept. of Peds. and Cardiovas. Res. Instit., Univ. Calif., San Francisco, and Postgrad. School Obstet. Gynecol., Univ. Auckland, Auckland, N.Z.

Prenatal corticosteroid therapy is efficacious in preventing RDS, but optimal treatment conditions are not yet defined. We determined corticoid concentrations in cord serum of 75 premature (25-36 wk) infants whose mothers received 100 mg hydrocortisone (HC) q 8° prior to delivery, and compared results with previous data for Betamethasone (Beta) therapy (12 mg q 24° or 6 mg q 12°). Corticoids were assayed by competitive protein binding after petroleum ether washing, free corticoids were assessed by charcoal absorption, and dissociation of tritiated steroid from nuclei was studied after washing fetal rabbit lung in culture. Total corticoids were maximal 1-2 hr after HC (mean 32.1 µg/dl vs. 8.4 for 84 untreated infants) and levels declined with a $t_{\frac{1}{2}}$ ~2 hr vs. 12 hr for clearance of Beta. Endogenous corticoids were suppressed 8-20 hr after the last dose of HC (5.1 ± 0.4 µg/dl, mean ± SE), but less so than with Beta (3.3 ± 0.3 and 3.6 ± 0.5 for 12 and 6 mg regimens, respectively). Maximal serum levels of free glucocorticoid activity were 11.6 µg/dl with HC therapy, 8.3 µg/dl with 12 mg Beta, and 5.1 µg/dl with 6 mg Beta compared with 1.6 µg/dl in untreated infants. Dissociation $t_{\frac{1}{2}}$ values were 1.4 and 7.4 hr for HC and dexamethasone, respectively. We conclude that the 100 mg HC regimen results in higher unbound serum corticoid concentrations, greater fluctuations and faster clearance of steroid from serum and lung tissue, and less suppression of endogenous cortisol than treatment with Beta.

1183 FAMILY VISITATION ON THE NEWBORN INTENSIVE CARE UNIT - PSYCHOLOGICAL IMPLICATIONS ON THE SIBLINGS. Jeanne Ballard, Michael Maloney, Margaret Shank, Barbara Barnes, Vivian Gutterman, Lauren Hollister, Children's Hospital Medical Center, Cincinnati

A randomized study of 38 families was conducted to determine the psychological effects of visiting a sick newborn on an intensive care unit. Twenty-three families with 31 children were randomized to enter the newborn intensive care unit under controlled conditions. Touching the infant was permitted. Fifteen families with 26 children (ages 2 to 16) were assigned to a control group. Fifteen boys and 16 girls were in the study group and 13 boys and 13 girls were in the control group. The mean age was 8.7 yrs for boys and 6.7 for girls, and was similar for both groups. Assessment tools included: the Missouri Behavior Checklist (MBC) administered just before and two weeks following the visit; a Modified Vernon Questionnaire (MVQ), a Family Changes Questionnaire (FCQ) and a Child Psychiatry evaluation given two weeks after the visit. The number of behavioral problems (MBC) did not change for either group. Apparent improvement occurred for both child (MVQ) and family (FCQ) functioning in study and control groups. Parents perceived improvement in 74% of the study and 40% of control families ($p<.05$). By psychiatric evaluation none of the study children were upset by the visit; 72% enjoyed and 28% enjoyed and demonstrated benefit. In summary, family visitation had no detrimental effect by behavioral assessment; child and family functioning improved under the conditions of the study; the actual visit enhanced parental well being and was reported as a positive experience by all of the siblings.

1184 THYROID HORMONE CONCENTRATIONS IN CORD SERUM AFTER PRENATAL CORTICOSTEROID THERAPY. Philip L. Ballard, Kenneth A. Woeber, and Alan H. Klein. Dept. of Peds. and Cardiovas. Res. Inst., Univ. California, San Francisco, Dept. Med., Mt. Zion Hosp., San Francisco, and Dept. Peds. Harbor-UCLA Medical Center, Torrance, CA.

Both glucocorticoids and thyroid hormones enhance lung maturation in fetal animals. Corticosteroid treatment increases serum T_3 concentrations in fetal sheep, raising the possibility that glucocorticoids could affect lung development in part through thyroid hormones. We have determined by radioimmunoassay the concentration of T_3, T_4 and rT_3 in cord serum of premature (≤35 wk) infants exposed prenatally for 8-72 hr to either betamethasone (12 mg q 24 hr or 6 mg q 12 hr) or hydrocortisone (100 mg q 8 hr). Results as mean ± SE are shown:

	T_3 (ng/dl)	T_4 (µg/dl)	rT_3 (ng/dl)
Untreated	39.1 ± 4.2	6.1 ± 0.7	236 ± 35
	(5) NS	(7) NS	(10) NS
Treated	41.8 ± 3.4	6.4 ± 0.4	266 ± 28
	(12)	(27)	(10)

T_3 was below the sensitivity of the assay (15.2 ng/dl) in 11 of 23 (48%) infants delivering < 48 hr after corticosteroid treatment vs. 3 of 10 (30%) infants delivering 80-193 hr after treatment and 2 of 7 (29%) untreated infants.

We conclude that prenatal corticosteroid therapy does not affect concentrations of T_4 and rT_3 in cord serum of premature infants, and may transiently suppress T_3. These findings suggest that glucocorticoids do not act indirectly through thyroid hormones to influence lung maturation.

1185 EFFECT OF EXCHANGE TRANSFUSION (ET) ON RESERVE BILIRUBIN BINDING CAPACITY (RBBC). Raul C. Banagale, (Spon. by R.P. Kelch), Iowa Methodist Medical Center, Department of Pediatrics, Des Moines, Iowa.

The effect of double volume ET on the serum albumin (SA), total bilirubin (TB) and RBBC was studied in 7 premature infants. There was no Rh or ABO blood group incompatibility. None of the infants exhibited clinical or laboratory signs of hemolysis. Two of the infants required a second ET. One to two day old whole blood with citrate-phosphate-dextrose as anticoagulant was used. The gestational age (mean ± SE) was 29 ± 1.5 weeks and the birthweight was 1347 ± 365 grams. RBBC was measured by Sephadex G-25 adsorption. The Table shows the values for SA, TB, RBBC before ET, immediately after ET, and 12 hours after ET.

ALBUMIN (gm/dl)		TOTAL BILIRUBIN (mg/dl)		RBBC (mg/dl)		12 HR FOLLOW-UP STUDIES		
Pre* (n=9)	Post** (n=9)	Pre (n=9)	Post (n=9)	Pre (n=9)	Post (n=9)	ALBUMIN (n=4)	TOTAL BILIRUBIN (n=4)	RBBC (n=4)
3.0	3.2	12.9	7.6	10.6	16.9	3.2	10.1	10.6
p value	NS		0.005		0.005		NS	

* = pre-exchange ** = post-exchange

The effect of ET on RBBC appears to be a transient phenomenon. Until more data are available, the criteria for a repeat ET should be the same as for the initial one, as previously recommended (Pediatrics, 59:881, 1977).

1186 SERUM THYROXINE (T_4) CONCENTRATION IN FORMULA FED (FF) AND BREAST FED (BF) PREMATURE INFANTS (PI) FOLLOWING RECOVERY FROM ACUTE NEONATAL PROBLEMS (ANP). Raul C. Banagale, (Spon. by R.P. Kelch), Iowa Methodist Medical Center, Department of Pediatrics, Des Moines, Iowa.

This study was to determine the pattern of T_4 values of PI (n=143) who had recovered from ANP and determine if the T_4 of FF (n=104) differs from the BF (n=39) infants. ANP were: RDS (n=57) asphyxia (30), sepsis (36) and hyperbilirubinemia (20). The gestational age (GA) at birth ranged from 24-37 weeks with a mean ± SD of 33.3 ± 3.1 weeks. At the time (11-45 days postnatal) of test (T_4 RIA), the corrected GA was 38.8 ± 2.4 weeks.

TABLE 1 T_4 (µg/dl, mean ± SE) Values, Corrected GA and Weight

(grams)	29-31 wks	(n)	32-34 wks	(n)	> 34 wks	(n)
1000-1500	5.16 ± 2.42	(4)	6.82 ± 0.93	(20)	8.20 ± 1.05	(13)
1501-2000			7.22 ± 1.51	(6)	9.29 ± 0.73	(26)
2001-2500					10.46 ± 0.59	(48)
> 2500					11.76 ± 0.80	(26)

TABLE 2

	MALES T_4 (µg/dl)	(n)	FEMALES T_4 (µg/dl)	(n)	MEAN SE T_4 (µg/dl)	(n)
Breast fed	10.1 ± 0.6	(28)	9.6 ± 0.9	(11)	9.8 ± 0.8	(39)
Formula fed	9.6 ± 0.5	(52)	9.3 ± 0.5	(52)	9.5 ± 0.5	(104)
p value	NS		NS		NS	

Table 1 shows the increase in T_4 as the postnatal weight and age increase. TSH values of PI (16) with T_4 below 6.5 µg/dl was 4.7 ± 2.9 µU/ml. No case of hypothyroidism was identified during the study and none developed clinical or laboratory evidence of hypothyroidism within a 1 year follow-up. Table 2 shows that breast feeding does not significantly affect the T_4 values in PI.

1187 USE OF PERIPHERAL INTRAVENOUS CANNULAS IN PREMATURE INFANTS - A CONTROLLED STUDY. Daniel G. Batton, M. Jeffrey Maisels, Peter Appelbaum. Penn State Univ Coll of Med, M. S. Hershey Med Ctr, Depts of Pediatrics and Pathology, Hershey, PA.

A randomized, controlled study was done to determine whether a 25-gauge steel needle or a 24-gauge teflon catheter was preferable for the administration of peripheral intravenous fluids and medications to premature infants. Thirty-four infants received a total of 58 cannulas: 28 steel needles and 30 catheters. The needles remained in place for 15.4±13.2 hrs (mean±SD) and the teflon catheters for 49.5±30.9 hrs (mean±SD). All of the steel needles had to be removed because of infiltration whereas only 17/30 (57%) of the catheters infiltrated. A local inflammatory reaction occurred with 11/30 (37%) of the teflon catheters but was not related to infection. Following removal, Staphylococcus epidermidis was grown from the culture of 1/19 steel needles and 1/25 catheters. In both instances blood cultures were negative and this was felt to be a contaminant. Teflon catheters remain functional three times longer than steel needles with no apparent increase in complications. The use of these catheters, therefore, appears to be the preferred method for administering intravenous fluids to premature infants.

1188 SERIAL RED BLOOD CELL(RBC) ANTIOXIDANT ENZYME LEVELS IN PREMATURE AND EXCHANGE TRANSFUSED INFANTS. Charles R. Bauer, Lee Frank, Aquannette White, Rosalyn Feller, M. Jayne Brennan and Shahid Sultan. (Spon. by E. Bancalari). University of Miami, School of Medicine, Departments of Pediatrics and Medicine, and V.A. Hospital, Miami, Florida.

Increased lung superoxide dismutase(SOD) and glutathione peroxidase(GP) activity during hyperoxic exposure has been shown to be associated with tolerance to pulmonary oxygen(O_2) toxicity in newborn animals of several species. Antioxidant enzyme RBC levels were monitored prospectively, as a reflection of lung changes, in 44 newborns requiring O_2 therapy and/or exchange transfusion, to determine if changes in SOD or GP could be related to the clinical course of these infants.

Clinical Grouping		(n)	Serial SOD Levels*	Serial GP Levels*
Severe	RDS	(13)	7- ↑ 4- ↓ 2- NC	8- ↑ 4- ↓ 1- NC
Mild-Mod	RDS	(13)	6- ↑ 0- ↓ 7- NC	8- ↑ 1- ↓ 4- NC
No	RDS	(8)	2- ↑ 2- ↓ 4- NC	4- ↑ 3- ↓ 1- NC
Exchange	Trans.	(10)	8- ↑ 2- ↓ 0- NC	9- ↑ 1- ↓ 0- NC

(* sampling began after birth thru 7 days. Infants with at least three samples were included. Enzyme values are expressed as Units of activity per gram of hemaglobin. ↑= increasing values with time, ↓= decreasing, NC=no change). These data indicate a trend for increasing blood enzyme values in infants with RDS. The six infants with RDS who died showed ↓ or NC in their serial SOD enzyme levels while no infants with RDS died if their SOD levels ↑. Additionally 8 to 10 infants with exchange transfusions had immediate post-transfusion values of SOD and G.P. that were significantly greater than the pre-transfusion values. This could not be explained by the enzyme levels contained in the donor blood alone.

1189 NECROTIZING ENTEROCOLITIS(NEC)- A SIX YEAR EXPERIENCE: MORTALITY AND MORBIDITY FROM MEDICAL AND SURGICAL MANAGEMENT. Charles R. Bauer, Ronald N. Goldberg and Michael B. Marchildon. (Spon. by E. Bancalari) Univ. of Miami, Sch of Medicine, Depts. of Pediatrics and Surgery, Miami, Fl.

One Hundred and Fourty cases of NEC have been diagnosed between 1975 and 1981 in this center. Sixty-Eight infants(49%) required only medical management. The mortality in this group was 24 percent(16 infants). Of the surviving 52 infants, follow-up evaluations ranging from 6 months to 5 years performed in 26 infants(50%) indicate that 73% are growing normally and 77% have normal develop mental exams. In marked contrast to these medically managed infants are the 51 percent who required surgical intervention. Ten of these infants required surgery late for strictures that developed after their initial medical management. One infant died during surgery, 57% had abnormal development exams and 43% had abnormal growth patterns. In the 62 infants undergoing immediate surgical interventions, there was a 69% mortality rate, almost triple that of the infants not requiring surgery. Of the 19 infants who survived, 12(63%) were seen in follow up between six months and five years. Sixty-Six percent of these infants have significantly retarded growth patterns and 66% are developmentally delayed for their age. This dismal outcome of infants requiring surgical intervention for NEC is in marked contrast to previously published reports. NEC is a frequent and often catastrophic event in critically ill infants who usually have already survived the initial insults of their acute disease. Prevention is manditory, as current therapy does not seem to offer an acceptable outcome in many of these infants.

1190 PEAK INFLATION PRESSURE VS. POSITIVE END EXPIRATORY PRESSURE IN PNEUMOPERICARDIUM WITH RDS. Stephen Baumgart, David J. Cohen, Frances Borian, Larry W. Stephenson. (Spon. by W.W.Fox). Univ. of Pa. Sch. of Med., Depts. of Peds. & Surg. Children's Hospital of Philadelphia, Phila. PA.

Pneumopericardium is the most critically acute complication in premature infants mechanically ventilated for RDS. Mortality is reported at 57%. Intermittent mandatory ventilation (IMV) with positive end expiratory pressure (PEEP) and peak inflation pressure (PIP) have been implicated in the pathogenesis of pneumopericardium. To investigate the significance of PEEP vs. PIP in pneumopericardium, 13 premature neonates (BW 1.25-2.90 kg, GA 29-38 wks) developing pneumopericardium while receiving mechanical ventilation for RDS were reviewed. Respiratory support (IMV, PEEP, PIP, FiO_2) and severity of disease (pH, $PaCO_2$, and PaO_2/FiO_2 ratio) were analyzed. Mean values for each parameter were calculated for 15 eight hour periods prior to the onset of pneumopericardium. The time from starting infants on IMV to the occurrence of pneumopericardium ranged 4 hrs to 13 days (mean 6.4 days). Ten infants developed pneumopericardium by 48 hrs. At the time of pneumopericardium, all infants had high PIP (mean 42, range 26-60 torr). Mean PIP increased significantly from 30 ± 10 S.D. torr 16 hr before pneumopericardium to 42 ± 8 torr just prior to the onset of pneumopericardium ($p < .05$). In contrast, mean PEEP was moderate at 3.1, range 2.1-5.7 torr (3-8 cm H_2O). Mean IMV was 60, range 15-120 cycles/min and mean FiO_2 was 90, range 60-100% at time of onset of pneumopericardium. There were no significant changes in PEEP, IMV, FiO_2, pH, $PaCO_2$, or PaO_2/FiO_2 ratio prior to onset of pneumopericardium. These data suggest an acute increase in PIP is the major parameter associated with pneumopericardium. There was no significant increase in PEEP.

1191 ATTENUATION OF WARMING AND COOLING CYCLES BY SHIELDING THERMISTOR PROBES IN INFANTS UNDER RADIANT WARMERS. Stephen Baumgart, Jeffrey Lavanier, Jacob G. Schwartz, Susan B. Hall. (Spon. by W.W. Fox). Univ. of Pa. Sch. of Med., Dept. of Peds., Children's Hosital of Philadelphia, Philadelphia, PA.

Infants nursed under servocontrolled radiant warmers are monitored continuously for skin temperature by an electronic thermistor taped to the abdomen. Skin temperature feeds back to the servocontrol mechanism which determines the radiant power density delivered to the infant. Characteristically, the radiant warmer cycles through warming and cooling phases. Shielding temperature probes with a small square of foam rubber covered by reflective foil is recommended to prevent artifactual heating of the thermistor by the radiant warmer during the warming phase. To determine the effect of thermistor shielding on infant heat demand, 10 premature neonates (birthweight 1.70 ± .12 SEM kg, gestational age 32.6 ± .7 wks) were studied to measure mean radiant power density for one hour with and one hour without probe shielding. Data were also analyzed to determine the average duration of warming and cooling cycles under the warmer. There was a significant increase in cycle duration with shielding (1.76 ± .15 min/cycle vs. 3.06 ± .39 min/cycle, $p < .02$). Shielding had no effect on mean radiant power density received by infants (15.6 ± 1.0 mw/cm^2 vs. 15.9 ± 1.2 mw/cm^2 shielded, $p > .5$). Shielding had no effect on skin temperature, heart and respiratory rates, or ambient temperature and humidity. These data demonstrate that shielding probes produces lower frequency cycling for infants under radiant warmers without changing radiant power density received at the infant's skin. The effect of attenuated warming and cooling cycles on peripheral vascular stability and oxygen consumption remains to be determined.

1192 GLUCONEOGENESIS IN HYPOGLYCEMIC NEWBORN INFANTS GIVEN NASOGASTRIC ALANINE. Alice G. Beard, Abdul Darki, Mark Boughter, Becky J. Williams (Spon. by Donald E.Hill). Dept. of Ped. University of Ark for Medical Sciences. Little Rock, AR.

Previous studies of intravenously and orally administered alanine to normoglycemic small and large for gestational age newborns have not resulted in increased gluconeogenesis. This study was done to evaluate the effect of alanine loading in the presence of hypoglycemia in the first hours of life. Twelve infants 1-3 hours of age (mean weight:3280 grams; 37 weeks gestational age with apgar scores of 7-10) who maintained initial blood glucose values of less than 38 mg/dl for 30 minutes were given 500 mg of L-alanine/kg as a 10% solution in .45% sodium chloride by nasogastric tube. Venous samples were taken pre-gavage and at 30,60 and 180 minutes thereafter for serum glucose, insulin, alanine and glucagon determinations with the following results:

TIME (min)	ALANINE (μmoles/L)	GLUCOSE (mg/dl)	INSULIN (μU/ml)	GLUCAGON (pg/ml)
0	305± 30	25.6±2.6	18.1±8.4	104.9±21.5
+30	1400±210	34.6±4.6*	22.2±8.6	136.2±22.1*
+60	2930±300	50.6±3.6**	26.7±7.7	175.7±32.5*
+180	2270±360	52.5±3.1**	23.6±7.2	156.7±22.0*

(All values ± SEM) Paired T-Test *p=<.05 **p=<.001

Mean glucose concentrations rose 98 and 105% at 60 and 180 minutes post loading while insulin values also rose. This coupled with a significant glucagon response suggests active gluconeogenesis in the presence of hypoglycemia.

1193 NOCTURNAL CARDIORESPIROGRAPHY: AN NICU DISCHARGE TOOL Ed J. Beaumont, Dietrich W. Roloff (Spon. by W. F. Howatt), Univ. of Michigan Hospitals, Department of Pediatrics, Ann Arbor, Michigan

Because of the increased risk of premature infants for infantile apnea and sudden infant death syndrome, we selected 11 of 38 infants ready for discharge for 12 hour nocturnal cardiorespirogram recordings. Birthweights were under 2000 g and gestational ages 34 weeks or less. They had completed a course of theophylline for apnea and/or had intraventricular hemorrhage, or neurologic abnormalities. 10 of 11 recordings were abnormal: excessive (>3.5%) periodic breathing (PB), apnea (>15 sec), or bradycardia (<80 bpm). After reinstitution of theophylline treatment (mean level 9.07; range 7.25-12.13 mcg/ml) the repeat recordings of 9 infants were normal; one required phenobarbital for normalization.

N = 10	Before	On Treatment
PB (% of record)	8.14% (0.72-18.0%)	0.44% (0-1.07%)
Apnea (events/12h)	2.71 (0-4)	0
Bradycardia (events/12h)	5 (0-12)	0

These abnormal studies were recorded in infants ready for discharge by our usual criteria including postmenstrual age of at least 37 weeks and the absence of apnea/bradycardia by conventional monitoring for 2 weeks. We conclude that routine heart rate and respiratory monitoring does not accurately identify premature infants at risk for infantile apnea. Cardiorespirograms should be added to the pre-discharge screening procedures in neonatal intensive care units.

1194 TRANSCUTANEOUS PO2 VARIABILITY:A PROGNOSTIC INDICATOR. Mary P. Bedard and Alfonso Pantoja (spon.by Ronald L. Poland), Wayne State University, Children's Hospital of Michigan, Department of Pediatrics, Detroit.

Transcutaneous pO2 (tc) monitoring has shown pO2 is continually fluctuating both spontaneously and in response to noise and handling. We retrospectively evaluated tc tracings of 122 newborns. Tracings were assigned to 1 of 3 groups. Group I showed good variability (N=88). Group II had no minute to minute fluctuations with preservation of long term changes or periods of normal and no variability (N=23). Group III had no variability (N=11). As can be seen, Group III infants were larger and older.

	I	II	III
Birthweight	1.8±0.1*	1.9±0.2	2.5±0.3*
Gestational Age	32.9±0.4*	33.4±0.8	36.1±1.4*

*p<.02

Congenital heart disease (p<.03 III vs I,II) and sepsis (p<.03 III vs I) were more common in group III and pulmonary hypertension and coagulopathy in group II (p<.01 II vs III). There were no differences in the incidence of asphyxia, CNS hemorrhage or PDA. Dopamine and isuprel were used more often in group II (p<.03 III vs I, II). Pavulon was used more often in group II (p<.03 II vs III). There was no difference in the use of tolazoline. The mortality of group III was 73% compared to 43% for group II and 22% for group I (p<.001 III vs I; p<.05 II vs I). Abnormalities in variability probably reflect poor peripheral circulation.

We suggest that evaluation of tc tracings for variability may provide information concerning the adequacy of the peripheral circulation and may be of prognostic value.

1195 SUBEPENDYMAL/INTRAVENTRICULAR HEMORRHAGE (SEH/IVH) IN PRETERM INFANTS WITHOUT NEONATAL DISEASE. Raul Bejar, T. Allen Merritt, Ronald W. Coen, Kao-Tai Tsai, Louis Gluck, University of Calif., San Diego, Dept. of Pediatrics, La Jolla, Calif.

To determine factors contributing to SEH/IVH, confounding variables related to neonatal disease were eliminated by analysis of 44 of 246 infants (<34 wks/2000gm) selected by Apgars ≥6 at 5 minutes, normal fetal pH, <15 hr intermittent mandatory ventilation (IMV), and no PDA. SEH/IVH was diagnosed by frequent tri-dimensional ultrasound within the first hours of life. Major (8) (ventricular enlargement and/or cerebral bleeding; $\bar{x}$ time DX=10 hr life); & minor (16) (SEH/IVH without ventricular enlargement; $\bar{x}$ time Dx 7 hr) hemorrhages were found in asymptomatic infants. None extended SEH/IVH after diagnosis. Stepwise logistic regression analysis of BW, GA, SGA, inborn, sex, maternal steroids, route of delivery, tocolysis, ROM, presentation, forceps, fetal cord pH, Apgars 1' & 5', resuscitation, mature lung profile, need for IMV, F_IO_2 need >.3, & apnea & bradycardia, lowest pH & Pa_{O_2}, highest Pa_{CO_2}, & volume expansion before diagnosis of SEH/IVH was made. Vaginal delivery, male, lowest Pa_{O_2} & BW were discriminant variables in the order of power differentiating SEH/IVH & no SEH/IVH groups. Infants born vaginally (28) & by C-section infants (16) were similar for all variables. Vaginally delivered infants had a higher incidence of total & major SEH/IVH than C-section infants (no major IVH/SEH). Follow-up (6-24 months) reveals only 2/16 infants with major neurologic deficit. The factors identified here for SEH/IVH represent the risks of prematurity alone for SEH/IVH and its consequences during development.

1196 HYPOXANTHINE CONCENTRATION IN CEREBROSPINAL FLUID (CSF) OF INFANTS WITH POSTHEMORRHAGIC HYDROCEPHALUS. Raul F. Bejar, Ola D. Saugstad, Hector James, Louis Gluck. Univ. of Calif., San Diego, Dept. of Pediatrics, La Jolla, Calif.

Hydrocephalus is a frequent complication of large intraventricular hemorrhages. Hypoxanthine, the end product of purine metabolism, which is elevated during brain ischemia indicating significant compromise of cell integrity, was measured in 13 hydrocephalic tiny infants (12 posthemorrhagic, 1 congenital hydrocephalus) to determine whether hydrocephalus is associated with anaerobic metabolism of brain tissue. Intraventricular hemorrhages & progressive ventricular size were diagnosed with repeated ultrasound studies of the infants' brains. Hypoxanthine concentrations in CSF (normal 0-3μm/L) increased significantly ($\bar{x}$=14.8μm/L, range 7.5-28μm/L) in progressive hydrocephalus, with or without overt signs of intracranial hypertension. Normal values or significant decrease in hypoxanthine were obtained when hydrocephalus was successfully treated or ventricular size was transiently stabilized by LP's or VP shunts. Actual ventricular size seemed not to correlate with hypoxanthine concentration although each case tended to have high concentrations when there was progressive ventricular enlargement. Patients with posthemorrhagic hydrocephalus in the first month of life had similar high concentrations ($\bar{x}$=14.5μm/L) as patients with "late" (age 1 or > mos) posthemorrhagic or with congenital hydrocephalus suggesting that anaerobic metabolism is mainly a consequence of ventricular enlargement.

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1197 PLEXIGLAS HEAD HOOD DOES NOT SIGNIFICANTLY ALTER BODY HEAT LOSS OF PREMATURE INFANTS IN INCUBATORS. Edward F. Bell and Gladys R. Rios (spon. by Allen Erenberg). Univ. of Iowa, Dept. of Pediatrics, Iowa City, Iowa.

Plexiglas head hoods (PGH) are often used to administer supplementary oxygen or to measure respiratory gas exchange of infants. Since Plexiglas is impermeable to heat energy radiated from the body, we theorized that PGH might reduce radiant heat loss (R) from the head and, thus, possibly reduce body heat loss (HL). We measured metabolic heat production (M) and HL of 6 AGA premature infants (BW 1.44-1.89 kg, age 7-16 d) in an incubator with PGH (top replaced with 0.013-mm polyethylene, Glad Wrap^R) and with a head hood (PEH) of polyethylene stretched over a rectangular frame made of thin tubular steel. Each infant was studied with PGH and PEH on the same day, with skin temperature servocontrolled to 36.5°C. After thermal equilibration, oxygen consumption ($\dot{V}O_2$), carbon dioxide production ($\dot{V}CO_2$), and insensible water loss (IWL) were measured continuously for 2 hours with each hood. M and HL were calculated and partitioned into evaporation (E), radiation (R), and the sum (C) of convection and conduction. The means are shown below, $\dot{V}O_2$ and $\dot{V}CO_2$ in ml/(kg·min), IWL in ml/(kg·h), and M, HL, E, R and C in kcal/(kg·h):

	$\dot{V}O_2$	$\dot{V}CO_2$	IWL	M	HL	E	R	C
PGH	7.90	7.45	1.18	2.36	2.40	0.68	0.98	0.74
PEH	8.61	8.01	1.36	2.56	2.61	0.79	1.08	0.74

None of these was significantly different, including total (HL) and radiant (R) heat loss. However, the estimated radiant loss from the head was lower with the PGH (17.9 vs 26.4 W/m^2, P<0.05).

1198 EARLY INFANTILE BRONCHOSPASM IN THE POST-RDS BABY - HEREDITARY INFLUENCE OR INITIAL MANAGEMENT? Judy Bernbaum, Frances Borian, Alan R.Spitzer. (Spon. by W.W. Fox). Univ. of Pa. Sch. of Med and Dept. of Peds., Children's Hospital of Philadelphia, Philadelphia, PA.

Premature infants treated for respiratory distress syndrome (RDS) may develop reversible bronchospasm during the first year of life. It is unclear whether this airway hyperreactivity is related to initial management or to hereditary factors. Twenty-one premature infants, mechanically ventilated for RDS, followed for bronchospasm beginning before 6 months of age, were matched with 21 similar infants with no bronchospasm during the first year of life. No significant differences existed between infants with bronchospasm (B) and their matched controls (C) for (mean ± SEM): birth wt. (1.15 ± .06 vs. 1.13 ± .09 kg); GA (30 ± 0.5 vs. 29 ± 0.4 wks); duration of oxygen exposure (35.6 ± 6.5 vs. 39.6 ± 6.4 days); and duration of ventilatory assistance (455 ± 108 vs. 451 ± 98 hrs). 13/21 B babies and 14/21 C babies had radiologic evidence of BPD. Family history of bronchospasm was considered positive if first or second degree relatives had asthma prior to age 20 requiring hospital treatment and bronchodilators. 14/21 (67%) infants with bronchospasm vs. 3/21 (14.3%) control infants had positive family histories (p <.001). Patients requiring continuous bronchodilator therapy for symptom control (n=15) were compared to those needing only intermittent therapy for acute exacerbations (n=6). 9/15 (60%) requiring continuous therapy had first degree relatives with positive histories vs. 1/6 (17%) in the intermittent therapy group (p <.02). Thus, a strong family history of bronchospasm may be a predisposing factor in the development of airway hyperreactivity in premature infants requiring ventilatory therapy for RDS. The closer the affected relative, the greater the tendency for the bronchospasm to be of a more severe nature.

●1199 INCREASED OXYGENATION WITH NONNUTRITIVE SUCKING DURING GAVAGE FEEDINGS IN PREMATURE INFANTS. Judy Bernbaum, Gilberto Pereira, George Peckham. Univ. of Pa. Sch. of Med., Dept. of Peds., Children's Hospital of Philadelphia, Philadelphia, PA.

Oxygenation decreases after nasogastric (NG) feeding but increases during nonnutritive sucking (NNS/pacifier) in premature infants recovering from RDS. To evaluate changes in oxygenation during NG feedings given with a pacifier, we studied 15 clinically stable premature infants (mean ± SEM birth wt. 1.2 ± 0.3 kg and GA 31.0 ± 1.5 wk) who were given a pacifier during and for 10 min. after an NG feed (NNS). The same infants were studied within 24 hrs. during an NG feed without a pacifier (control). Studies were done during transition from NG to oral feeds when the sucking reflex was well-developed. Transcutaneous O_2 ($TcPO_2$) was monitored prior to, during and for 30 min. after each NG feeding. Pre-feeding $TcPO_2$ levels were comparable in both studies (58 ± 3.0 vs. 59 ± 2.9 mmHg, (N.S.)). $TcPO_2$ values during NNS rose significantly to 64.7 ± 3.0 mmHg (p< 0.001) by the end of the feeding, remained elevated for 20 min. and returned to baseline levels by 25 min. after feeding. Conversely, $TcPO_2$ measurements in control studies fell to 57.2 ± 2.8 mmHg (p< 0.01) immediately after feeding, continued to fall for 20 min. (52.2 ± 3.0 mmHg, p < 0.001) and gradually returned to baseline levels by 30 min. Significant differences in $TcPO_2$ values between the 2 study periods were noted immediately after feeding and for 20 min thereafter (p< 0.1). Conclusion: Our study suggests that NNS during NG feedings prevents the decrease in oxygenation found after routine gavage feedings in premature infants. The improved $TcPO_2$ values while sucking might represent a physiologic response that is important to meet the increased caloric demands associated with feedings.

1200 EARLY NEUROLOGIC ABNORMALITIES IN PRETERM INFANTS: AN INDICATOR OF DEVELOPMENTAL PROGRESS. Judy Bernbaum, Linda Spungen, Frances Borian, Anne Farran. (Spon. by D. Cornfeld). Univ. of Pa. Sch. of Med., and Dept. of Peds., Children's Hospital of Philadelphia, Phila., PA.

Neurologic abnormalities occur commonly in low birthweight (LBW) premature infants during the first year of life, but often are transient. Developmental problems may be identified by the age at which abnormalities of muscle tone, reflex activity, and posture normalize. To determine the relationship between the age of normalization and developmental sequelae, we studied 21 infants with birthweight (mean ± SD) 1.25 ± 1.89 kg and gestational age 31 ± 1.5 wks. Infants were evaluated for neurologic abnormalities at 3,6,9 and 12 mos adjusted age (AA). Development was assessed at 12 mos AA using the Bayley Scales of Infant Development. Neurologic exam revealed that infants were either 1) normal at 3 mos; 2) normalized by 6 mos; 3) normalized by 12 mos; or 4) abnormal at 12 mos. Bayley scores varied in accord with these different ages of neurologic normalization. Mean scores were: Groups 1 and 2 (n=8) = 93.4 ± 5.8 (normal range); Groups 3 and 4 (n=13)=70.5 ± 11.2 (borderline to abnormal range), p <.001. Our study demonstrated a clear relationship between age of neurologic normalization and developmental progress. Early absence or resolution of abnormalities suggested favorable development at 12 mos. Persistence of abnormalities to 12 mos or beyond was related to either borderline or abnormal functioning. Conclusion: Although neurologic abnormalities are common in LBW preterm infants, they are not merely a transient phenomenon without significance. Regular neurologic assessment during the 1st year of life may be used to distinguish, as early as 3-6 mos, those infants with promising development vs. those at risk for developmental sequelae.

1201 ABSORPTION OF ORALLY ADMINISTERED GENTAMICIN IN PRETERM INFANTS by Abdul M. Bhat, Robert G. Meny, Chigozie N. Ogbu, Epifania A. Aranas; Hurley Medical Center, Division of Neonatology, Flint, Michigan 48502.

16 preterm infants were given gentamicin (2.5 mg/kg/dose q 6 hours) orally as a prophylaxis against necrotizing enterocolitis (NEC). None of these infants received systemic gentamicin. Infants with NEC or NEC like symptoms were excluded from the study. Their weight and gestational age was 1.39 ± 0.37 kg and 30.6 ± 2.7 weeks respectively. Their mean apgar score was 5 and 8 at one and five minutes respectively. All infants had respiratory distress syndrome and 12 out of 16 needed artificial ventilation. 12 infants had umbilical arterial catheters inserted. 9 out of 16 infants had serum gentamicin levels done at mean postnatal age of 1.7 days. 1 of those 9 infants had no detectible gentamicin level. The serum gentamicin level of the remaining 8 infants varied from 1.2 to 7 µgm/ml with mean of 2.5 µgm/ml. Serum gentamicin level on other 7 infants was done at a mean postnatal age of 12 days. No gentamicin could be detected in the serum from 3 infants. The serum gentamicin levels on the remaining 4 infants was less than 2 µgm/ml. We suggest that orally administered gentamicin can be absorbed in preterm infants especially during the first few days of life. Infants on simultaneous oral and systemic gentamicin may be at a greater risk of toxicity.

1202 URINARY EXCRETION OF BIOGENIC AMINE METABOLITES IN APNEA OF PREMATURITY by Abdul M. Bhat, John W. Scanlon, Bennett Lavenstein, L. Chuang, Farouk Karoum; Georgetown University Hospital, Department of Pediatrics, Washington, D.C. 20007.

12 hour urinary excretion of VMA, HVA and MHPG were studied in 24 premature infants, 14 with apnea and 10 without apnea. Their birth weight and gestational age was 0.95 ± 0.21 kg, 27.9 ± 2.2 weeks and 1.22 ± 0.19 kg, 30.3 ± 1.8 weeks respectively. All infants were studied before apnea (1-3 days of postnatal age). Non-apneic infants were also studied at 10-15 days. Apneic infants were studied again 24 hours after apnea. The concentration of various biogenic amine metabolites expressed as µgm/kg body weight (BW) and ugm/mg of creatinine (C) are given in the table (Mean±SE

Metabolites		Non-Apneic Infants		Apneic Infants	
		1-3 days	10-15 days	Before Apnea	After Apnea
VMA	µgm/mg C	7.3±1.6	14.5±4.9	8.5± 0.88	10.7±2.4
	µgm/kg BW	32.9±7.1	52.9±15.8	38.1±7.4	35.9±6.5
HVA	µgm/mg C	14.7±1.7	20.0±3.5	20.8±2.9	16.5±2.9
	µgm/kg BW	69.2±10.4	74.9±9.6	79.8±6.4	54.5±6.6
MHPG	ugm/mg C	37.3±4.6	57.8±16.1	49.3±20.7	33.1±6.9
	µgm/kg BW	173.1±24.9	216.6±50.0	176.6±44.0	117.0±25.5

The excretion of VMA and MHPG did not significantly decrease with the onset of apnea. Only HVA when expressed as µgm/kg body weight was significantly lower in apneic infants. We conclude that apnea of prematurity is not associated with inhibition or immaturity of adrenergic pathways.

1203 IN VITRO COMPARISON OF VARIOUS MILK & CA.PREPARATIONS (PREPS)AFFECTING OSMOLARITY(OSM)IN NEONATAL USAGE. Madhu Bhogal,Yucel Atakent,Mathilda Klupsteen,Angelo Ferrara.NYU/Bellevue Med.Ctr.Dept.Peds.NYC.

Sick newborns(NB)often receive Ca.c̄ oral feeds for hypocalcemia.The Ca.preps.are given as 75mg.ele.Ca/K/day QID.OSM by these drugs has not been studied comparatively.3 preps.of Ca.mixed in 3 types of milk in 4 different dilutions were used to measure 36Δ indiv.OSM(done by the freezing-point method).Each OSM was done 2X to detect any coeff.of variations exceeding 5%(Those 5%were re-measured).The ANOVA was used to detect mean OSM diff.RESULTS(1)s̄ Ca.milk(A)*had lower OSM compared to(B)&(C).(2)CaGluc.in the same milk dilutions produced a signif.lower OSM(esp.in small vol.dilutions)compared to the other Ca-milk mixture(P<.05),(3)All Ca.in more concentrated forms(5ml)produced a signif.higher OSM compared to all Ca.in larger vol.(more dilute).(4)Ca/P ratio of 4:1 didn't differ in OSM compared to high vol.dilution(120ml)(5)To avoid hyper-OSM loads it's best to(a)use Ca.in high vol.dilution(120ml) or 4:1(b)use CaGl.in smaller vol.which delivers lower OSM(c)&/or give same amt.more frequently.TABLE I:MEAN OSM(m.osm/L)BY MILK,BY CA.PREPS***& BY DILUTION FOR SICK NB.(Glubinate=Gb.;Gluconate=Gc)
**Signif.diff.in OSM among 4 dilut.F^3_{19}=28, P<.01 (ΔFor 1.8Kg.NB)

	PM60/40*(A)			Prem.Enf.24*(B)			Similac 20*(C)		
MILK	$CaCl_2$	CaGc.	CaGb.	$CaCl_2$	CaGc.	CaGb.	$CaCl_2$	CaGc.	CaGb.
**In 5cc.	590	370	672	608	327	685	599	326	679
**In 10cc.	446	307	535	459	318	534	464	326	526
**In 120cc.	291	284	301	307	303	317	316	307	326
**c̄ C/P 4/1	298	281	318	346	318	358	354	315	394

***Same Ca.prep.(all dilutions)didn't differ signif.in OSM in milk (B)&(C).But.OSM (B)&(C) differed from (A) P<.01.

1204 SARALASIN INFUSION TESTS FOR EVALUATING HYPERTENSION IN INFANCY. Ellen M. Bifano, Ernest M. Post, Alan D. Bedrick, David H.P. Streeten and Robert A. Richman. SUNY Upstate Medical Center, Departments of Pediatrics and Medicine, Syracuse, New York.

Saralasin, an angiotensin II antagonist, has been used extensively to evaluate hypertension in adults. We measured the blood pressure (BP, mmHg) response to an infusion of saralasin in four hypertensive infants to determine its safety and efficacy in that age group. Prior to each infusion, we performed a renal scan and measured basal plasma renin activity (PRA, ng/ml/hr). Means of 6 BP measurements are shown:

Patient	Age	PRA	BP:Basal	Saralasin	Diagnosis
A.	10 days	35	134/74	97/60	Renal Art Thromb
B.	14 days	>50	151/116	78/60	Renal Ischemia
C.	7 days	8.5	112/76	100/67	? Renal Ischemia
D.	3 months	0.2	125/73	112/52	Hyperaldosteronism

The patients with high PRA levels (A and B) had marked decreases in BP during the infusion, while those with normal (C) or low (D) PRA had little or no response. The saralasin infusion was continued for two days in patient B, who had malignant hypertension unresponsive to conventional antihypertensive therapy, including nitroprusside. Patient D had normal findings on aortogram, renal angiogram, and renal vein PRA measurements, but a high plasma aldosterone level (36.7 ng/dl).

We have demonstrated that the change in BP during an infusion of saralasin can rapidly and safely determine the contribution of the renin-angiotensin system to hypertension in infants and aid in the selection of appropriate antihypertensive therapy.

●**1205** NEONATAL HYPERVISCOSITY: RANDOMIZED STUDY OF PARTIAL PLASMA EXCHANGE IN ALTERING LONG-TERM OUTCOME. V. Black, L.O. Lubchenco, B.L.Koops, R.L.Poland. University of Colorado Health Sciences Center, Wayne State University, Hutzel Hospital, Denver Children's Hospital, Departments of Pediatrics, Detroit.

Ninety-four patients with polycythemia and hyperviscosity (HV) were assigned randomly to partial plasma exchange (Exch) or observation (NExch) and were matched with a non-polycythemic control. No group differed in socioeconomic class, apgar scores, resuscitation, meconium staining, weight or gestational age. Maternal pre-eclampsia was more common in HV patients (p<0.02). HV patients more commonly had necrotizing enterocolitis (NEC) and cyanosis (p<0.005) and required more IV's (p<0.001).

Comparison of hyperviscous Exch and NExch groups revealed that maternal pre-eclampsia was more common among the Exch group (p<0.05) as was maternal smoking (p<0.01). Brazelton exams evaluated showed no differences at the time of diagnosis. Following Exch, GI symptoms were more frequent among Exch compared to NExch patients (p<0.02) as was NEC (p<0.001).

At one year HV patients did not differ from controls in mental or motor scores. Abnormal neurologic exams were more common among HV patients (p<0.05) and speech was more likely to be delayed (p<0.02). At two years HV patients had more motor delays and neurologic diagnoses (p<0.001). Comparison of the HV patients (Exch vs NExch) revealed no differences at one year. At two years abnormal neurologic exams were more common among NExch patients (p<0.01).HV patients had more problems at follow up than controls. Exch seems to increase NEC but reduce neurologic problems.

● 1206 LUNG FLUID BALANCE DURING VIBRATORY VENTILATION IN LAMBS.

Richard D. Bland, J. Usha Raj, Thomas A. Hazinski, Gunnar E. Sedin, and Robert B. Goldberg. Cardiovasc Res Inst, Dept Pediatr, Univ California, San Francisco

In 1942 Warren and Drinker reported that breathing movements have an important influence on filtration of fluid into the lungs (Am J Physiol 136:207). What happens when normal breathing movements stop, as they do during high-frequency vibratory ventilation? To answer that question, we measured pulmonary arterial (PA) and left atrial (LA) pressures, pleural (PL) and airway (AW) pressures, lung blood flow and lymph flow, and concentrations of protein in lymph and plasma of 7 healthy lambs, 2-3 wks old, during a 2-4 h period of spontaneous breathing (SB), followed by 4-8 h of mechanical ventilation (MV) at 30 breaths/min and 4-8 h of vibratory ventilation (VV), in which the lambs received 1500 whiffs of air/min from an Emerson Airway Vibrator. The lambs were unmedicated during SB, but received pancuronium and morphine during MV and VV. We alternated the sequence of MV and VV. Results (X ± SD):

	MEAN PRESSURES (torr)				BLOOD FLOW	LYMPH FLOW	LYMPH:PLASMA
	PA	LA	PL	AW	(l/min)	(ml/h)	PROTEIN RATIO
SB	18 ± 2	3 ± 1	-2 ± 1	0	2.0 ± .4	2.2 ± .6	.61 ± .05
MV	22 ± 2	7 ± 1	0 ± 1	7 ± 1	1.9 ± .4	2.1 ± .6	.58 ± .04
VV	27 ± 4	8 ± 2	1 ± 2	8 ± 4	1.7 ± .4	1.7 ± .7	.63 ± .06

Lymph flow was less and lymph:plasma protein ratio greater in VV than in MV, consistent with reduced lung fluid filtration during VV. In lambs killed after 8 h of VV, extravascular lung water was normal and microscopy showed no edema. We conclude that VV has no adverse effect on lung fluid balance and may provide a benefit to lambs by decreasing net filtration of fluid into their lungs.

1207 THE ROLE OF RED CELL TRANSFUSION IN THE PREMATURE INFANT.

John Blank, Thomas G. Sheagren, Jayshree Vajaria, Henry H. Mangurten, Raghbir Benawra and Bhagya L. Puppala (Spon. by Celia Kaye), Lutheran General Hospital, Department of Pediatrics, Park Ridge, Illinois.

In order to access the value of "booster transfusion" in the premature infant, a randomized trial was performed. Infants less than 1500 gms. at birth were randomized to be transfused to keep their hemoglobin level above 10.0 g/dl. or they were allowed to drop their hemoglobin. There were 56 infants enrolled on the study: 26 in the transfusion group and 30 in the non-transfused group. Analysis at the end of the study shows that the groups were well-matched for gestational age (mean 29.6 wks.) and birth weight (mean 1160 gms.). All children were transfused to replace iatrogenic blood loss, and in clinical states associated with acute blood loss or shock. Exchange transfusion was performed as necessary for the management of jaundice. In the non-transfused group, patients could also be transfused if required for surgery, if no weight gain for seven days on 140 cal/kg/day, or tachycardia greater than 170 BPM consistently for four days. Statistical analysis of the clinical course of these patients shows no difference between groups in terms of length of stay in the hospital, discharge weight, incidence or severity of apnea. There was a difference at the P <.001 level between groups in the discharge hemoglobin level and reticulocyte count. The non-transfused infants also had increased weight gain/day significant at the P <.05 level. This unexpected finding was not due to a difference in the incidence of clinical PDA. Our conclusion is that there is no clinical advantage to maintaining the hemoglobin above 10.0 g/dl in the pre-term infant.

1208 DOPPLER ULTRASONOGRAPHY DURING LIGATION OF THE PATENT DUCTUS ARTERIOSUS (PDA).

Carl J. Bodenstein, William J. Daily, St. Joseph's Hospital and Medical Center, Department of Pediatrics, Phoenix.

Continuous anterior cerebral artery doppler ultrasonography was performed during PDA ligation in seven neonates to assess changes in cerebral blood flow (CBF). Mean gestational age was 32 wks. (range 28-35), mean birth weight 1470 gms. (range 822-2240). Ages at ligation were 2-32 days. Pre and postligation pulsatile index (PI) and systemic blood pressure (BP) values are presented below.

Pre and Postligation PI, BP (torr): Range (mean)

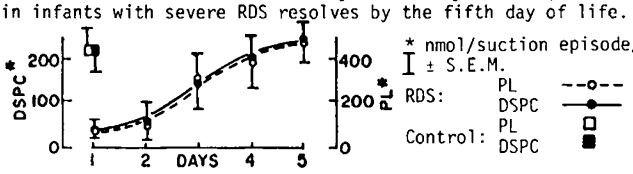
	PI	systolic BP	diastolic BP	mean BP
pre	.80-1.0 (.94)	54-85 (73)	27-51 (40)	45-64 (55)
post	.55-.86 (.74)	76-96 (87)	54-73 (60)	66-75 (71)
Δ	-.09--.45 (-.20)	0-28 (14)	7-33 (20)	7-25 (16)

Systemic BP increased and PI decreased in all cases. These data are consistent with universal but variable increase in CBF. The largest change was seen in the most immature patient. Postoperative cranial ultrasonography documented one new, and extension of one previous, intraventricular hemorrhage (IVH). These data suggest that PDA ligation is associated with increase in systemic BP and CBF values. The magnitude of CBF increase may be related to the degree of BP elevation relative to cerebral autoregulatory competence. When the limits of cerebral vascular integrity are exceeded IVH may result.

1209 POSTNATAL RECOVERY OF TRACHEAL EFFLUENT PHOSPHOLIPIDS IN SEVERE RESPIRATORY DISTRESS SYNDROME (RDS).

Carl L. Bose and Brian Wood, (Spon. by Lowell Glasgow). University of Utah School of Medicine, Salt Lake City, Utah.

During the first 5 days of life, the phospholipid content of tracheal effluent from 12 infants (28-35 GA) with severe RDS was measured to identify specific deficiencies and to determine their rate of recovery. On each infant's daily pooled specimen, total phospholipid (PL) and disaturated phosphatidylcholine (DSPC) were quantified and the presence of phosphatidyglycerol (PG) determined. Values in the RDS group were compared to measurements on specimens collected during the first day of life from 7 control infants (27-36 GA) being ventilated for apnea or transient tachypnea. Compared to controls, infants with RDS had less PL and DSPC on Day 1 (p<.01). A gradual increase in both PL and DSPC began on Day 3 and reached values similar to controls after Day 4. No change in %DSPC in the RDS group was observed; %DSPC in RDS and control groups was similar. PG was always absent in the RDS group on Day 1 but appeared coincident with the rise in DSPC and PL. PG was a variable finding in controls. We conclude that the early deficiency of DSPC, PG, and PL in infants with severe RDS resolves by the fifth day of life.



●1210 AMPICILLIN PROPHYLAXIS OF GROUP B STREPTOCOCCAL TRANSMISSION IN HIGH-RISK PARTURIENT WOMEN.

Kenneth M. Boyer, Cecile A. Gadzala, Peggy C. Kelly, Samuel P.Gotoff. Univ. of Chicago, Pritzker Sch. of Med., Michael Reese Hosp., Dept. of Pediatrics, Chicago.

Most cases of GBS early-onset sepsis appear to have an intrapartum pathogenesis. Attack rates are increased in infants born to women with premature labor or prolonged rupture of membranes. We have carried out a randomized study of the effect of intrapartum parenteral ampicillin (2 gm IV, followed by 1 gm IV Q4H) on GBS vertical transmission in infants born to high-risk parturient women with prenatal GBS colonization. Cultures of throat, umbilicus, rectum, external ear, gastric contents, and blood were obtained from study infants in the delivery room at birth.

No. of surface cultures positive	No. of infants: Ampicillin	Controls	X^2	p
0 sites	69	82		
1-2 sites	1	17	27.49	<.001
≥ 3 sites	1	29 ****		

A dramatic reduction in GBS vertical transmission occurred in infants born to high-risk mothers who were treated with ampicillin. Blood cultures were positive (*) in 4 heavily colonized infants whose mothers were not treated with ampicillin; no blood cultures were positive among infants whose mothers were treated (p = .17). Intrapartum ampicillin treatment of mothers with perinatal risk factors and prenatal GBS colonization significantly reduces GBS vertical transmission.

1211 GLOMERULAR AND TUBULAR FUNCTION AFTER MODERATE PERINATAL ASPHYXIA (A).

Luc Brion, A. Pardou. Clinique E. Cavell, Hospital Erasme, Free University of Bruxelles.

To confirm Aperia's (1981) suggestion that asphyxia was more damaging to tubular than to glomerular function, we studied 50 A during the 1st 2 days of life:

Birthweight	Gest. Age	Apgar(1')	Apgar(5')	Base Excess(1h)	pH(1h)
2.68±0.71kg	36.9±3.3wk	4.0±2.3	6.7±2.4	-14.5±5.7mEq/l	7.14±.12

Hematuria(gross in 3, micro in 6)was noted in 18%, proteinuria in 36%(100mg/dl in 28%, 100-200mg/dl in 8%). Fraction of excretion of Na was<2.5% except in1patient in renal failure. Fraction of excretion of phosphate was 20% except in 1 patient. Arginine vasopressine urine concentration test was normal in 17/17(514±95mosm/kg). Urine output >3ml/ g.h & <.4 were present in 4 & 6 patients respectively. BUN was 25mg/dl in 3/10 oliguric A, only 1 had renal failure. Creatinine clearance(Ccl)was similar in A & controls(C), but 10 values were <.4ml/kg.min in A & none in C.

	Ccl Day 1	Ccl Day 2	ml/kg.min
A	.51 ± .17	.75 ± .45	
C	.87 ± .49	1.11 ± .66	

The usual negative correlation between Ccl & serum B_2 microglobulin (B_2M) was found in C ($r = -0.78$, $p < .001$) but not in A. FEB_2M was normal in 5/5.

We conclude that oliguria, hematuria, proteinuria & decreased Ccl are common in A. In contrast to previous studies in perinatal asphyxia, we showed relatively good tubular electrolyte & water handling.

1212 AMNIOTIC FLUID VOLUME AND FETAL SWALLOWING RATE. Y. Brans, T. Kuehl, R. Hayashi, D. Shannon and P. Reyes. Univ. of Texas Health Science Center, Perinatal Research Laboratory, Departments of Pediatrics and of Obstetrics and Gynecology, and Southwest Foundation for Research and Education, San Antonio.

Extreme similarities in the anatomy and physiology of the feto-placento-uterine units in baboons and humans make the baboon an ideal model to investigate aspects of reproductive physiology. In order to obtain baseline data on normal baboon pregnancies, amniotic fluid volume (AFV) was determined by para-amino-hippurate (PAH) dilution in 39 pregnancies ranging from 88 to 173 days in duration. Amniotic fluid volume averaged 257±(SD) 71.1 ml (range: 126-392ml) and did not vary with gestational maturity. Fetal swallowing rate (FSR) was determined in 6 pregnancies at 138-149 days in animals whose PAH-determined AFV's ranged from 178 to 309 ml. Inulin dilution was used, AF samples being obtained prior to injection and approximately 4, 8 and 24 hours later. The Ln of AF inulin concentrations decreased as a straight line whose slope multiplied by PAH-determined AFV yielded FSR's that averaged 18.8±5.37 ml/hour (12.3-25.8ml/h). These data suggest (1) that AFV of baboons is similar to that of humans, considering the differences in body weight for mother and fetus (1/3 of human); and (2) that mean FSR in 138 day baboon fetuses is similar to that reported in term human fetuses.

1213 URINE OUTPUT AND SODIUM EXCRETION AFTER MODERATE PERINATAL ASPHYXIA (A). Luc Brion, Anne Pardou, Clinique E. Cavell, Hospital Erasme, Free University of Bruxelles. Sponsored by Dr. Paul Swyer.

In order to study water & sodium homeostasis after A, 50 (32 term & 18 preterm) newborns were investigated during the first 2 days of life: (Mean ± ISD):

	I=Intake ml/kg.d	O=Urine ml/kg.d	O/I %	Na Intake mEq/kg.d	Na Excreted mEq/kg.d	GFR ml/kg.m
Day 1	59.5±12.3	11.8±11.8	26±26	2.98±3.94	.35±.40	.51±.17
Day 2	71.6± 5.8	41.3±27.4	60±45	.13±.70	.67±.55	.75±.45

	Cw=Free Water Clearance ml/kg.min	Cosm=Osmolar Clearance ml/kg.min	FENa=Fraction of Excretion of Na %	FEK=Fraction of Excretion of K %
Day 1	.0014±.0040	.0143±.0096	.64 ± .44	24.7±11.7
Day 2	.0066±.1112	.0178±.0±67	.71 ± .84	18.0±17.4

Negative Cw was present in 9/26 patients. On Day 2, O was <.4ml/kg.h in 6 &>3ml/kg.h in 4 patients. Changes in O/I were related to Cosm($r=.52$, $p<.01$) & to CNa ($r=+.60$, $p<.001$) but not to CW, FEK & GFR. No osmotic diuresis was seen. Urinary Na/K ratio was<1 in 25/40 patients. A negative correlation was seen between FENa & GFR ($r=-.38$, $p<.05$). Serum Na was normal.

Usually tubular water & Na reabsorption is not impaired after A in the absence of renal failure. Low values of CW are probably related to ADH hypersecretion. The absence of hyponatremia seems related to fluid restriction. O/I variation could be dependent on the degree of stimulation of prostaglandins & renin system (Weissman, 1981).

1214 SYSTOLIC BLOOD PRESSURE (BP) AND GLOMERULAR FILTRATION RATE IN MODERATELY ASPHYXIATED NEWBORNS (A): EVOLUTION DURING THE FIRST 48 HOURS. Luc Brion, Anne Pardou, Clinique E. Cavell, Hospital Erasme, Free University of Bruxelles. Sponsored by Dr. Paul R. Swyer.

Neonatal asphyxia has been associated with an increased BP during the first hours of life (DIMICH, 1974). Gentamycin tI/2 is related to mean blood pressure in asphyxiated prematures (FRIEDMAN, 1981). We studied 50 A (Apgar 4.0 ± 2.3 at 1' & 6.7 ± 2.4 at 5'). Shock (S: BP> 2SD below mean, BE > -10mEq/l & oliguria) was present in 3 prematures (PT) & 8 term (T)infants.

In appropriate for GA controls (C), BP was related to B.Wt.($r=.43$, $p<.01$) but not in A. In PT, BP was higher in A than in C at the end of the first day:

	GA(wk)	BP h.0-6(mmHg)	BP h.6-12	BP h 12-24	BP h 24-48
T:A:S:	39 ± 1*	50 ± 14	48 ± 12	52 ± 9	61 ± 4
No S:	39 ± 1	61 ± 7	71 ± 8	71 ± 7	75 ± 8
C:	39 ± 1	65 ± 7	72 ± 13	69 ± 6	75 ± 6
PT:A:S:	32 ± 4	50 ± 14	48 ± 12	52 ± 9	61 ± 4
No S:	33 ± 1	61 ± 13	69 ± 10	81 ± 10 (I)	72 ± 9
C:	33 ± 3	59 ± 8	63 ± 9	62 ± 8 (I)	68 ± 5

(I): ≠($p<.05$) *mean ± ISD

No relation was found between BP, Apgar scores, pH at 1 h. of age & GFR in A.

Most of our patients were moderately asphyxiated only: this may explain the differences in the evolution of BP and its relation to GFR from previously reported studies in asphyxiated newborns.

1215 ELECTRONIC MONITORING OF JAUNDICE: BETTER AND QUICKER THAN THE EYE. Audrey K. Brown, Mae Hee Kim, Praewpun Nuchpuckdee, Gloria Valentia, Yi Zheng, SUNY-Downstate Medical Center, Dept. of Pediatrics, Brooklyn, N.Y.

Previously, we and others have reported that non-invasive electronic measurement of cutaneous bilirubin is useful in screening for significant bilirubinemia in neonates who are not receiving phototherapy. In a study involving 146 infants we found that any infant whose electronic jaundice meter (EJM)* index was ≤12 had a serum bilirubin level ≤4mg/dl; any infant whose EJM index was ≥19 had a bilirubin ≥6mg/dl. Further, all infants whose serum bilirubin was ≥10mg/dl had an EJM index ≥19. Such EJM indices could be used to determine the necessity for performing a serum bilirubin. To determine whether the EJM detected degrees of jaundice unperceived by regular nursery personnel (who were unaware that such a comparison was being made), EJM indices and serum bilirubins were performed and compared with records of initial visual detection of jaundice in 119 infants during the first 96 hours of life. In 21/119 infants, jaundice had not been detected visually despite serum bilirubin ranging from 6 to 14mg/dl. All had EJM readings >13. 15 of these 21 infants had EJM readings >17. Almost half of the infants (10/21) whose jaundice had not been detected visually had bilirubin values >8.5mg/dl. One Black infant whose jaundice had not been perceived visually at a serum bilirubin of 14mg/dl, had a very high EJM index of 27.

The EJM represents a non-invasive objective means of identifying infants who need or may be exempt from serum bilirubin determinations.

*Air-Shields

1216 ASSESSMENT OF PULMONARY FUNCTION AND RESPONSES TO THERAPY BY A REBREATHING TECHNIQUE. DS Brudno, GB Avery, FM Galioto. Childrens Hospital National Medical Center, Washington, D.C. A new technique to assess the pulmonary status of critically ill neonates employs a low dead space (2cc) valve interfaced into the ventilator circuit allowing rebreathing and non-rebreathing modes. Parameters measured are effective pulmonary blood flow (QEP, L/min), lung tissue fluid (Vt, cc), diffusion (DL, cc/cm/min) and functional residual capacity (FRC, cc.) The test gases are 10% Helium, 0.5% Acetylene, 0.3% Carbon Monoxide balanced with Oxygen and Nitrogen. The concentrations of the gases are measured by a mass spectrometer and analyzed by a microcomputer. This has been used in 16 neonates with HMD, PFC, chronic lung disease and a variety of cardiovascular diseases. A neonate, mechanically ventilated for PFC, was tested with various modes of therapy: hyperventilation, tubocurarine, leg wraps and tolazoline (2mg/kg bolus.)

	QEP	Vt	DL	FRC
pretreatment.....	.632	6.20	.052	20.30
hyperventilation.....	.692	6.03	.051	24.60
tubocurarine & leg wraps.....	.721	8.73	.057	24.82
tolazoline.....	.850	8.16	.058	26.07
predicted..... Indexed>	3.000	14.61	--	45.23

Improvements in QEP resulted from hyperventilation (+9%) or with tubocurarine (+4%) but more favorably with tolazoline (+18%.) Vt increased with leg wraps (+14%), used to reduce the hypotensive effects of the medications, suggesting a tendency to develop an increase in interstitial lung water and/or pulmonary edema. FRC improved with hyperventilation (+19%.) This rebreathing technique is sensitive in assessing pulmonary dysfunction and therapy.

1217 THE EFFECT OF POSITIVE END EXPIRATORY PRESSURE (PEEP) ON FUNCTIONAL RESIDUAL CAPACITY (FRC) IN NEONATES WITH RESPIRATORY DISTRESS SYNDROME (RDS) AND PNEUMONIA (PN). Richard L. Bucciarelli, Carl L. Bose, Peter Richardson (Spon. by Lowell Glasgow). University of Utah College of Medicine, Dept. of Peds. Salt Lake City, Utah.

The effect of PEEP on the FRC of 14 ventilated neonates (10 RDS and 4 Pn) was evaluated. A total of 48 FRC determinations were made. Initial measurements were made at the clinically prescribed level of PEEP. PEEP was then varied by 2cmH_2O over the range of 2 to 8cmH_2O. Infants with clinically severe RDS (Gr I) showed a markedly reduced initial FRC; whereas, infants with mild to moderate RDS (II) had an FRC at the lower limits of normal. In infants with Pn, FRC was initially at the upper limits of normal (TABLE). As PEEP was changed, the ΔFRC/2cmH_2O PEEP changed by a significantly greater margin if initial FRC were low-normal or slightly elevated. These data indicate that changes in PEEP in infants with RDS will effect lung volumes more if FRC is within normal ranges and will have little effect at low lung volumes. Infants with Pn have significantly greater lung volumes than infants with RDS and show the greatest change in volume for a given change in PEEP.

TABLE

Gr (N)	BW(gm)	FRC(cc/kg)	ΔFRC/2cmH_2O
I (4)	1615±285	7.16±4.83*	.6*
II (6)	1475±518	20.50±6.27*	2.0*
III(4)	1628±528	29.20±8.30*	7.5*

*$p < 0.005$ between all groups. All values = Mean ± S.D.

1218 NEONATAL MORBIDITY IN LEVEL III NURSERIES: ROLE OF THE REFERRING HOSPITAL? L. Joseph Butterfield, Lula O. Lubchenco, Beverly L. Koops, Virginia D. Black, Edward Goldson, Catherine Manchester, Departments of Perinatology and Pediatrics, Denver Children's Hospital and University of Colorado Health Sciences Center, Denver.

When Level III nurseries accept outborn infants, their neonatal mortality, morbidity and long-term outcome could depend on practices at the birth hospital. The study presented herein shows a wide variation in neonatal morbidity associated with the hospital of birth.

All births in 5 metropolitan Denver hospitals (MDH) which had Level I nurseries and regularly transported high-risk infants to Denver Children's Hospital (DCH) were compared with infants born at University Hospital (UH). During the 4-year period 1/1/75 to 12/31/78, 297 infants with birth weights <1500 grams were born in the 5 MDH and 393 in UH.

The fetal death rate in MDH was 26%, twice that of UH, 12% ($p<.001$). The fetal death rate varied from 21-43% among the 5 hospitals.

Hyaline membrane disease (HMD) ranged from 32 to 70% among the 5 hospitals ($p<.01$). The overall was 52% compared with 56% in UH (p=NS).

Patent ductus arteriosus (PDA) varied between 11 and 42% ($p<.005$). The hospital with the highest incidence of HMD and PDA also had the highest incidence of chronic lung disease.

Morbidity data can identify hospitals at risk which are not recognized through mortality figures alone.

1219 INFLUENCE OF HYPOXEMIA ON THE METABOLIC RATE OF PREMATURE INFANTS. Luis A. Cabal, Felipe Gonzalez, Abel Chaves, Toke T. Hoppenbrouwers, Enrique I. Cardenas, Bijan Siassi, Manuel Durand and Joan E. Hodgman. Univ. of So. Calif. School of Med., LAC-USC Med. Ctr., Dept. of Ped., Los Angeles.

Moderate hypoxia has been considered responsible for reducing the metabolic rate. This effect has not been explored in premature infants in relationship to their dependency on external heat sources. We evaluated the influence of inhalation of 4% CO_2 + 40% O_2 and 4% CO_2 + 16% O_2 gas mixtures given during ventilatory response studies, on the metabolic rate (MR) of 9 preterm infants. All infants had appropriate body weight (mean ± SD: 1641 ± 279 gms) for gestational age (31.5 ± 1.9 wks) and were studied during active sleep while on a radiant heat warmer servocontrolled at 36.5°C skin temperature. MR was measured by indirect calorimetry and PO_2 by a transcutaneous sensor. During the studies, 4 infants produced heat (HP) and 5 were dependent on external heat sources (HD). MR increased in HP infants while receiving both 4% CO_2 + 40% O_2 and 4% CO_2 + 16% O_2; whereas HD infants had a significant decrease ($P < 0.001$) in MR while breathing 4% CO_2 + 16% O_2, accompanied by significantly lower transcutaneous PO_2 levels (mean ± SD: 68.8 ± 11.6 mm Hg). These data suggest that: 1) Moderate hypoxemia blunts the metabolic rate of preterm infants who are dependent on external heat sources; 2) Moderate hypoxemia does not decrease the metabolic rate in infants who are heat-producing and 3) The relationship of heat dependency and oxygenation should be considered in the evaluation of energy metabolism.

1220 BEHAVIOURAL STATE IN LOW-BIRTH-WEIGHT INFANTS: ASSOCIATIONS WITH AGE, WEIGHT AND THE USE OF THEOPHYLLINE. Dugal Campbell, Robin K. Whyte, Susan Shannon, Henry S. Bayley and John C. Sinclair. McMaster University, Departments of Psychiatry and Pediatrics, Hamilton, Ont., Canada.

An investigation of the energy balance in healthy growing low-birth-weight infants called for observation of behavioural "states" to estimate the energy costs of each state. Each child was seen for 10 two-hour watches at intervals during a fortnight. Observers assessed state every minute using the criteria of Prechtl; the observations were compared with a continuous physiograph record of eye movements, activity, respiration and heart rate. Overall the infants passed 18% of the watches in quiet sleep, 21% in indeterminate sleep, 49% in REM sleep, and 12% awake. There were significant changes in the distribution of states due to gestational age and weight: the proportion of time passed in quiet sleep increased and the amount of time passed in indeterminate sleep fell, from 29 weeks to 37 weeks; and from .8 to 1.8 kg. weight. This pattern of states was seen in infants fed both formula and human milk, in SGA infants, and in infants with patent ductus arteriosus. Infants given theophylline for apnea had their waking time reduced (from 14% to 5%) and the REM time augmented (from 47% to 56%). These results show that the distribution of states varies systematically with normal development; alterations in the state pattern are associated with recurrent apnea treated with theophylline.

1221 ORIGIN AND IMPORTANCE OF TRACHEAL POLYMORPHONUCLEAR LEUKOCYTES IN NEONATES. Katherine M. Chance, Jay M. Milstein, Michael P. Sherman, and Boyd W. Goetzman, Univ. of CA School of Medicine, Dept. of Pediatrics, Davis.

We obtained tracheal aspirates (TA) during the first eight hours of life from male infants with respiratory distress and other risk factors for fetal infection. We determined if the tracheal polymorphonuclear leukocytes (PMNs) were of fetal or maternal origin using quinacrine fluorescence. We tested for an association between the presence of fetal cells to positive TA or blood cultures, neutropenia, and increased immature/total neutrophil (I/T) ratios. Eleven of 15 newborns had predominantly male PMNs (57±9% fluorescent cells) while four babies had fewer male PMNs (29±4% fluorescent cells), $p<0.001$. PMNs from normal adult males and females had 55-65% and 13-15% fluorescence, respectively. Gastric aspirates were obtained in eight babies. Seven had predominantly female PMNs and one an intermediate number. Seven TA were culture positive consisting of four babies with congenital pneumonia and three colonized infants. Two infants with congenital pneumonia had positive blood cultures. These infants had normal leukocyte counts, increased I/T ratios, but low numbers of PMNs on their TA which may have placed them at risk for dissemination. Eight TA were culture negative including four with large numbers of fetal cells. The presence of fetal cells in TA were not associated with positive TA or blood cultures, neutropenia, or increased I/T ratios. TA PMNs were predominantly fetal. The presence of these cells was not specific for bacteremia or congenital pneumonia, and in certain infants, may be indicative of non-bacterial inflammation.

1222 PULMONARY MECHANICS IN EXPERIMENTAL MECONIUM ASPIRATION. Chun T. Chen, Thomas Toung, and Mark C. Rogers. Dept. of Anesthesiology/Critical Care Medicine, Johns Hopkins Medical Institutions, Baltimore, MD

To evaluate the effect of meconium on the pulmonary surfactant, the pulmonary mechanics of a total of thirty-six (36) excised, separated canine pulmonary lobes were studied. Meconia were blended in normal saline to produce a solution of 10% and 20%. They were either filtered or centrifuged and then instilled endobronchially into the canine lobes. The Quasi-Static pressure-volume deflation curve of each lobe was determined before and 4 hours after instillation of either normal saline or meconium solutions. The results showed that in the saline controlled group (8 lobes), the curve was essentially unchanged before and after instillation of saline. In the 10% filtered meconium solution group (14 lobes), the curve was markedly depressed especially at the transpulmonary airway pressure of 10 ($p<0.06$) and 5 cm H_2O ($p<0.005$). In the 10% centrifuged meconium solution group (6 lobes) the result was similar. In the 20% filtered meconium solution group (8 lobes), the lobes exhibited similar but not significantly greater depression of the pressure-volume curve than that of 10% solution groups. It is concluded that meconium contains an agent or agents that can inhibit the pulmonary surfactant.

1223 CUTANEOUS BILIRUBINOMETRY DURING PHOTOTHERAPY (P). Raul F. Cifuentes, Andre J. Nelson, James Levine, and Rolf R. Engel. University of Minnesota, Hennepin County Medical Center, Department of Pediatrics, Minneapolis.

Increased tanning and decreased bilirubin in skin exposed to P compromises cutaneous bilirubinometry. To circumvent this, an opaque patch was placed over the mid sternum throughout the period of P on 19 infants with GA 32.6 ± 3.4 weeks and BW 1.7 ± 0.6 kg ($\bar{x}$ ± 1 SD). When serum was sampled for bilirubin determinations, a Minolta cutaneous bilirubin meter was applied to the area under the patch and to the adjacent exposed skin to obtain a mean value for five consecutive readings at each site.

By one hour after starting P, the readings from exposed skin decreased by 14% and in two hours by 21% ($p< .001$). In contrast, both bilirubinometry readings of the skin under the patch and serum bilirubin levels did not change significantly during the initial two hours of P.

The table presents correlations between serum bilirubin levels and Minolta meter readings before and during P.

Combination	P	Opaque patch	n	Regression line: Intercept	Slope	r
A	-	+	19	10.4	1.51	0.88
B	+	+	107	10.2	1.47	0.87
C	-	-	19	9.8	1.54	0.86
D	+	-	107	8.8	1.05*	0.75

*$p< 0.01$ for D vs B

In conclusion, an opaque patch improves the predictability of cutaneous bilirubinometry in infants receiving phototherapy.

1224 THE INACCURACY OF APGAR SCORING. David A. Clark, David O. Hakanson and Ellen M. Bifano, Dept. of Pediatrics, SUNY, Upstate Medical Center, Syracuse, New York (Spon. by M. L. Williams).

The Apgar score is frequently assigned hurriedly, casually or retrospectively. We developed 8 neonatal case descriptions with sufficient information to provide a single Apgar score but also included additional distracting information. These 8 cases were then scored by 148 individuals including 28 obstetrical nurses, 54 neonatal nurses, 23 nurses who care for both maternity and newborn patients in small community hospitals, 27 pediatricians and pediatric houseofficers and 16 obstetricians and obstetrical houseofficers.

The results (table) indicated that pediatric attendings and houseofficers assigned the Apgar score more accurately than any other group. Their accuracy was still only 61%.

	Physicians		Nurses		
	Peds	Obs	Neo	Obs	Small Hosp.
% Correct Apgar Scores	61	44	42	34	24

Only two individuals, both pediatric houseofficers, scored all eight patients correctly. Item analysis commonly revealed incorrectly high Apgar scores assigned to very low Apgar cases. We conclude the Apgar score will only be accurate and meaningful for developmental prognosis when the simple criteria are carefully and conscientiously applied.

1225 STRESS AMONG NEONATOLOGISTS. Thomas Clarke, William Maniscalco, Susan Taylor-Brown, Catherine Hannon-Johnson, Donald L. Shapiro, Univ. of Rochester, Dept. of Pediatrics & Div. of Social Work, Rochester, New York.

Neonatology is reputed to be a stressful pediatric subspecialty. To objectively quantify this stress and assess the factors involved, a questionnaire was mailed to neonatologists in the northeastern United States. 97 (70%) replied. A 5-point scale was used to determine level of satisfaction with neonatology as a career and stress experienced at work. Preliminary analysis of these questionnaires has indicated the following: almost all neonatologists experienced stress at work: 32% moderately severe and 16% very severe stress. Open-ended questions indicated the major causes of stress were (a) excessive work load, e.g., on call too often or late calls (36%), (b) patient care (36%) especially dealing with infant death, and (c) staff disagreements (32%) especially nurse or housestaff conflicts. 20% of those surveyed suffered a stress related illness in the past 5 years. One sixth of the neonatologists were either moderately or very dissatisfied with neonatology. Major dissatisfactions were: (a) too much work (48%); (b) lack of resources (32%) including inadequate salary; (c) stress of clinical responsibility (20%); and (d) administrative demands (16%). Satisfactions included patient care (62%); teaching (24%), intellectual stimulation (22%) and research (15%). Altering subspecialty has been considered at some time by 58% (15% very seriously). Preliminary results of this study confirm that neonatology is a highly stressful career. Identification of causes of stress among neonatologists may ultimately lead to appropriate intervention strategies.

● **1226** DO CIRCULATING CONCENTRATIONS OF PROSTAGLANDIN E_2 REGULATE THE DUCTUS ARTERIOSUS? R.I. Clyman, F. Mauray, M.A. Heymann, Dept. of Peds., Mt. Zion Med. Center & Cardiovascular Research Inst., Univ. of CA, San Francisco

According to current views, the Prostaglandin E_2 (PGE_2) that maintains patency of the ductus arteriosus (DA) is formed intramurally and exerts its action locally on muscle cells. We recently found that newborn lambs with patent ductus arteriosus (PDA) have higher plasma PGE_2 concentrations (pulmonary artery (PA)=169±52, aorta (Ao)=80±11 pg/ml, n=6) than those with a constricted DA (PA=23±3 Ao=20±3 pg/ml, n=8). To see if these concentrations of PGE_2 could produce patency of the DA, we used 5 near-term lambs (137-147 days) delivered by C-section, paralyzed and ventilated with 100% O_2. Cardiac output and DA flow were measured by radioactive microspheres. PGE_2 concentrations (PA= 64±22, Ao=69±31 pg/ml) and the DA resistance (1892±733 torr/l/min/kg) stabilized by 2 hr after delivery. We then started a continuous PGE_2 infusion into the superior vena cava; PGE_2 concentrations and DA resistances were measured 20 minutes after each increase in rate (.005 to .133 µg/kg/min PGE_2). We observed the first significant persistent decrease in DA resistance (889±493 torr/l/min/kg) at PGE_2 concentrations of PA=193±33 and Ao=84±15 pg/ml. At the maximum PGE_2 concentrations obtained in each animal (PA=635±195, Ao=105±pg/ml) the DA resistance was even lower (468±288 torr/l/min/kg). The PGE_2 infusions had no significant effect on systemic or pulmonary vascular resistances. We conclude that elevated plasma PGE_2 concentrations found in newborn lambs with PDA may be responsible for the DA patency after delivery.

1227 THE ROLE OF LABOR IN RESPIRATORY DISTRESS OF TERM NEONATES AFTER ELECTIVE CESAREAN SECTION. Morris Cohen, Bonita S.Carson (Spon. by Frederick C.Battaglia). Univ. of Colo.Sch.of Med.,Rose Med.Center, Dept.of Peds.,Denver, Colo.

Elective cesarean section (C/S) has been increasing over the last decade. This study was performed to determine if respiratory morbidity (RM) is different if labor has occurred.

The records of all neonates assessed by prenatal clinical evaluation as 38-42wks gestation and born by non-emergent C/S at Rose Med. Center from Jan-Dec, 1980, were reviewed. Of these, 196 were free of significant maternal and fetal illness. C/S was performed in 111 after the onset of labor and in 85 without labor.

RM defined as >15minutes O_2 requirement after admission to the nursery, occurred with greater frequency in the no-labor group ($p<.001$), as indicated in the table below which also gives the incidence of RM by gestational age (GA) on postnatal examination. Even in the sub-group 39-40wks, the difference was significant.

	All pts.	38-42wks	<38wks	39-40wks only
Labor (L)	12/111=10.8%	9/103= 8.7%	3/8 =37.5%	5/71= 7.0%
No Labor (NL)	25/85 =29.4%	19/74 =25.7%	6/11=54.5%	13/52=25.0%
	$p<.001$	$p<.002$	n.s.	$p<.005$

Regardless of GA, the severity of RM was also greater in the no-labor patients. In the study group RM>4hrs occurred in 1.8%(L) vs 9.4% (NL, $p<.001$). The average cost of hospitalization for NL patients was also excessive being 3 times that of study infants without RM and 1.5 times the cost for L group patients with RM.

RM was greater in neonates born by non-emergent C/S without labor. Awaiting the onset of labor may significantly reduce RM in neonates delivered by non-emergent C/S.

1228 CORD ERYTHROPOIETIN AND BILIRUBIN PRODUCTION IN MACROSOMIC INFANTS. Ronald S. Cohen, Andrew O. Hopper, Louis R. Bucalo, Clinton R. Ostrander, Joseph Garcia, Herbert C. Schwartz, and David K. Stevenson. Dept. of Ped., Stanford Univ. Sch. of Med., Stanford, CA, and Univ. of California, Donner Lab, Berkeley, CA.

Erythroid cell lines are a major heme source in the newborn. The most important humoral stimulus for erythropoiesis is erythropoietin (Ep). Elevated Ep levels have been noted in the cord blood of hyperinsulinemic rhesus monkey fetuses, infants of diabetic mothers (IDM), and hypoxic neonates. Evidence of stimulated erythropoiesis also has been found in each of these instances. Therefore increased heme catabolism in IDM may be related to stimulated erythropoiesis. We studied 6 IDM, 7 infants who were large for dates (LGA), and 6 infants who were appropriately grown for their gestational age (AGA); they were delivered at $\geq$ 36 weeks gestation, and had a mean birthweight of 3.70 ± .53 (SD) kg (range 2.32-4.37 kg). Cord blood samples were analyzed for Ep levels. The pulmonary excretion rate of carbon monoxide (Ve_{CO}), a valid means of determining the bilirubin production rate, was measured in the first few days of life, and found to have a positive linear correlation with Ep ($n=19$, $r=.55$, $p<.02$). The two infants with the highest Ve_{CO} results also had the highest Ep values, and were both IDM. These data suggest that increased erythropoiesis, effective or ineffective, mediated by Ep, may be a significant factor in the hyperbilirubinemia seen in certain neonatal populations such as IDM and LGA infants.

1229 POSTROTATORY NYSTAGMUS (PR-N) IN FULL-TERM AND PREMATURE INFANTS. Leandro Cordero, Jr., David L. Clark, and Craig W. Anderson (Spon. by Grant Morrow, III) OSU Col. of Med., Dept. of Pediatrics and Anatomy, Columbus, Ohio.

Postrotatory nystagmus is an easily elicited reflex reported to be abnormal in developmentally delayed children. PR-N has been recorded in newborns, but methodological difficulties have compromised its full understanding. Eight healthy adults were compared with 19 full-term and 13 prematures, all neurologically normal, tested at 2,6,9, and 12 months. All subjects were positioned in a rotational chair, spun for 1 minute at a constant angular velocity (150°/sec) and then abruptly stopped. Electronic recording of PR-N in absolute darkness continued for 5 min. Two types of PR-N were observed. Primary PR-N consisted of an average of 80 eye movements (beats) lasting 40 sec., in direction opposite to the rotation and was followed by Secondary PR-N (mean of 130 beats, 200 seconds duration, same direction as the original rotation). ANOVA and Scheffe's method of post hoc multiple comparisons were used. Results for full term and prematures were similar in all recorded variables, hence the entire group of infants was compared to adults. The number and frequency of beats in both Primary and Secondary PR-N were significantly greater in adults. However, the angular displacement, duration and velocity of each beat was significantly higher in infants of all ages. All components of PR-N, whether Primary or Secondary, can be recorded and identified under 1 year of age and are significantly different from that obtained from adults. These differences may reflect anatomical and neurophysiological immaturity of eye movement control in the infant.

1230 GLUCOSE INFUSION TO THE CELIAC AXIS INDUCES SUPPRESSED GLUCOSE PRODUCTION (Ra). Richard M. Cowett, Denis Tenenbaum, and William Oh. Brown Univ., Women & Infants Hosp., Dept. of Pediatrics, Providence, RI.

Hypoglycemia has been reported in infants whose aortic catheter (UAC) was placed above the celiac axis. It was postulated that hypoglycemia resulted from direct infusion of glucose into the pancreas stimulating the beta cell. To evaluate this hypothesis, 9 term lambs [birthweight 5.2±0.3 kg (M±SEM); age 4.8±0.6 days] were infused with 6 mg/kg/min of dextrose into a UAC below the celiac axis for 2 hrs following which 25 μCi/kg D-[6-3H] glucose was given by the prime constant infusion technique to measure Ra. After a recovery period of 1 hr, the study was repeated with dextrose infusion above the celiac axis. Blood was drawn for pl. glucose, insulin and glucose specific activity from the carotid artery and Ra was calculated.

Position of UAC	Pl. Glucose mg/dl	Pl. Insulin μU/ml	Insulin Glucose	Ra mg/kg/min
Below Celiac Axis	175±11	70±14	0.39±0.06	5.9±0.8
Above Celiac Axis	140±6†	63±9	0.46±0.08†	4.0±0.5*

Paired T - *p <.05 †p <.01

Following infusion of dextrose above the celiac axis, there was a decrease in pl. glucose, increase in the insulin to glucose ratio and fall in Ra. There was no detectable difference in peripheral pl. insulin concentration, which may be due to more efficient hepatic extraction of insulin. We speculate that direct glucose infusion to the pancreatic artery results in increased insulin delivery to the portal system and suppressed Ra by the liver, which may account for the potential risk of hypoglycemia.

1231 Incidence and Risk Factor Analysis of Subependymal(SEH)/Intraventricular Hemorrhages(IVH) in<1500Gm Infants Born at a Perinatal Center. C.S.Crawford (Spon.by A.Bongiovanni) U.ofPa.,Sch. of Med. Pa.Hosp.,Phila.Pa. Cranial ultrasound(US) has become routine in our management of<1500 gm infants because of the reportedly high incidence of SEH/IVH and the impact on mortality/morbidity. 99 infants had US from 7/80-11/81. 9 died before US but had autopsies. 11/108(10.2%)had SEH and 23/108(21.3%) had IVH±SEH. Combined SEH/IVH=31.5%.

Risk Factor	SEH/IVH(n=34)	No Bleed(n=74)	p*
Perinatal Bleeding	10	12	N.S.
Cesarean Section	10	45	<.005
Vaginal-Vertex	21	26	<.01
Maternal Hypertension	5	21	N.S.
Tocolytic Agents	15	22	N.S.
No Prenatal Steroids	28	54	N.S.
Gestational Age ≤27 wk	12	11	<.02
Gestational Age 28-29wk	15	21	N.S.
Birth Weight ≤1000grams	18	21	<.02
PDA	21	24	<.005
RDS	27	45	N.S.
Male	20	41	N.S.
Death	12	13	<.05

SEH/IVH in<1500 gm,inborn infants was less than expected and was associated with Vaginal-Vertex delivery,≤27 wks gest.age,PDA,≤1000gm,increased mortality and was reduced with C-Section delivery. *Yates correction applied

1232 WHY DO INFANTS BORN AT HIGH ALTITUDE HAVE A HIGH INCIDENCE OF HYPERBILIRUBINEMIA? Linda S. Crnic, Mark A. Newberry, and Lorna Grindlay Moore (Spon. by Donough O'Brien), University of Colorado School of Medicine, Departments of Pediatrics, Psychiatry and Medicine, Denver.

We have found a five-fold increase in incidence of neonatal hyperbilirubinemia (>12 mg/dl) in full term normal weight infants born at 3000 m. In order to assess the contributions of altitude-induced polycythemia and impaired conjugation and excretion of bilirubin to this problem, rats kept at a simulated altitude of 4600 m for 6 weeks were given loading doses (0.5, 1.5, and 3.0 mg/100 g) of bilirubin and hematocrit, hemoglobin, total and unconjugated bilirubin determined on samples taken 17 min. later.

Hematocrit rose from 42.5% to 67.2% and hemoglobin rose from 14.6 to 20.9 g/dl with exposure to simulated altitude and contribute to the significant ($p<.05$) increase in serum bilirubin in rats given no exogenous bilirubin. However, the loading dose conditions indicate that an impairment in conjugation, but not excretion, also contribute to the altitude effect: at every dose, the high altitude rats had significantly higher total serum bilirubin levels than sea-level rats, due entirely to a rise in unconjugated bilirubin as conjugated bilirubin levels were significantly reduced in high-altitude rats at all doses. Impaired excretion would have led to increased rather than decreased conjugated bilirubin in the serum.

We conclude that both polycythemia and an impairment in bilirubin conjugation, but not in excretion, occur at high altitude. Supported by NIH grant HD 08315 and the American and Colorado Heart Associations.

1233 RESPIRATORY LOOP-AREA ANALYSIS: POSSIBLE EARLY INDICATOR OF BAROTRAUMA. M. Douglas Cunningham, Deborah J. Boyer, W. Andrew Litzenberger, Diane M. Gagel, Nirmala S. Desai, Department of Pediatrics, College of Medicine, University of Kentucky, Lexington.

Effects of mechanical ventilation upon pulmonary dynamics of the premature newborn lung were studied during the 1st week of life for 13 infants. Dynamic compliance (C_L) and lung resistance (R_L) were determined for spontaneous and mechanical breaths of pressure-cycled intermittent mandatory ventilation using a multichannel recorder with scalar and loop output. Volume-pressure and pressure-flow loops were measured by planimetry (mm^2/g) to determine compliance loop-area (C_L/area) and resistance loop area (R_L/area). Seven infants (1311g ± 62) recovered from respiratory distress syndrome (RDS) and were extubated on day 13(±3).Six infants (1178g ± 95) developed bronchopulmonary dysplasia (BPD) by week 3 of life and required mechanical ventilation until day 56(±12). During the 1st week of mechanical ventilation, mean airway pressure for both groups decreased progressively from 10.4 to 6.3 cmH_2O (r=0.932). Mechanical vs spontaneous breath C_L/areas for RDS patients on day 7 were 2.40 vs 0.45 (p=0.001) and for BPD patients were 1.62 vs 0.52 (p=0.003). R_L/areas of mechanical breaths for BPD patients on day 7 were 6 times greater than spontaneous breaths (8.42 vs 1.17; p=0.02). We conclude: 1) C_L/areas revealed that excessive mechanical volumes and pressures were maintained, despite conventional ventilator settings and changes, 2) R_L/areas increased during the 1st week for infants susceptible to BPD, and 3) respiratory loop-area analyses may identify degrees of barotrauma to be avoided.

●1234 MILD COOLING TO TREAT APNEA INCREASES OXYGEN CONSUMPTION (VO2), Robert A. Darnall, (Spon. by John Kattwinkel), University of Virginia School of Medicine, Department of Pediatrics, Charlottesville.

Reducing skin temperature (Tab) from 36.8 C. to 36.0 C. has been shown to decrease the frequency of apnea in premature infants. We monitored 11 premature infants to determine the effect of mild cooling on VO2, % time apneic (%AP), the frequency of apnea, >2, >5, and >10 seconds in duration and periodic breathing (PB). Tab was maintained in each infant at both 36.8 C. and 36.0 C. for 2-4 hours under a radiant warmer (RW), while simultaneously measuring VO2 and respiratory pattern. Each of 808 one min. sleep epochs was scored for PB (+ or -), length of longest apnea (LAP), %AP, and VO2.

	WARM	COOL
VO2 (cc/kg/min)	9.11±.07	10.05±.11*
%AP (%)	16.4 ±.7	11.8 ±.9*
PB (%)	38.4	25.8*
LAP> 2 sec (% min)	74.3	56.2*
LAP> 5 sec (% min)	57.9	42.2*
LAP>10 sec (% min)	8.5	4.0

MEAN±SEM; * p<.001

We conclude that maintaining Tab at 36.0 C. 1) decreased the frequency of pauses >2 and >5 sec in the RW. 2) did not alter the frequency of pauses >10 sec. 3) decreased the %AP and % PB in the RW, and 4) increased VO2. We speculate that the reduction in the frequency of short pauses (<10 sec) associated with PB during even mild cooling may reflect the effect of an increased metabolic rate.

●1235 ROLE OF ANGIOTENSIN II, CATECHOLAMINES, AND OXYGEN TENSION IN SYSTEMIC CIRCULATORY ADJUSTMENTS AT BIRTH. Dennis Davidson, S. Alex Stalcup, Robert B. Mellins, Columbia U, Coll. of P & S, Babies Hospital, Dept. of Peds., N.Y.

Angiotensin converting enzyme activity in the fetus is modulated by PaO_2 and enzyme activity increases 3-fold with elevation in PaO_2 from fetal to neonatal values. Because of the synergism between angiotensin II (AII) and catecholamines (CATS), we hypothesized that both play a role in the systemic circulatory adjustments with oxygenation at birth. Six unanesthetized lambs, chronically instrumented in utero, were delivered by C-Section near term and ventilated with O_2 to insure an unasphyxiated birth. Systemic arterial pressure (SAP), PaO_2 (mmHg), plasma renin activity (PRA), AII and CATS (pg/ml) were measured before and immediately after birth. Simultaneously we determined systemic vascular resistance (SVR, mmHg/L/min) and blood flow distribution postnatally (PN). Table shows mean values; * = significant from fetal.

	PaO_2	PRA	AII	CATS	SAP	SVR
Fetal	21	9.0	65	427	48	-
2' PN	141*	13.0*	623*	13463*	62*	48.3
5' PN	150*	15.6*	493*	2910*	56*	43.8
10' PN	111*	12.4*	205*	1901*	55*	35.7
30' PN	101*	12.0*	306*	1602*	54*	42.8

Significant blood flow changes were limited to elevated brain and adrenal values at 2'. Because the high AII and CATS levels coincide with the peaks in SAP and SVR, we suggest that: 1) these synergistic mediators foster the high SVR required for normal birth; and 2) hypoxemia at birth may alter the levels of these mediators, producing pathophysiologic circulatory patterns.

● 1236 VITAMIN D METABOLISM IN PRETERM INFANTS (PI): EFFECTS OF CA-GLUCONATE INFUSIONS. Edgard E. Delvin, Bernard Salle, Francis H. Glorieux, and Louis David. McGill Univ., Shriners Hosp., Genetics Unit, Montreal, Qué., Canada and Hôp. E. Herriot, Neonatal Dept., Lyon, France.

We have previously reported that in PI, during the first 5 days of life, vitamin D (D) was hydroxylated in the kidney after 32 w of gestation (J. Ped. 99,640 1981) without altering the course of the hypocalcemic episode. We have now evaluated whether a rapid correction of the latter modified the renal activation of D. Two age (31-36 w) and birthweight - (1800-2200 g) matched groups of PI received from birth and throughout the study 2100 IU D_3/d. On day 4, one group (I, n=9) was infused with Ca-gluconate (70 mg Ca/kg x 24 h). The other (II, n=7) served as control. Serum samples were obtained from all infants on day 4 and 24 hrs afterward. The following analysis were carried out (mean sem):

Group	day	n	Ca mM	Pi mM	25-OHD ng/ml	1,25(OH)$_2$D pg/ml	iPTH mlEq/l
I+II	4	16	1.90±0.06	1.92±0.10	25±3	100±14	94±16
I	5	9	2.35±0.11 (p<0.0005)	1.54±0.09 (p<0.025)	30±3 (NS)	75±8 (NS)	30±5 (p<0.01)
II	5	7	2.04±0.09 (NS)	2.09±0.12 (NS)	28±4 (NS)	155±20 (p<0.025)	168±50 (p<0.05)

The data show that, by 31 w: 1) Pi levels dropped significantly in group I with no apparent renal 1α-hydroxylase stimulation; 2) an increased supply of calcium corrects the hypocalcemic episode with appropriate response of PTH secretion and 1,25(OH)$_2$ D synthesis.

1237 RECURRENT BILATERAL PLEURAL EFFUSIONS SECONDARY TO SUPERIOR VENA CAVAL OBSTRUCTION AS A COMPLICATION OF CENTRAL VENOUS CATHETERS. Vijay G. Dhande, John Kattwinkel, and Bennett A. Alford. University of Virginia Medical Center, Department of Pediatrics, Charlottesville.

We describe five babies (birth weights 730-1120 grams) who developed bilateral pleural effusions as a complication of central venous catheters (CVC). The effusions occurred 11-15 days after initial placement or change of a CVC (the latter necessitated because of clotting). A preceeding sign in all was selective pitting edema of the shoulders and above. All required repeated thoracenteses to remove fluid accumulation of up to 200 ml/Kg/day. Fluid composition was a clear transudate or chylous depending on state of enteral nutrition. Four of 5 developed calcifications in neck and shoulder veins 19-35 days after catheter placement or change. All 5 developed sepsis following onset of symptoms.

Three babies had venograms demonstrating obstruction of the superior vena cava with upper drainage occurring through collaterals to the azygous and inferior vena cava. Silastic gas-sterilized catheters implanted in animals for 4 hours showed fibrin deposition on 2/4 when scanned by electron microscopy. No deposition occurred on 2 autoclaved controls.

We hypothesize that the effusions resulted from obstruction of lymphatic duct outflow and that vena caval thrombosis may have been triggered by 2-chloroethanol or ethylene oxide residues from gas sterilization of the silastic catheters. We recommend that gas sterilization be avoided for any silastic material intended for intravascular use.

1238 PRONE POSITION REDUCES APNEA IN PRETERM INFANTS. Vijay G. Dhande, John Kattwinkel, and Robert A. Darnall, University of Virginia School of Medicine, Department of Pediatrics, Charlottesville.

Body position has been shown to influence pulmonary function in newborns. In prone position, tidal volume and minute ventilation are significantly greater than in supine. To assess the effect of body position on the incidence of apnea and the pattern of breathing, we studied 5 preterm infants with birthweights 1030 to 1817 grams. Each infant was studied for 2 hours in each position, after a stabilization period of 1-2 hours. Heart rate, respiratory pattern by impedence pneumography and nasal air flow, and $TcpO_2$ were recorded continuously. Fewer apneas occurred in prone (table). There was no difference in the type of apnea (obstructive vs central). $TcpO_2$ was higher in prone ($p < 0.005$). Periodic breathing occurred 14.1% in supine and 10.3% in prone.

APNEA EPISODES/HR (MEAN ± SE)			
Duration	Supine	Prone	
2 to 10 sec.	65 ± 8	55 ± 10	p < 0.001
> 10 sec.	6 ± 3	7 ± 3	NS
TOTAL	71 ± 10	62 ± 13	p < 0.001

We speculate that the reduced apnea in prone may result from better ventilation and improved oxygenation. The compliant chest wall of the premature baby may be better stabilized in prone, thus improving coordination between rib cage, diaphragm and abdomen. This may result in decreased intercostal inhibitory afferents and improved oxygenation.

1239 SERUM BILIRUBINS AT 2 WEEKS OF AGE. Vincent A. DiMaria, Roger M. Barkin, Sylvia F. Villarreal, Keith B. Hammond (Spon. by Frederick C. Battaglia). University of Colorado Health Sciences Center, Department of Pediatrics, Denver.

Hyperbilirubinemia is a common clinical presentation in children during the first month of life, however normal values for 2 week old infants do not exist. One hundred seventy-five healthy full term infants seen for their routine 2 week health maintenance evaluations had total and fractionated bilirubins determined. A subset of 33 children with bilirubins of 2.0 mg/dl or greater at 2 weeks of age were studied in depth.

The bilirubins reported by the type of feeding revealed markedly higher bilirubins in breast fed infants than in those fed entirely by formula.

Feeding Technique	N	(%)	Total Bilirubin (mg/dl) Mean	S.D.	Direct Bilirubin (mg/dl) Mean	S.D.
Breast only	81	(46)	5.6	3.8	0.4	0.4
Breast and formula	28	(11)	3.8	3.2	0.3	0.2
Formula only	66	(38)	2.7	2.2	0.3	0.2

No etiology for hyperbilirubinemia was determined in those children studied in detail with the exception of one infant with cytomegalovirus in the urine.

Most children with prolonged hyperbilirubinemia require no intervention. The standards developed provide important guidelines in the evaluation of the jaundiced infant.

1240 INCIDENCE OF SUBEPENDYMAL (SEH) AND INTRAVENTRICULAR HAEMORRHAGE (IVH) IN THE LOW BIRTHWEIGHT INFANT BORN IN A PERINATAL UNIT. **Dolfin, T.; Fong, K.; Hoskins, E.; Skidmore, M.; Shennan, A.; Regional Perinatal Unit, Women's College Hospital, Toronto, Ontario, Canada.**

Over a 4-month period, 45 premature infants weighing less than 1500 grams or below 32 weeks gestation were subjected to serial cranial ultrasound examinations from just after delivery, then every 12 to 24 hours. Four babies were excluded because they died or were transferred before 24 hours of age. Ultrasounds on these infants were normal and deaths unrelated to IVH.

Overall incidence of SEH/IVH was 27.5%. One infant died due to extensive IVH. Haemorrhage occurred before 72 hours in all, and in two, was present at 2 hours of age.

	Mean B.W.	Mean G.A.	Sex(F/M)	Apgar(1',5')	C/S-Sp.	Pneumo.	
Non-Haem. 30 newborns	1143 gr (550-2600)	28 wks	16/14	6 - 8	21/9	3/30	*
Haem. 11 newborns	1075 gr (890-1470)	28 wks	7/ 4	5 - 7	7/4	4/11	*

* **Non-significant**

The incidence of SEH/IVH reported in the literature in this group of infants is 45 to 90 percent. Our findings suggest that this incidence can be significantly reduced by delivering premature infants in a Perinatal Unit.

1241 ALVEOLAR-TRANSCUTANEOUS OXYGEN TENSION DIFFERENCES DURING HYPERCARBIC VENTILATORY RESPONSES IN PRETERM INFANTS. Manuel Durand, Luis A. Cabal, Abel Chaves, Toke T. Hoppenbrouwers, Enrique I. Cardenas, Joan E. Hodgman, USC School of Med., LAC-USC Med. Ctr., Dept. of Ped., Los Angeles.

The reliability of transcutaneous PO_2 ($PtcO_2$) in reflecting arterial PO_2 during hypercapnic ventilatory responses to hypoxia and hyperoxia has not been studied. In order to determine alveolar-transcutaneous O_2 gradients, $(A\text{-}s)DO_2$, we studied changes in alveolar PO_2 (PAO_2) and $PtcO_2$ before and during the fifth minute of breathing 4% CO_2 in 16% O_2 and 4% CO_2 in 40% O_2 in 9 healthy preterm infants. The studies were performed during active sleep using a nosepiece and a pneumotachograph. End-tidal PO_2 was measured with a PE-20 catheter and an O_2 analyzer, and transcutaneous PO_2 with a $PtcO_2$ sensor. We found the gradient between alveolar and transcutaneous PO_2 was normal for control values in air and during 4% CO_2 in 16% O_2. However, during administration of 4% CO_2 in 40% O_2, PAO_2 increased more than $PtcO_2$, leading to an increased gradient.

	PAO_2 mmHg	$PtcO_2$ mmHg	$(A\text{-}s)DO_2$ mmHg
AIR	108.9	74	35
4% CO_2 16% O_2	96.7	72	24 ($p<0.02$)
AIR	110.5	68	43
4% CO_2 40% O_2	261.4	136	125 ($p<0.001$)

Our findings indicate that: 1) In healthy preterm infants the $(A\text{-}s)DO_2$ is normal in air, 2) the gradient decreases significantly with decreased ambient oxygen but remains within normal range, and 3) $(A\text{-}s)DO_2$ significantly increases during hyperoxia, indicating that $PtcO_2$ does not reliably reflect arterial PO_2 at higher levels of alveolar PO_2.

1242 EFFECT OF CONTINUOUS POSITIVE AIRWAY PRESSURE ON THE VENTILATORY RESPONSE TO CO_2 IN PRETERM INFANTS. Manuel Durand, Ellen McCann, June P. Brady. Children's Hosp. Dept. of Ped., Cardiovasc. Res. Inst. Univ. of Ca., San Francisco.

The effect of continuous positive airway pressure (CPAP) on the ventilatory response to CO_2 in newborn infants is unknown. We studied the CO_2 response to 4% CO_2 in air in 9 preterm infants without lung disease before and during administration of CPAP delivered by face mask (4-5 cmH_2O). We measured minute ventilation, tidal volume, respiratory frequency, end-tidal PCO_2, and calculated the slope and intercept of the CO_2 response. Respiratory pattern and changes in oxygenation were also analyzed by measuring inspiratory and expiratory time, mean inspiratory flow, mean expiratory flow, effective respiratory timing, end-tidal PO_2 and $tcPO_2$.

We found that administration of CPAP decreased minute ventilation from 278.7 to 197.6 ml/min/kg ($p<0.001$). Tidal volume and respiratory frequency were also significantly decreased. The slope of the CO_2 response during CPAP was not significantly different from the slope before CPAP (36 vs 33 ml/min/kg/mmHg), but the intercept was shifted to the right ($p<0.001$). The decrease in respiratory frequency was primarily due to a prolongation of expiratory time ($p<0.05$). In addition, $tcPO_2$ increased during administration of CPAP ($p<0.001$).

Our findings indicate that: 1)CPAP significantly decreases ventilation in preterm infants without lung disease, affecting both tidal volume and respiratory frequency, 2)CPAP does not appreciably alter the ventilatory response to CO_2, 3)the changes in respiratory frequency are primarily accounted for by a prolongation of expiratory time, 4)CPAP improves oxygenation.

1243 THE PATHOGENESIS OF INTRACRANIAL HEMORRHAGE (ICH) IN THE NEWBORN DOG. William H. Edwards, Eugene E. Nattie, and Miguel Marin-Padilla. (Spon. by Robert Z. Klein) Dartmouth Medical School, Depts. of Maternal & Child Health Physiology, and Pathology, Hanover, New Hampshire.

Clinical studies have reported a relationship between infusion of hypertonic $NaHCO_3$ and ICH. The term newborn dog is a good model for ICH because the brain is histologically similar to the 28-30 week human neonate. We studied the separate and combined effects of prolonged partial asphyxia and hypertonic $NaHCO_3$ infusion on the incidence of ICH in spontaneously breathing newborn dogs. Group I animals (N=5) received a 5 mEq/kg IV bolus infusion of molar $NaHCO_3$. Group II animals (N=6) were asphyxiated (FiO_2 2-3%, $FiCO_2$ 7-8%) for 30 min. and then resuscitated. Group III animals (N=9) were asphyxiated as above, but received a 5 mEq/kg IV bolus infusion of molar $NaHCO_3$ during resuscitation. The animals were sacrificed 2-4 hrs. after asphyxia and/or $NaHCO_3$ infusion. The brains were examined for gross subarachnoid or intraventricular hemorrhage (SAH or IVH) then fixed. No animal in Groups I or II had gross SAH or IVH. Three animals in Group III had SAH, 4 had IVH, and 6 had either gross SAH or IVH. Microscopic results were similar. The most frequent site of bleeding in Group III was the choroid plexus or its subependymal base (6 animals). Factors which may relate to the increased incidence of hemorrhage in Group III include a 2.5 fold greater rise in serum osmolality than Group II immediately post $NaHCO_3$ infusion and a lower PCO_2 during the hour post asphyxia in Group II compared to Group III (20-27 mmHg vs 34-38 mmHg). Our study suggests that rapid infusion of $NaHCO_3$ during resuscitation may lead to ICH.

●1244 DIURESIS AND RESPIRATORY DISTRESS SYNDROME(RDS): A ROLE FOR PROSTACYCLIN(PGI_2)? William D Engle, Billy S Arant, Jr, Suvipa Wiriyathian, and Charles R Rosenfeld. Dept Ped, Southwestern Med Sch, Dallas, TX.

Spontaneous diuresis precedes pulmonary improvement in RDS. To examine factors which may be important in this diuresis, 8 infants with RDS (EGA=30 wks, BW=1205g) were studied prospectively with timed-urine collections. Fluid intake(I) and urine output(O) were recorded. Alveolar-arterial oxygen gradients ($AaDO_2$) were calculated. Urine(U) and/or plasma(P) were analyzed for creatinine (Cr), osmolality(osm), and arginine vasopressin(AVP), prostaglandins and cAMP by RIA. Diuresis (O/I >80%) occurred at 24-32h; improvement in $AaDo_2$ at 48-56h*. Results of sequential studies were (X ± SE, *p<.05):

	I	II	III	IV
Age (hrs)	7.8±1.9	28.9±2.7	52.3±3.5	74.7±3.4
C_{Cr} (ml/min)	.64±.18	1.03±.34	1.03±.24	.88±.30
UV (ml/min)	.04±.01	.08±.02	.08±.01	.06±.02
Posm (mosmol/kg)	276±2	282±6	294±7*	291±6*
Uosm (mosmol/kg)	185±15	166±28	268±43	260±23
P-AVP(μU/ml)	1.6±.2	1.9±.4	1.9±.1	2.6±.7
P-6KetoPGF$_{1\alpha}$ (ng/ml)	2.3±.3	1.1±.4*	.8±.1*	.7±.1*
U-PGE_2 (ng/min)	.10±.02	.09±.02	.10±.02	.06±.02
U-cAMP (nmol/min)	.03±.01	.03±.01	.03±.01	.02±.01

P-6KetoPGF$_{1\alpha}$ (P-6K, PGI_2 metabolite) varied directly with weight change and inversely with mean BP*. Diuresis in RDS occurs without significant changes in renal function or P-AVP. The decrease in P-6K may result in decreased capillary permeability and/or decreased vasodilation and may be important in the subsequent improvement in pulmonary function.

1245 NEONATAL INFORMATION SYSTEM USING AN INTERACTIVE MICROCOMPUTER PROGRAM. Stephen C. Engelke and Walter LaMondola (Spon. by J. Kenny). East Carolina Univ. School of Medicine, Dept. of Pediatrics, Greenville, NC.

A neonatal information system has been developed using an interactive microcomputer data base management system (DBMS). This previously unreported application has important advantages: low cost ($5,000); Z80A, 64K RAM, 900K storage for stand alone computing; fast assembly language, relational DBMS allows powerful data operations comparable to main frame computers; rapid development of custom data bases by a non-programmer physician (SCE) with minimal technical assistance.

The system is being used to evaluate the growing ECU Regional Perinatal Program, which serves 29 counties with 17,000 annual births and one of the highest perinatal and neonatal mortality rates in the U.S. Validated Transport Score, Psycho-Social Inventory, Neonatal Perception Inventory, Parmelee neuro exam, and Bayley Scales of Infant Development are part of 600 patient variables being used to analyze initial management and referral patterns, hospital care and infant follow-up through 3 years of age. The system can score and generate individual patient summaries or automatically produce periodic group reports. Sophisticated statistical analysis can be done on site or can be transferred to SPSS or SAS.

In conclusion, this report describes the use of a low cost, interactive microcomputer DBMS to rapidly develop and implement a neonatal information system with minimal technical assistance.

1246 PERINATAL LISTERIOSIS, J. Ewing, A. Allen, D. Stinson, R. Bortolussi, L. Peddle, Dalhousie University, the Grace Maternity and the Izaak Walton Killam Hospitals, Depts. of Pediatrics and Obstetrics, Halifax, Nova Scotia.

Between April and August, 1981, 22 confirmed cases of perinatal L. monocytogenes infections were identified in N.S. Fifteen of these 22 cases were delivered at the Grace Maternity Hospital and form the basis of this report. An additional 3 infants colonized with listeria but otherwise normal are not reported here.

Of the 15 mothers, 8 had flu-like symptoms in the 2 weeks prior to delivery, 3 had symptoms of URI, 3 a history of fever alone; only one reported no illness. During labor, 11 mothers had fever >38°C. and 8 had green-stained amniotic fluid.

Of the 15 infants, 4 died in utero and 3 died as neonates (case fatality rate = 46.7%). Twelve (80%) were born at a gestational age < 37 wks. Of the 11 liveborns, 9 had clinical evidence of infection. Two infants who were born at term had no evidence of infection; their mothers had received treatment for listeriosis in the third trimester. Of the 9 symptomatic infants, 6 had birth asphyxia, 8 had respiratory distress and 4 (as well as 2 stillbirths) had a rash at birth. Eight of the 9 had positive blood cultures. One had positive surface cultures only, following maternal ampicillin treatment in labor.

Maternal disease appeared to precipitate premature labor. Infants < 37 wks. accounted for all the deaths and all of the severe neonatal disease. The delivery of healthy fullterm infants to 2 mothers who were treated for listeriosis occurring in pregnancy suggests that early recognition and prompt treatment of maternal disease will improve perinatal outcome.

1247 PERINATAL FACTORS ASSOCIATED TO NEONATAL POLYCYTHEMIA HYPERVISCOSITY SYNDROME (PHVS). Horacio S. Falciglia, J. Robert Johnson, Perinatal Center Good Samaritan Hospital, Cincinnati, Ohio. (Spon. by Reginald Tsang).

Over 2 years 109 pts with PHVS were identified. Diagnosis of PHVS was made when peripheral (venous) hematocrit was ≥ 65%. The study pts were retrospectively compared with a control group of 5136 pts without PHVS. The study group consisted of 83 (76%) full term infants, 16 (15%) premature and 10 (9%) post-term according to the Dubowitz score. 69% were AGA, 18% SGA and 13% LGA. Control pts had similar distribution. Incidence of PHVS was 2%. No significant difference was found in the mode of delivery (vaginal, C-section and mid forceps) between the two groups.* There were no attempts to control the volume of placental transfusion in these pts. Maternal preeclampsia, maternal diabetes, multiple pregnancy and cigarette smoking were not significantly associated with PHVS*. Complications during labor, failure to progress (FP) and Meconium Staining (MS) were increased in PHVS pts. 21 PHVS pts had FP (19%) vs 158 FP control (3%), 24 PHVS pts had MS (22%) vs 572 MS control (10%), but it did not reach statistical difference*. Incidence of asphyxia (A) was increased in PHVS pts. 19 PHVS pts (17%) had low APGAR vs 591 control A (11%). Asphyxia was not significantly associated with PHVS*. In most of the cases the cause of PHVS remains obscure. It is speculated that complications during labor resulting in asphyxia increase the risk of PHVS.

* X^2 Test.

1248 THE EFFECT OF TIME OF CORD CLAMPING (C) ON PLACENTAL BLOOD VOLUME (PBV) AND NEONATAL BLOOD VISCOSITY (V) IN INFANTS OF DIABETIC MOTHERS (IDM) BORN BY CESARIAN BIRTH (CB). Horacio S. Falciglia, J. Robert Johnson, Eldridge A. Baker, Donald J. Frank. Good Samaritan Hospital. (Spon. R. Tsang).

IDM are relatively hyperviscous (HV) at birth and the contribution of the time of cord clamping on their viscosity is unclear. 27 IDM (20 insulin dependent 7 gestational) born by CB and positioned between the abdominal wall and the back of the mother were studied. Time of cord C was checked by one of the authors with a stop watch from the time the chin was delivered. The mean gestational age of the study group was 37± 2.8 wks. Controls were born under the same circumstances and gestation. Time of cord C was randomized in both groups. PBV was determined by Redmond's method. PBV in IDM was 46.0± 27 ml/kg (range 18.8 - 73.2) and cord C of 38.7" (range 0 - 78") (r = 0.377, not significant.) Controls were 34.63 ml/kg (range 0 - 74.6) and 42.6" (range 4 - 80") (r = 0.116.) Both groups of pts underwent cord and 3 hrs V. 3 IDM became HV at 3 hrs (from 3.5 to 7.2 centipoises (CP), 5.8 to 8.7 CP, and 4.4 to 6.4 CP.) Cord V was 4.06± 2.0 CP and 3 hrs 5.08± 2.56 CP in IDM ($P<0.001$) vs cord V 4.08± 1.64 CP and 3 hrs 4.96± 1.78 CP in controls ($P<0.01$.) 3 hrs V was significantly increased in both groups. In IDM a small increase in cord V was followed by a greater increase at 3 hrs than in controls. This change in V was not affected by the time of cord C (r = 0.077, $P>0.10$.) PBV for IDMs were the same as the normal Cesarian group. Under these conditions, time of cord clamping did not affect the viscosity in IDMs. Infants born by Cesarian did not receive placental transfusions that are thought to occur in normal vaginal delivery.

1249 NEONATAL POLYCYTHEMIA HYPERVISCOSITY SYNDROME (PHVS) SYMPTOMATOLOGY (S) AND PARTIAL EXCHANGE-TRANSFUSION (PET). Horacio S. Falciglia, J. Robert Johnson. Perinatal Center, Good Samaritan Hospital, Cincinnati, Ohio. (Spon. by R. Tsang).

The relationship between neonatal hyperviscosity and symptomatology and the effects of partial exchange-transfusion are unclear. Over 2 yrs 109 pts with PHVS were identified (peripheral venous hematocrit (hct) ≥ 65 or a viscosity (V) ≥ 6 centipoises (CP). These pts were matched with 109 controls without Polycythemia. Trisomies and congenital heart disease were excluded. Study pts hct was 67.7% ± 7.0 (mean ± 2 SD). Out of 109 PHVS pts, 45 had V studies (8.4 ± 1.6 CP). Control pts hct was 51.8% ± 11.4 (V 4.8 ± 1.8 CP). V was matched against S ie, CNS, cardiopulmonary, GI, hematological and GU. Among PHVS pts with a V ≥ 6 CP, 86% had S vs 3% in controls. V ≥ 6 CP was significantly associated with symptoms ($P<0.001$). Among control, 2 pts had CP ≥ 6 and both had S. S in the PHVS group were: 34 jitteriness, poor suck and lethargy, 43 respiratory distress and cyanosis, 14 heart murmur, 9 bradycardia, 3 arrhythmia, 42 plethora, 1 N.E.C., 7 abdominal distension, 1 DIC, 8 hyperbilirubinemia, 6 thrombocytopenia, 1 melena, 1 kidney enlargement. 43 pts had hypoglycemia, significantly associated with PHVS ($P<0.001$). 103 PHVS pts underwent PET at a mean age of 14.5 hrs. Mean hct before PET was 67.7% ± 7.0 and after 55.1% + 9.2 . Mean V before PET was 8.3 ± 2.8 CP and after 5.6 ± 2.9 CP. S subsided after PET in all pts, but 2 showed residual neurological sequelae. Neonatal Polycythemia is associated with viscosity ≥ 6 centiposes. Hyperviscosity is a major cause of symptoms and exchange transfusion effectively reduces hyperviscosity without complications.

1250 PREDICTABILITY OF CEREBRAL VENTRICLE SIZE IN NEWBORN INFANTS. Donald Fisher, Golde Dudell and Alan Zubrow. (Spon. by Kwang-sun Lee) University of Chicago, Pritzker School of Medicine, Department of Pediatrics, Chicago, IL and Columbia University, New York, N.Y.

This study reports the relationship of lateral ventricle size with various parameters; post-conceptional age, weight and head circumference in newborn infants. Cortical size (CS), ventricle size (VS) and skull size (SS) were measured by linear ultrasound. CS is calculated by deducting VS from the total distance (skull to inner wall of lateral ventricle) or SS. There were significant linear correlations of varying degree between CS, VS and SS post-conceptional age, weight and head circumference (all $p<.01$).

	CORRELATION COEFFICIENT (r) df=132			
	CS	VS	SS	VS/SS
Post-Conceptional Age (26-49 wks)	0.72	0.59	0.74	-0.06
Weight (610-3830 gms)	0.79	0.62	0.80	-0.10
Head Circumference (21-35.75 cm)	0.82	0.61	0.82	-0.15

VS/SS does not correlate with the latter parameters. In fact, VS/SS is rather constant among all infants, 0.322±0.031 (M±S.D.) with coefficient variation of 9.6%.

Subsequently, 15 infants with suspected brain pathology were studied with both CAT scan and ultrasonography. Nine showed enlarged VS by both methods with VS/SS of 0.49±.05, but six infants with normal VS on CAT scan had VS/SS of 0.34±.04 ($p<.01$).

Results of this study suggests that 1) increment in cortical thickness and lateral ventricle size is proportionally constant and thus, 2) VS/SS can be used as an index for abnormal ventricle size in newborn infants.

1251 ARTIFICIAL SURFACTANT (AS): A THERAPEUTIC TRIAL IN INFANTS WITH HYALINE MEMBRANE DISEASE (HMD). ZVI FRIEDMAN AND MICHAEL DOODY. Depts. of Ped., OB & GYN., Baylor College of Medicine, Houston, Texas.

HMD is the consequence of Surfactant (S) deficiency. AS, a protein free mixture of: dipalmitoyl phosphatidylcholine (DPPC), dioleyl (DO) PC, DOP glycerol and cholesterol was developed in our laboratories. The following physical properties of the AS were matched to human S isolated from amniotic fluid at term and mature rabbit lung S: 1. Monolayer surface balance measurements 2. Gel/Liquid Crystalline phase behavior of the lipid mixtures 3. Pressure-volume studies in premature rabbits. Three infants with severe HMD who were mechanically ventilated received 1 or 2 doses of AS, 25 mg/kg (30 mg/ml) into the endotracheal tube. Clinical data is shown in the table.

Infant	1	2	3
Birth weight (gms)	1100	1150	1060
Gestation (wks)	27	28	27
F_iO_2 pre S	0.80	0.87	0.60
Age instillation S (hrs)	14	8½,12½	13
Time to F_iO_2 0.21 (hrs)	48	120	24

Patients 1, 2 developed air leaks and patient 2 developed grade II IVH and PDA. Rapid clearing of chest-x-ray was seen in patients 1, 3 before clinical improvement. AS clearly modified the course of HMD in patients 1, 3. Further studies are required to assess AS as an effective substitute S in premature infants.

●1252 SUCCESSFUL RESUSCITATION OF PRETERM FETAL LAMBS WITH AN EXTRACORPOREAL MEMBRANE LUNG. Roberto Fumagalli, Theodor Kolobow, Paolo Arosio, Victor Chen Delwin Buckhold, Joseph Pierce, NIH, Bethesda, MD, (Spon. by Dr. James Sidbury

We have explored the use of the extracorporeal membrane lung (ML) in the treatment of 128-130 d fetal lambs, in whom state of the art resuscitation has failed, with death imminent. 16 fetal lambs were exposed by C-section, intubated, and cannulated for possible extracorporeal bypass using a single double lumen catheter in the external jugular vein. All animals were placed on a mechanical ventilator (MV). In 5 lambs, by 10 minutes the PaO_2 78 + 47 torr (FIO_2 0.80), $PaCO_2$ 86 ± 23 torr, pH 7.179 ± 0.09: these animals were successfully managed on MV and were on room air after 24 hrs of MV, with excellent compliance and blood gases. Eleven other animals showed a progressive deterioration with a pH 7.073 ± 0.112, $PaCO_2$ 113 ± 26 torr, PaO_2 18 + 11 torr. Two of those lambs were kept on MV and died after 2 and 5 hrs respectively; nine other lambs were placed on extracorporeal bypass at a blood flow of 60 ml kg^{-1} min^{-1} and kept on CPAP at 15 cm H_2O. Within 1 hr of bypass pH 7.337 + 0.076, $PaCO_2$ 43 ± 8 torr, PaO_2 47 + 23 torr After 7 ± 9 hrs of bypass the lung fields by chest X-ray films showed substantial clearing, total lung compliance rose to 0.705 ± 0.35 ml $(cm\ H_2O)^{-1}kg^{-1}$, and lambs were placed on MV for 24 hrs, at the end of which time pH 7.42 ± 0.09 torr, $PaCO_2$ 40 ± 6 torr, PaO_2 59 + 9 torr (FIO_2 0.21). The effective lung compliance rose from 0.22 ± 0.02 to 0.78 ± 0.15 ml $(cm\ H_2O)^{-1}kg^{-1}$. At autopsy the lungs appeared normal and well aerated. CPAP less than 15 cm H_2O was ineffective. One animal with extreme hypoxia (PaO_2 3 torr) prior to bypass remained severely hypotenisve, with severe metabolic acidosis, and died.

Extracorporeal bypass with a ML, performed without much delay, can rapidly restore good arterial blood gases while permitting high levels of CPAP not otherwise tolerated. This treatment within a few hours leads to improvement in lung function, and survival.

1253 THE IMPACT OF PROM(PROLONGED RUPTURE OF MEMBRANES)IN NEONATES <1000G. Assefa Gebreselassie, Angelo Ferrara. NYU/Bellevue Med. Ctr. Dept. Peds. NYC.

A link of PROM,↓resp.morbid.&↑surviv.has been noted(Bauer Ped. 53:7,'74).To test a similar hypot.all charts of neonates <1000G. transported to III ctrs.in NYC over 4 yrs(1/77to12/80)were reviewed.5 variables,each at2. levels(wt,age of pickup,stabil.score*PROM >24hr,5'APGAR)were used to correl.c̄ mortality.The mean wts.+1SD in Gm.of those c̄ PROM(N=77)was 822.05±133.98,didn't differ signif. from those(N=183)s̄ PROM:820.46G±127.52G(t_{260}=.09,P>.90).Cases of PROM receiving steroids prior to deliv.weren't recorded.χ^2testing &Mantel-Haenszel tests were used in analysis.RESULTS(1)Within wt. specific categories,diff.in mortality were noted by levels of stabil.scores(↑score c̄↑surviv.,P<.05)APGAR(5'APGAR>6 c̄↑surviv.P<.05)PROM(PROM present,↑surviv.,P<.05)but no signif.diff.was noted in age of pickup(2)In asphyxic,(APGAR5'<6)well stabil.neonates(N=124)c̄ PROM,there was a signif.↑in surviv(54%)compared to those s̄ PROM(27%),P<.01(3)Those asphyxic&poorly stabil(N=49)had an improved but not sig.diff.surviv.c̄ PROM(38%)compared to those s̄ PROM(28%).(4)The remaining non-asphyxic gp.(N=87)didn't show any sig.dif. in mortality(χ^2=.57,P>.5).Correl.of PROM&surviv.in asphyxic <1000 G.may be related to lung maturation but early stabil.is also essential.TABLE I: PROM & SURVIVAL OF NEONATES <1000Gm.

*Ped.Res.15:517,'81

	N=260	%Survival c̄ PROM(N=77)	%Survival s̄ PROM(N=183)	P <
Asphyxic(well stabil APGAR 5'≤6)	124	54% (N=34)	27% (N=90)	.01 signif.
Asphyxic-Poor stabil	49	38% (N=13)	28% (N=36)	NS
Non-asphyxic gp.	87	55% (N=30)	64% (N=57)	NS

1254 SERIAL PULMONARY FUNCTION IN INFANTS WITH CHRONIC LUNG DISEASE (CLD). Tilo Gerhardt, Steven L. Goldman, Dorothy Hehre, Rosalyn Feller, Rajeswari Sonni, Eduardo Bancalari. University of Miami, Department of Pediatrics, Miami.

Serial measurements of lung function up to 6 months of age were obtained in 20 preterm infants (BW 1200±370g, GA 30.6±2.4 wks) with CLD. The infants required mechanical ventilation for>3 days because of severe HMD, were oxygen dependend for >4 wks and their chest radiographs showed increased haziness and prominent interstitial markings. Tidal volume was determined by pneumotachography, esophageal pressure with a saline filled feeding tube, and FRC by measuring the amount of exhaled N_2 while breathing a N_2 free gas mixture. The results are shown in the table:

Age (Weeks)	2	4	12	26
Wt (grams)	1200 ± 250	1270 ± 380	2830 ± 1230	5840 ± 1580
RR (breath/min)	54 ± 18	56 ± 13	57 ± 13	43 ± 13
V_T (ml/kg)	5.4 ± 1.3	6.4 ± 1.5	6.5 ± 1.5	5.7 ± 1.1
C_L (ml/cmH_2O/Kg)	0.77 ± 0.17	0.83 ± 0.24	0.88 ± 0.29	0.75 ± 0.18
R_L (cmH_2O/l/sec)	136 ± 45	161 ± 65	114 ± 27	123 ± 43
FRC (ml/kg)	15.0 ± 3.3	15.6 ± 3.2	15.1 ± 3.3	16.5 ± 3.2
P_ACO_2 (mmHg)	45.7 ± 3.6	45.9 ± 5.3	40.5 ± 5.3	40.3 ± 3.4

At 2 and 4 wks of age the infants show a higher RR, smaller V_T, and higher P_ACO_2 than normal. The FRC and C_L are only half of the expected normal value while R_L is three times higher than normal. Growth was associated with an increase in FRC and C_L proportional to weight gain but without catch up towards normal values. R_L remained elevated. These findings suggest that abnormal pulmonary mechanics in CLD persist for at least 6 months without evidence of recovery with growth. (Funded by NIH#1R01-HL/HD-25023-01A1)

●1255 THE OPTIMAL POSITION FOR SPINAL TAP IN PRETERM INFANTS C.A.Gleason, R.J.Martin, J.V.Anderson, K.Sanniti, W.A.Carlo, A.A.Fanaroff. CWRU, RB&C Hosp.,D.Peds, CLE

Spinal taps in preterm infants are frequently associated with clinical deterioration. Thus we sought the optimal position for this procedure. 17 healthy infants (GA 31.5±2.5 wks, BW 1.5±0.3 kg) were studied at a mean postnatal age of 20 days. 3 positions were randomly tested in each infant without actual needle insertion: a) Flexed(FP)-lateral recumbent, b) Extended(EP)-lateral recumbent, neck free, c) Upright(UP)-sitting with neck, spine and hips flexed. Each position was maintained for 5 min. with equal control periods before and after. Transcutaneous oxygen ($TcPO_2$) and CO_2 ($TcPCO_2$), heart rate(HR) and blood pressure were monitored continuously. Minute ventilation(MV) was measured via pneumotachometer in 7 infants. HR increased in each position. $TcPO_2$ fell in all positions, greatest in FP. Mean $TcPCO_2$ increased significantly only in FP and strikingly was still elevated 5 mins. after FP had been discontinued ($p<0.01$). No episodes of airway obstruction or apnea >10 secs. were observed. Despite the greatest decrease in $TcPO_2$ in FP, MV did not fall accordingly. Thus, we speculate that V-Q abnormalities predominantly account for the fall in $TcPO_2$. The blood gas fluxes may be reduced by assuming UP or minimizing neck flexion during spinal tap.

	$TcPO_2$(mmHg)		$TcPCO_2$(mmHg)		MV(cc/min)	
	Control	Study	Control	Study	Control	Study
FP	72±12	44±12*	55±7	58±9*	660±260	600±340
EP	71±11	54±15*	57±9	57±9	690±170	620±190
UP	73±12	58±13*	56±8	57±9	710±360	670±270

*$p<.05$ (All values = Mean ± SD)

1256 MORPHOMETRIC CORRELATION OF FRESH PLACENTAL MEASUREMENTS & BIRTH WT. - A MATHEMATICAL MODEL. Tilak Gooneratne, Angelo Ferrara, Rita Demapoulos. NYU/Bellevue Med.Ctr. Depts.of Peds.& Pathology, NYC.

It has been stated that placenta(PL)wt.at term is approx.1/6-1/7 that of the NB wt(BW).The study was undertaken to correlate PL measurements ⊂ neonatal wt. 31 consecutive PL at Bellevue between 3/81&8/81 were studied morphometrically&histologically.Abnormalities of cord insertion,lobulation of the PL& LGA PL were eliminated.Diameters of the maternal surface&thickness&wt.were recorded by a pathologist soon after delivery.The neonatal staff recorded maturity&sex.Coefficients of correlation & regression analysis were calculated for PL surface area,PL vol.,PL wt.& BW. RESULTS(1)In AGA PL wt.correlates signif.better to log of BW ($r=.81$)than does PL vol.to log of BW($r=.41$),$P<.002$(2)SGA PL wt.to birth wt. have a.higher correl.coeff.($r=.90$)than do AGA PL wt.to BW($r=.81$),$P<.2NS$)(3)PL wt.of ♂NB correlates better to BW than do ♀ PL wt.(4)Both PL wt.&vol.explain more of the variance to BW than either variable alone(5)Surface area did not correlate well ⊂ BW(6)No correlation was noted between morphometric PL measures & outcome(mortality). TABLE I - CORREL. COEFF. & P VALUES

		#	r PL WT,BW, & P VALUES	r PL VOL &BW	R^2BW,PL WT, VOL.&P VALUES
AGA(N=25)	PRETERM 9 ♂	6	.86 P<.05	.48 NS	All AGA .61
	PRETERM 9 ♀	3	.99 NS	.53 NS	F^3_{21}=10.9, P<.001
	TERM 16 ♂	8	.87 P<.005	.20 NS	
	TERM 16 ♀	8	.43 NS	.46 NS	
SGA(N=6)	PRETERM ♂	2	.99 --	.99 --	ALL SGA .85
	PRETERM ♀	4	.90 NS	.69 NS	F^1_4=22.7 P<.01

●1257 FUROSEMIDE ENHANCES THE INCIDENCE OF PDA IN INFANTS WITH RDS. T.P. Green, T.R. Thompson, D. Johnson, J.E. Lock. Dept. of Ped., U of MN, Mpls(spons by B. Mirkin).

Furosemide (FSM) stimulates the renal synthesis of prostaglandin E_2, a potent dilator of the ductus arteriosus. A prospective, double-blinded study was conducted to test the hypothesis that FSM use enhances PDA incidence. Infants with RDS who required mechanical ventilation and weighed less than 2500g were randomized to FSM or chlorothiazide (CTZ) groups (CTZ does not increase PG synthesis). The blinded diuretic was begun after the 1st day of life if an infant did not initiate the expected diuresis and was not showing pulmonary improvement. Infants were fluid restricted (70 ml/kg /d) and 67% of the infants received diuretic. Subjects were examined daily by a blinded investigator and 2 consecutive days with findings consistent with PDA were required for this diagnosis. Sequential statistical analysis terminated the study when PDA incidence was significantly greater in the FSM group (FSM 18/33; CTZ 7/33; $p<.02$). The groups were comparable in other respects including birth weight (FSM 1491±471 g; CTZ 1532±500), initial severity of disease as assessed by mean airway pressure (FSM 14.6±4.5 cm H_2O; CTZ 15.5±4.5) and fluid intake on each day. Diuretic effect was greater in the FSM treated patients: weight on day 5 was less in the FSM group (FSM 93.2±7.0% of birth weight; CTZ 96.3± 6.5%; $p<.05$). Despite the effect on PDA incidence, multivariate analysis identified FSM use as a factor significantly enhancing survival; diuresis (loss of weight by day 5) was a factor related to the early cessation of mechanical ventilation. The relationships among diuresis (spontaneous and drug induced), PDA, and pulmonary recovery in RDS require further examination.

1258 COPING STRATEGIES UTILIZED BY STAFF NURSES IN AN NICU AS A FUNCTION OF EXPERIENCE IN THE UNIT. Ronald E. Gribbons, Richard E. Marshall. Washington University School of Medicine, Dept. of Pediatrics, St. Louis, Missouri.

An emerging NICU problem is the retention of experienced nurses. We have previously reported that stresses encountered by NICU nurses change with length of employment (LE). The present study examined coping strategies and their relationship to LE.

A Neonatal Nurse Stress Assessment Inventory (NNSAI) was developed and administered to 23 full-time nurses. The sample was stratified by LE into 4 periods: LE-1, orientation; LE-2, two months to 1 year; LE-3, 1 to 3 years; LE-4, more than 3 years.

Coping strategies utilized included: 1) talking with individuals outside the NICU, 2) talking with other nurses, 3) attending meetings with psychotherapists, 4) attending meetings with neonatal staff physicians, and 5) developing a personal style that included setting priorities, confrontation and humor.

Nurses in orientation remain quiet at work and rely on those outside the NICU. During LE-2 nurses seek out their peers and this continues during LE-3 and 4. LE-2 nurses attend the psychotherapist and physician meetings with enthusiasm while nurses in LE-3 and 4 increasingly felt that they accomplished little. In contrast, nurses during LE-3, and especially during LE-4, developed more autonomous coping strategies. They set priorities, used more humor, and were more easily able to confront physicians about problems.

Our results suggest that, as the nurse gains experience, she relies more on her coping skills and less on assistance from either others or organizationally based meetings.

1259 AMNIOTIC FLUID PHOSPHATIDYLGLYCEROL (AFPG) AND RISK FOR TRANSIENT TACHYPNEA OF THE NEWBORN (TTN). Thomas L. Gross, Robert J. Sokol, Melinda S. Kwong, Margaret V. Wilson, Paul M. Kuhnert, Victor Hirsch (sponsored by Satish Kalhan) Case Western Reserve Univ., Metropolitan General Hospital/Perinatal Clinical Research Center, Depts. Ob/Gyn and Peds., Cleveland.

Disagreement as to the importance and etiology of TTN persists. In this prospective study of AF maturity tests 55 neonates with TTN were compared with 355 in whom no respiratory distress occurred. All were classified by one neonatologist based on strict clinical and radiographic criteria. The 2 groups were compared for 22 neonatal complications and procedures related to preterm delivery. The TTN group had significantly increased cyanosis, shock, necrotizing enterocolitis, suspected sepsis, central nervous system depression, admission to the NICU, prolonged hospital stay, umbilical artery catheterization, and prolonged oxygen therapy (all $p<.05$). Ten perinatal factors were evaluated as potential risks for TTN using stepwise discriminant analysis. Only 3 factors, negative AFPG (<2%), prematurity (<38 weeks pediatric gestational age) and 1 minute Apgar <7 were found to contribute significantly to the classification into TTN and non TTN groups ($p<.01$). The most important factor was negative AFPG. Lecithin/sphingomyelin ratio <2, maternal diabetes mellitus (DM), cesarean birth, general anesthesia, large for gestational age infants, male infants and polycythemia did not contribute independently. These findings suggest that TTN is an important cause of neonatal morbidity. In addition several factors such as DM and cesarean birth previously reported to correlate with TTN may be mediated through the most important factor of mild pulmonary immaturity.

1260 EARLY IDENTIFICATION OF INFANTS AT RISK OF DEVELOPING CHRONIC LUNG DISEASE. Steven L. Goldman, Tilo Gerhardt, Radjeswari Sonni, Dorothy Hehre, Rosalyn Feller, Eduardo Bancalari, Univ. of Miami, Department of Pediatrics, Miami.

To predict which infants with acute HMD are at higher risk for developing chronic lung disease (CLD), we performed pulmonary function (PF) studies on infants requiring > 72 hours of mechanical ventilation or > 7 days of supplemental O_2. CLD was defined as requiring > 28 days of supplemental O_2 and having hazy lung fields and increased interstitial markings on chest x-ray. Of 14 infants studied, 7 developed CLD (Group I), 6 did not (Group II), and 1 infant died while requiring supplemental O_2, but for< 28 days and is therefore excluded.

Group I was more premature than Group II (BW:1141±91 vs 1586±80g ($p<.01$); GA:30.1±0.7 vs 32.6±0.6 weeks ($P<.05$)). Although the amounts of ventilatory support were similar in the two groups during the first week of life, Group I ultimately required more days of mechanical ventilation (14.7±4 vs 4.5±1 days; $p<.05$) and supplemental O_2 (71±13 vs 10±2 days; $p<.01$). However PF studies done in the first week of life did not show any statistically significant differences between the groups although resistance tended to be higher in Group I ($p=.08$).

	Group I	Group II
Compliance (ml/cmH_2O/kg)	.46 ± .06	.41 ± .06
Resistance (cmH_2O/L/sec)	227 ± 50	90 ± 19
Pulmonary Clearance Delay (%)	22 ± 3	33 ± 8
a-A O_2 (mmHg)	187 ± 56	217 ± 38
a-A CO_2 (mmHg)	9.2 ± 1.4	9.6 ± 1.9

We conclude that PF testing in the first week of life may not identify those infants at risk of developing CLD.

1261 MORBIDITY AND MORTALITY AMONG INFANTS WITH BIRTHWEIGHTS OF 1000 GRAMS OR LESS. E. Goldson, M. Kemper, J.A. Hernandez. Department of Perinatology, The Children's Hospital, Denver, Colorado

This paper reports our experience with 124 infants weighing 1000 grams or less at birth who were admitted to The Children's Hospital between January 1, 1978 and December 31, 1979. There were 57 males and 67 females with 106 infants being AGA and 18 being SGA. Sixty-four of the group (51.6%), 43 males and 21 females, expired within the first 18 months of life. Fifty percent died in the first 24 hours, 73.4% by the seventh day and 87.5% by day 27. An additional 12.5% died between the second and eighteenth month of life, 4 of them after discharge. Appropriateness for gestational age was not a factor in survival but birthweight was, with an increase in survival among the infants with birthweights greater than 800 grams. Factors associated with mortality were IVH, particularly Grade IV and air leaks. Among the 60 survivors at 2 years of age, 58.4% had PDA's, 63.3% had BPD, 31% had hydrocephalus and 3.2% had NEC.

Our data suggest that infants with birthweights of less than 800 grams with IVH and/or air leaks are at high risk for developing a clinically significant PDA, BPD and/or hydrocephalus.

1262 METOCLOPRAMIDE HAS NO EFFECT ON ALBUMIN BINDING OF BILIRUBIN, Glenn R. Gourley, William Mogilevsky and Gerard B. Odell, University of Wisconsin Hospitals, Department of Pediatrics, Madison, Wisconsin.

Metoclopramide (M) is a commonly used drug in Europe and is receiving increasing attention in the U.S. as more indications for its use are proposed. Since M increases both gastric emptying and lower esophageal sphincter tone, it might be thought useful in infants with feeding problems. However, if binding of M displaces bilirubin from albumin, its use in neonates would be limited. There is conflicting data regarding the albumin binding of M. We measured the ability of M to displace bilirubin from albumin while doing salicylate saturation (SI) tests on serum from hyperbilirubinemic neonates.

Pt	Serum Bilirubin (mg/dl)	SI	ΔOD-460 Sal-B	M_1-B	M_2-B
1	14.8	4.1	.009	0	-.001
2	21.0	4.2	.013	-.001	.001
3	4.0	6.7	.004	-.002	0
4	6.0	6.7	.006	.001	.001
5A	14.0	2.4	.005	0	.001
5B	14.6	3.2	.007	.001	0
5C	16.0	3.4	.008	0	.002
6	17.6	8.0	.021	0	0
7	16.4	4.3	.011	.001	.002

(B=buffer; M_1=200 ng/ml; M_2=220 µg/ml)

M causes no significant displacement of bilirubin from albumin in serum from hyperbilirubinemic neonates.

1263 DELAYED ONSET OF HEAD GROWTH AND DEVELOPMENT IN CALORICALLY DEPRIVED PREMATURE INFANTS. Michael Georgieff, Gilberto R. Pereira, Rosalind Ting. (Spon. by W.W. Fox). Univ. of Pa. Sch. of Med., and Dept. of Peds., Children's Hospital of Philadelphia, Philadelphia, PA.

The effect of caloric intake in the neonatal period on head growth and subsequent development was studied in 19 neurologically normal, appropriate for gest. age 32 wk premature infants who had no clinical evidence of congenital anomalies, clinical intraventricular hemorrhage, seizures, hypoglycemia, severe acidosis (pH 7.10), or retrolental fibroplasia. At followup 2 groups were identified: 10 infants, who exhibited developmental catch-up for their 2 mos of prematurity before a chronologic age of 12 mos (Group I), and 9 infants who exhibited this catch-up between 12 and 18 mos of age (Group II). The 2 groups were comparable in Mean ± SEM gest. age (32 ± 0.4 vs. 32 ± 0.6 wks), birthweight (1.48 ± .04 vs. 1.61 ± .12 kg), birth head circumference (28.1 ± 0.2 vs. 28.6 ± 0.4 cm), Apgar scores, degree of hyperbilirubinemia, days of intubation (3.0 ± 0.9 vs. 6.2 ± 1.6 days) and socio-economic status. During the first 2 wks of life infants in group II had: 1) significantly lower caloric intake (mean ± SE 65.0 ± 7.6 vs. 83.7 ± 5.1 Kcal/kg/d, $p=.05$). 2) delayed time of onset for head growth (Mean ± SEM 2.1 ± 0.4 vs. 0.5 ± 0.2 wks, $p < .02$) and 3) decreased cumulative head growth (Mean ± SEM week 1: 0.38 ± .07 vs. 0.00 ± 0.00 cm, $p < .001$; week 2: 1.35 ± .15 vs. 0.25 ± 0.10 cm, $p < .001$) as compared to patients in Group I. The differences in cumulative head growth between the 2 groups persisted through 6 wks of hospitalization and remained significantly different at 6 mos and 12 mos followup. This study indicates that inadequate caloric intake and delayed onset of head growth in the neonatal period are two factors that are associated with subsequent head size and delayed developmental catch-up of premature infants.

1264 NEONATES RECEIVING PROLONGED INTENSIVE CARE: OUTCOME AT TWO YEARS. Steven J. Gross and Carol O. Eckerman (Spon. by Samuel L. Katz). Duke University Medical Center, Department of Pediatrics, Durham.

Advances in perinatal care have resulted in prolonged hospitalization for some infants who otherwise would have died soon after birth. These infants incure the greatest expenditure of resources for an uncertain long-term outcome. From Oct., 1978 to Oct., 1979, 23 of 351 (6.6%) infants admitted to our nursery required intensive care for ≥90 days (mean: 148 days; range: 90-386). Underlying conditions included bronchopulmonary dysplasia, necrotizing enterocolitis, and extreme prematurity. Nine (39%) subsequently died- 6 prior to discharge (mean age: 157 days; range: 110-198), and 3 after discharge (at 10, 19, and 22 months). These latter 3 infants were developmentally handicapped at the time of death. All 14 infants alive at 24 months were evaluated. Five (36%) were microcephalic, 5 (36%) had major neurological defects (spastic diplegia, hydrocephalus and blindness), and 10 (71%) had Bayley Mental Developmental Indices (MDI) <80 (6<50). Poor outcome was associated with slow postnatal head growth (<3rd percentile), prolonged mechanical ventilation, and longer hospitalization. All 9 infants requiring mechanical ventilation for >90 days subsequently died or survived with major neurological defects and MDI<50. Only 4 infants were free of neurological defects and had MDI>80; none of these had mechanical ventilation for >90 days, poor head growth or hospitalization >107 days. In summary, outcome for infants requiring ≥90 days of intensive care was disappointing; 83% subsequently died or survived with a major developmental handicap.

1265 TRANSIENT DECREASE IN HEART RATE WITH RESPIRATORY PAUSES IN NORMAL AND ABORTED SIDS INFANTS DURING SLEEP. G.G. Haddad, R.B. Mellins, Columbia U, Coll. of P & S, Babies Hospital, Department of Pediatrics, N.Y.

We have shown that the frequency and average and maximum duration of respiratory pauses (RP) in infants with aborted Sudden Infant Death Syndrome (A-SIDS) do not differ from those in normal infants (Amer.Rev.Resp.Dis. 123:183,1981).Because the heart rate (HR) is increased and HR variability decreased in A-SIDS throughout REM and quiet sleep, we studied the HR pattern during RP (expiratory time > 2 sec).We studied all 252 RP seen in 19 studies of 5 normal infants and all 171 RP seen in 16 studies of 5 A-SIDS infants during sleep in the first 4 months of life.HR was measured with an accuracy of 0.2 msec and ventilation and respiratory timing were measured using the barometric method.Sleep was staged with EEG,EOG and EMG.Only half of all RP were associated with a change in HR and these were 1.5-3 times more frequent in quiet than in REM sleep in both groups of infants.The typical HR pattern (>75%) consisted of a transient decrease in HR beginning within 0.5-3 sec of the onset of the RP;return of HR towards baseline occurred within the RP and was completed before or shortly after the end of the RP.The maximum drop in HR was 54% of baseline (lowest HR=85 bpm) in both groups of infants,and there was no difference in HR pattern between normal and A-SIDS infants.We conclude that during sleep in the first 4 months of life: 1)a decrease in HR is seen in only half of RP in both normal and A-SIDS infants; 2)the rapid onset of the drop in HR suggests that hypoxemia is not the cause for the HR slowing and 3) the HR pattern associated with RP in A-SIDS infants is not different from that in normal infants.

●1266 INTRALIPID(IL) ALTERATIONS IN PULMONARY PROSTAGLANDIN (PG) METABOLISM AND GAS EXCHANGE. Joseph R. Hageman, Kristine McCulloch, Bruce R. Ouade, Michael A. Cobb, Lauren Pachman, and Carl E. Hunt. Northwestern Univ., Children's Memorial Hosp., Department of Pediatrics, Chicago.

IL contains PG precursors(linoleic acid 56 mg/ml). To assess the effects of IL on pulmonary gas exchange and PG metabolism, we have studied 64 unanesthetized rabbits with chronic right atrial and aortic catheters; 40 received IL 4.0 ml/kg over one hour and 24 received a control saline infusion. Half of each group had oleic acid(OA)-damaged lungs, and half of each group received indomethacin(I). PG levels were measured by RIA. There were no baseline differences between the IL and control groups for pH, $PaCO_2$, $P(a-A)CO_2$, blood pressure, triglyceride(TG) level, or for arterial(a), venous(v), or a-v difference (PG gradient) for PG E_2 and PG 6-keto $F_{1\alpha}$. Blood sampling was repeated after the infusion and the difference (± SEM) between baseline and one hour was compared by paired t test. Significant differences occurred only in the OA groups receiving IL (Table). The only

Group	TG mg/dl	$P(a-A)CO_2$ mmHg	PaO_2 mmHg	PULMONARY GRADIENT(pg/ml) PG E_2	6-keto $F_{1\alpha}$
IL	543 ± 76 (p<.001)	6.0 ± 2 (p<.01)	−12 ± 3 (p<.001)	1030 ± 500 (p<.05)	700 ± 430 (p=.05)
IL + I	792 ± 144	3.0 ± 4	1 ± 9	−720 ± 700	100 ± 62

significant difference with I was the TG increase (p<.001). Without I, IL infusion resulted in significant differences for all parameters (p values in Table). In summary, the gas exchange impairment occurring with IL infusion is related not to hyperlipemia but rather to increased pulmonary PG synthesis.

1267 HUMAN SURFACTANT (HS) SUBSTITUTION IN A CASE OF RDS. Mikko Hallman, Howard Schneider, T. Allen Merritt, Louis Gluck. Univ. of Calif. San Diego, Dept. of Pediatrics, La Jolla, California.

Surfactant substitution is hampered by lack of effective synthetic surfactant & possible side effects of animal protein. Biologically active HS was isolated from amniotic fluid of 6 term pregnancies at C-section & we report the 1st case of treatment of RDS with HS. The 1st possible patient was twin B (B), male, BW 960 gm, GA 27 wks, chosen for a potentially greater benefit from treatment than twin A (A) female, BW 980 gm, ruptured membranes for 24 hr. Both infants required ventilation from birth. RDS was diagnosed by x-ray & phospholipid analysis of lung effluent. At 4.5 hr of age 70 mg HS in 3.5 ml of saline was instilled into the endotracheal tube, followed by 2 min. hand ventilation. Within 5 min. Pa_{O_2} rose from 70 mmHg to 265 (F_{IO_2} 1.0). Improved respiratory condition [↓mean airway pressure (MAP), ↓oxygen requirement, ↓PC_{O_2}, improved chest x-rays] was evident for at least 12 hr.

Time From	Birth HS	0.8 -3.6	4.5 0.0	6.5 2	9.5 5	15 10	20 15	25 20	35 30	45 40	75 70
MAP	A	11.0	10.5	10.5	10.3	8.3	5.9	5.4	5.2	7.5	4.7
(cmH_2O)	B	10.0	8.3	6.8	6.3	4.4	3.9	4.2	4.5	Hood	2.7
F_{IO_2}	A	.90	.80	.71	.77	.51	.41	.35	.34	.74	.32
	B	.80	1.00	.27	.27	.27	.70	.62	.33	.34	.22
Pa_{O_2}	A	44	94	90	74	66	59	66	60	66	60
(mmHg)	B	42	70	63	58	55	70	74	62	61	51

HS aborted the course of RDS. Further trial of HS is indicated.

Supported by NIH Grant No. HD10622.

1268 OUTBREAK OF C.DIFFICILE NECROTIZING ENTEROCOLITIS (NEC): A CASE FOR ORAL VANCOMYCIN THERAPY? VICTOR K.M. HAN, HAMDY SAYED, GRAHAM W. CHANCE, WAGIH A.K. SHAHEED, & DAVID G. BRABYN. Departments of Paediatrics and Microbiology, University of Western Ontario, London, Canada.

During a two-month period, thirteen infants in this NICU developed NEC, increasing the prevalence in inborns from 5.2 to 20.5/1000 live births. Fifty-seven perinatal and neonatal factors, many of which have been previously associated with NEC, were compared between the NEC infants and 17 unaffected inborn controls admitted concurrently. Apgar scores were higher ($p<0.05$), cord blood gases did not differ, vaginal delivery was more frequent ($p<0.05$), high umbilical catheters were used somewhat more frequently and prior exposure to broad spectrum antibiotics did not differ - in the affected group.

C.difficile cytotoxin was detected in the stools of 12 affected infants (92.3%) compared to 2 controls (11.8%) ($p<0.001$) and the organism was isolated in 8 affected neonates (61.5%) compared to none of the controls ($p<0.001$). Subsequent study revealed an endemic carrier rate in our NICU to be 14.2%.

The outbreak ceased upon institution of oral vancomycin therapy in cases and infant contacts and strict anti-infective measures in the NICU. This indicates an etiologic role of C.difficile in NEC. Oral vancomycin in the management of NEC was assessed by therapeutic response, drug levels and occurrence of side effects.

1269 PATENT DUCTUS ARTERIOSUS (PDA): A 19 MONTH EXPERIENCE WITH INTRAVENOUS (I.V.) INDOMETHACIN (INDO). J. Peter Harris, Thurman A. Merritt, (Spon. by Louis Gluck), University of Rochester and University of California, La Jolla.

Over a 19 month period 23% of preterm infants were found to have a symptomatic PDA. Spontaneous closure occurred in 44 and 67 infants required I.V. INDO (B.W. $\bar{x}$ 1256 ± 422 gm.; G.A. $\bar{x}$ 29 ± 4 wks.; age 8.6 ± 11.7 days). Successful closure with INDO occurred in 91% and 83% <1000 gm B.W. No differences were found between the number of doses required and B.W., G.A., or age at initial therapy.

34/67 exhibited ≥ 30% decline in urine output and 25/67 had transient ↑ BUN and/or creatinine but these subgroups were not identical. 4/67 developed acute renal failure. Occurrence of intraventricular hemorrhage and necrotizing enterocolitis in INDO infants were not different from the total preterm population. 1/67 developed cicatricial retrolental fibroplasia. Bronchopulmonary dysplasia was more frequent in infants with PDA but early closure revealed a decreased incidence. Only a single instance of late PDA reopening occurred. 6/67 died and only 1/67 was temporally related to PDA closure. Our data suggests that I.V. INDO successfully closes the PDA in infants ≤1000 gms. without significant complications owing to its administration.

1270 THE ESTIMATION OF TOTAL SERUM BILIRUBIN CONCENTRATION BY TRANSCUTANEOUS BILIRUBINOMETRY. Harry Harrison, Jr., (Spon. by Louis Gluck). Univ. of California, San Diego, Dept. of Pediatrics, La Jolla, California

A transcutaneous bilirubin meter (Minolta Camera Co.) was tested for accuracy on full-term and pre-term infants. This study differs from previous reports because the device was tested on ill full-term & pre-term infants. A linear relation exists between transcutaneous meter readings & serum bilirubin concentration. The transcutaneous meter can be used to predict total serum bilirubin concentration accurately in full-term infants off phototherapy (r=.90), pre-term infants with medical complications (r=.86), pre-term infants under phototherapy (r=.79), and infants with moderate skin pigmentation (r=.93). The accuracy of the transcutaneous meter is improved when patients are grouped by weight, independent of medical complications. The close standard errors of estimate bewteen the spectrophotometric determination of bilirubin (± 1 mg%) & the readings of the transcutaneous bilirubin meter (+ 1.5 mg%) makes the device useful in the neonatal ICU.

●1271 ESTIMATION OF THE VENTILATORY RESPONSE TO CARBON DIOXIDE IN NEWBORN INFANTS USING SKIN SURFACE ELECTRODES. Thomas A. Hazinski, John W. Severinghaus, Mark S. Marin, William H. Tooley. Dept. of Pediatrics, Anesthesia, and the Cardiovas. Research Inst., Univ. of California, San Francisco.

Skin surface blood gas measurements are particularly useful in the study of ventilatory control since they reduce the tactile stimuli to breathing. We have used the change in skin surface CO_2 tension ($PsCO_2$) as a measure of ventilation. The calculation is based on the fact that if CO_2 production is constant, the change in ventilation from one level to another is inversely proportional to the change in $PsCO_2$. When CO_2 is in the inspired gas, the fractional change in ventilation relative to air breathing (VI) is equal to $Ps_oCO_2/Ps^*CO_2-P_ICO_2$; Ps_oCO_2 is the $PsCO_2$ during air breathing and the denominator is the difference between skin surface and inspired CO_2. We studied 14 infants from 28-40 wks gestation at weekly intervals. Six infants had serious apnea. The infants breathed each gas for 10 minutes during quiet sleep with electrodes attached. We calculated a VI while the infants breathed 0, 2, and 4%CO_2, and derived a slope of VI, which is similar to a standard ventilatory response slope. 35 studies were divided into 3 groups: Infants with apnea(11), infants whose apnea had resolved (9), and non-apneic infants(15). Apneic infants had a significantly reduced VI slope compared to non-apneic infants. When apnea disappeared, the VI slope increased into the range measured in normal infants. In each group, the VI slope was significantly related to post-natal age. Using this new method, we conclude that apneic infants have a reduced response to CO_2, and that the resolution of apnea is associated with a normal CO_2 response.

●1272 THE DIURETIC PHASE OF RESPIRATORY DISTRESS SYNDROME (RDS) AND RELATIONSHIP TO PULMONARY PHYSIOLOGY. David P. Heaf, Jaques Belik, Alan R. Spitzer, Michael H. Gewitz, William W. Fox. Univ. of Pa. Sch. of Med., Dept. of Peds, Children's Hospital of Philadelphia, Phila., PA.

Previous studies have shown clinical improvement in infants with RDS around the time of spontaneous diuresis. To evaluate the relationship between improvement in pul. function and spont. diuresis in RDS, 9 premature infants, B.W. 1570 gm (range 955-1985 gm), G.A. 32 weeks (range 28-36 wks) requiring mechanical ventilation for RDS were studied. Observations were made at a mean age of 11.9 hrs prior to the onset of diuresis, at onset of diuresis, at maximum urine output (mean age 44.9 hrs) and at 24 hours after maximum urine output. Inspired oxygen, ventilator frequency (f), peak inflating pressure (PIP), art. blood gases, functional residual capacity (FRC), dyn. lung compliance (C_L) and 8 hourly fluid input (I) and urine output (O) were recorded. Diuresis was defined as output/input>100%. Data were analyzed for O/kg/hr, I/kg/hr, FRC, C_L, alveolar arterial oxygen gradient ($AaDO_2$), f and PIP. Prior to diuresis FRC decreased from mean ± SEM of 16.2 ± 2 ml/kg to 13.3 ± 1.2 mlg/kg, C_L decreased from 2.5 ± 0.3 ml/cmH_2O (P< 0.05), indicating worsening of disease. There was no change in $AaDO_2$, PIP or f over this period. 17.2 hrs later at the time of urine output FRC had increased 36% to 18.1 ± 1.0 ml (P < 0.005), C_L had increased 60% to 2.88 + 0.42 ml/cmH_2O (P< 0.025), $AaDO_2$ had decreased from 246 ± 27 to 184 ± 30 torr (P< 0.005) and PIP had decreased from 14.9 ± 2.2 cm/H_2O to 11.3 ± 2.1 cm/H_2O (P <0.05). 24 hrs after max. urine output there was no further improvement in FRC, C_L or PIP, but f and $AaDO_2$ continued to decrease. These data show that the pulmonary function in RDS rapidly improves after the onset of diuresis. Thus, diuresis can act as a marker for weaning the ventilator.

1273 PARENTAL INFORMATION AND CIRCUMCISION IN HIGHER EDUCATED, HIGHLY MOTIVATED COUPLES. Alfredo J. Herrera, Bevi Cochran, Anne Herrera, Barbara Wallace (Sponsored by John Neff), St. Agnes Hospital, Department of Pediatrics, Baltimore, Maryland.

	Group I	Group II
Maternal Age	29.5+3.6	27.1+4.2
Parity	0.75±0.70	0.65±0.89
College Education	73%	83%
Single Mothers	0%	3.85%
Teenage Mothers	0%	2%
Breast Feeding	81%	92%
Circumcised Males	88%	88%

Circumcision is performed in most male neonates born in America. The American Academy of Pediatrics emphasizes the importance of parental information in the decision making process.

If correct medical information is going to make a difference in the performance of this procedure, the population more likely to show this difference is the higher educated, highly motivated one. Parents attending childbirth classes (Lamaze) were randomized in two groups. Group I was given verbal and written information on the risks and benefits of circumcision following the guidelines of the Ad Hoc Task Force on circumcision at about the 7th month of pregnancy; Group II was not given any special counseling.
There were 125 couples involved in our study, 61 in Group I and 64 in Group II; both populations were closely matched. There was not statistical significant difference in the incidence of circumcision in these two groups.
Correct medical information does not seem to make any difference in the performance of this surgical procedure, even in the higher educated, highly motivated parents.

1274 RELATIONSHIP OF PRENATAL AND NEONATAL FACTORS TO SIDS: PRELIMINARY RESULTS OF THE NICHD COOPERATIVE EPIDEMIOLOGICAL STUDY OF SUDDEN INFANT DEATH SYNDROME (SIDS) RISK FACTORS.
L.Hillman, H.J.Hoffman, M.Jones, G.vanBelle, J.Goldberg, D.T.Janerich, J.F.Kraus, J.Pakter, D.R.Peterson, K.Damus, E.G.Hasselmeyer. National Institute of Child Health and Human Development, NIH, Bethesda, Md.

Preliminary analyses of interview and medical record data, using 400 of 800 pathology confirmed singleton SIDS cases and living controls matched for age only (control A) and for age, birthweight, and race (control B), confirmed an increased risk of SIDS with a) young maternal age, b) increased parity with marked sparing of firstborn, c) black race, d) male sex, e) maternal smoking, f) prematurity, and g) in-utero growth retardation. Growth retardation involved weight, length, and head circumference, failure to "catch up", and was seen primarily in SIDS cases with maternal smoking. There were no differences between cases and control A or B in prenatal factors (prepregnancy conditions, pregnancy complications including toxemia or anemia, weight gain, premature rupture of membranes) or in delivery factors (C-sections, presentation, lengths of labor, anesthesia, analgesia, complications of delivery). Apgar scores at 1 and 5 minutes were not different. Need for other than usual types of care after birth was greater for SIDS infants than for control A's, but not control B's. Yet, in the nursery, SIDS infants, independent of prematurity, growth retardation, or type of feeding, had a significantly greater incidence than either control A's or B's of tachypnea, respiratory distress, apnea, cyanosis, bradycardia, tachycardia, vomiting, abnormal cry, irritability, and temperature instability including fever. The data suggest, although prenatal abormalities were not identified, that SIDS infants as a group are different at birth.

1275 CLONIDINE IN NEONATAL NARCOTIC ABSTINENCE SYNDROME, Hoder, E.L., Leckman, J.F., Poulsen, J., Ehrenkranz, R.A., Cohen, D.J., (sponsored by Ian Gross) Yale University School of Medicine, Yale Child Study Center, Yale New Haven Hospital, Department of Pediatrics, New Haven, Connecticut.

The neonatal narcotic abstinence syndrome (NNAS) is characterized by hyperirritability, feeding problems, autonomic instability and seizures in newborns born to mothers addicted to narcotic agents. We report the successful treatment of NNAS in 4 infants of addicted mothers with clonidine hydrochloride, a centrally active α-adrenergic agonist that reduces noradrenergic sympathetic activity. After the onset of NNAS severe enough to warrant pharmacologic intervention, clonidine was begun at 0.5-1.0 µg/kg/day. Response was measured by means of serial physical examinations and by a 14 item check-list that was completed non-blindly by the nursing staff. The major symptoms of NNAS were rapidly ameliorated in each of the infants after a total daily dose of 2-4 µg/kg/day was achieved. The length of required treatment with clonidine, averaging 1-2 weeks, compares favorably with other treatment regimens. No toxic side effects of clonidine were seen. Clonidine blood levels obtained during the treatment course ranged between 0.1-0.3 ng/ml with peak values occurring within 3 hours of an oral dose.

These findings suggest that clonidine may be a safe therapeutic agent for the treatment of NNAS. A double-blind study to determine the relative efficacy of phenobarbital vs. clonidine in NNAS is underway.

● 1276 TRANSCUTANEOUS OXYGEN ($P_{tc}O_2$) LEVELS IN NORMAL INFANTS AND SUBSEQUENT SIBLINGS OF SIDS (SSIDS). Toke T. Hoppenbrouwers, Joan E. Hodgman, Luis A. Cabal, Helen Carney, Ruth Kidd. Univ. of So. Calif. School of Med., LAC-USC Med. Ctr., Dept. of Ped., Los Angeles.

$P_{tc}O_2$ tracings were obtained in 12 control infants and 12 SSIDS at 1 and 3 months of age as part of a larger polygraphic study. The first hour of recording was selected and every fifth minute was sampled. Electrode placement and temperature were held constant. Although the variability was elevated in Active sleep, no significant sleep state differences in $P_{tc}O_2$ levels were found and the values were therefore averaged for each infant. Gender distribution was uneven. Although to date no data suggest gender differences in oxygenation, this variable needs to be examined further. In both study groups 7 infants (63.6%) exhibited lower values at 1 than at 3 months of age. With increasing age the skin is expected to thicken, resulting in poorer diffusion; consequently, the elevated value at 3 months of age represents a true phenomenon. The levels at 1 month here are lower than those reported in normal newborns. Normal infants, therefore, have a period of reduced oxygenation which precedes the age of highest risk for SIDS. SSIDS at 3 months of age exhibited significantly lower $P_{tc}O_2$ levels than controls ($p < 0.05$). Indirect evidence suggests that infants dying of SIDS have had preexisting mild chronic hypoxia. This is the first direct evidence of reduced O_2 levels in infants at increased risk for SIDS.

	Oxygen Levels in mm Hg	
	1 month	3 months
Control	69.7(±11.8)	75.9(±7.8)
SSIDS	62.8(± 6.9)	66.7(±9.2)

1277 TOTAL BILIRUBIN FORMATION AND VITAMIN E LEVELS IN PRETERM INFANTS. Andrew O. Hopper, Ronald S. Cohen, Susan M. Shahin, Cynthia H. Meyers, Clinton R. Ostrander, and David K. Stevenson (Spon. by Philip Sunshine), Dept. of Ped., Stanford Univ. Sch. of Med., Stanford, CA.

Total bilirubin formation (TBF) in the first few days of life was evaluated in 48 preterm infants [28-37 wks; mean birth weight 1.72 ± .54 (SD) kg] breathing room air and receiving no supplemental vitamin E. The pulmonary excretion rate of CO (Ve_{CO}) was used to estimate TBF. Ve_{CO} was elevated [16.4 ± 6.5 µl/kg/hr; n=32] compared with term infants [13.9 ± 3.5; n=20]. Serum tocopherol (ST) levels in preterms [n=22], as noted by others, ranged widely [0.33-1.95 mg%; mean = 0.75 ± 0.37], and did not correlate with gestational age, birth weight or Ve_{CO}. Despite routine treatment with a minimum of 25 mg per day of α-tocopheryl acetate, Ve_{CO} and Ve_{CO}/Hb values were elevated over the first month.

Week	Hb(mg%)	Ve_{CO} (µl/kg/hr)	Ve_{CO}/Hb	Vit.E (mg/dl)
1	16.05(48)	16.6(32)	1.04(32)	0.75(22)
4	11.7(11)	15.2(10)	1.52(8)	3.07(9)

In addition, TBF relative to an estimate of the circulating RBC mass (Ve_{CO}/Hb) appeared to increase during these four weeks. These findings suggest that preterm infants may have prolonged elevation of TBF after birth, despite attaining vitamin E levels previously shown to insure "sufficiency." Hemolysis caused by other deficiencies, ineffective erythropoiesis, or turnover of hepatic heme may contribute to this phenomenon.

1278 OBSTETRICAL FACTORS ASSOCIATED WITH PERIVENTRICULAR-INTRAVENTRICULAR HEMORRHAGE (PIH). Jeffrey D. Horbar, Marykay Pasnick, Kathleen Leahy and Jerold F. Lucey. University of Vermont College of Medicine, Department of Pediatrics, Burlington, Vermont

Obstetrical factors may have a role in the pathogenesis of PIH. We performed a retrospective analysis of infants with birthweights ≤ 1200 grams in order to investigate this possibility. Data was available for 60 of 63 infants admitted consecutively over a two-year period ending 11/81. Obstetrical data was obtained from hospital records. PIH was diagnosed using ultrasonography or at autopsy. Six infants without evidence of PIH were excluded from the study. Three died prior to age 48 hours, and 3 did not have ultrasound scans after 48 hours of age. Fifty-four infants were included in the study. Fifty-one had one or more diagnostic ultrasound brain scans after 48 hours of age and 3 had autopsy-proven PIH. Twenty-nine study infants had evidence of PIH. The combined length of the first and second stages of labor was recorded for each infant (< 6 hours or ≥ 6 hours). Associations between length of labor and PIH (χ^2 = 4.80, p = 0.03) and between mode of delivery and PIH (χ^2 = 4.80, p = 0.03) were demonstrated using the method of Mantel-Haenszel. Labor < 6 hours and c-section were associated with lower risk of PIH than labor ≥ 6 hours and vaginal delivery. The mean birthweights and gestational ages did not differ significantly among the labor and mode of delivery groups. We conclude that labor ≥ 6 hours and vaginal delivery may be associated with an increased risk of PIH in infants with birthweights ≤ 1200 grams.

1279 FEASIBILITY OF STERILE COLLECTION AND ANTICOAGULATION OF AUTOLOGOUS CORD BLOOD (ACB) FOR TRANSFUSION. Joan Hulme, Margaret N Watkins, W M Gooch, L Bucciarelli (Spon. by M E Lahey) Univ of Utah, Dept of Peds & Path, SLC, Utah

While transfusion with ACB has theoretical advantages, its safety remains to be adequately tested. We therefore studied anticoagulation, sterility & effects of filtration of ACB obtained at term deliveries. Immediately after clamping cord & preparing it with iodophor obstetricians drew blood by puncturing the umbilical vein successfully 76/77 times with yield of 28.9±0.5 ml ($\bar{X}$±SE). Since we observed that syringes flushed with aqueous heparin contained 20-2000 IU, sterile 30 ml syringes with 60 IU lyophilized heparin were prepared. Adequacy of anticoagulation with 1.5 to 2.5 IU/ml heparin was determined by 2 methods. Whole blood clotting time was assayed by a continuous thromboelastogram over 4 hrs & showed no evidence of thrombin formation. A sample assayed until it clotted showed a pattern of normal clotting factors. Fibrin split products determined by latex agglutination were normal: 2 ug/ml (17/25) & 10-40 ug/ml (8/25). Platelet counts did not decrease (291,600± 64,440/mm^3 initially vs 332,400±67,830/mm^3 at 3.5 hrs). In the 2 instances of positive cultures, sterile technique was known to have been compromised. After filtration of ACB, microscopic examination of the filter (20u) showed no debris (11/48), small clots (3/48), & Wharton's jelly and/or small strands of fibrin (34/48). Plasma Hgb following filtration of ACB during 1st hr was 15.7±6.0 mg/dl & after 1st hr 29.1±7.0 mg/dl - values within transfusion standards. We conclude that sterile ACB can be drawn in sufficient quantity for transfusion, anticoagulated with 1.5 to 2.5 IU/ml heparin for 4 hrs, & filtered without excessive hemolysis.

●**1280** INHIBITION OF SURFACTANT FUNCTION IN THE RESPIRATORY DISTRESS SYNDROME (RDS). Machiko Ikegami, Harris C. Jacobs, and Alan H. Jobe, UCLA School of Medicine, Harbor-UCLA Medical Center, Department of Pediatrics, Torrance.

The surface active properties of airway secretions collected by routine suctioning following intubation of 10 infants with severe RDS and 10 infants without RDS (control) were studied. The minimum surface tension (Min.ST) in dynes/cm of each airway sample (AS) was measured using the dynamic alveolar model. The Min. ST of AS from the infants with RDS versus control were 27.3±3 versus 6.3±1.1. Surfactant with Min.ST of 1.4±1 was recovered by centrifugation from samples from infants with RDS. A supernatant fraction from AS from RDS infants raised the surface tension of natural sheep surfactant, while similar fractions from control infants raised the ST much less per mg protein. The AS from control infants contained 2.1±0.6 μmoles phosphatidylcholine (PC)/mg protein, significantly more PC than those from infants with RDS (0.4±0.2 μmoles PC/mg protein). The phospholipids of the surfactant recovered from the initial AS from infants with RDS versus controls contained no or trace amounts of phosphatidylglycerol (PG) versus 6.5±1.7% PG in control infants. Sequential daily samples documented a continuous fall in Min.ST from 27.2± 2.8 over 5 days until extubation of 6 infants with RDS. At extubation the mean Min.ST was 5.7±2.3, a mean value very similar to that measured for control infants. This study documents the presence of substances that inhibit the surface tension lowering properties of surfactant in the airways of premature infants with respiratory distress syndrome.

1281 HOW LAMBS WITH RDS ACCUMULATE A SURFACTANT POOL WITH TIME. Harris C. Jacobs, Alan H. Jobe, Machiko Ikegami, Sally J. Jones, UCLA School of Medicine, Harbor-UCLA Medical Center, Department of Pediatrics, Torrance.

Isotope dilution curves with ^{3}H labeled natural surfactant (^{3}H-NS) and measurements of surfactant phosphatidylcholine (PC) were used to measure changes in PC pool sizes with time in lambs with RDS. All lambs were delivered by C-section at 135-136 days gestational age and were supported with infant ventilators with constant settings, except peak inspiratory pressure (PIP) was varied to normalize pCO_2. The lambs had normal blood gases at sacrifice. 11 lambs received a tracer dose of ^{3}H-NS mixed in fetal lung fluid at birth and airway samples were collected hourly for 10 hours. When the 11 individual curves were grouped (n= 3 or 4) based on final PC pool size, the shapes of the curves were similar, indicating equivalent accumulation kinetics of PC, independent of final pool size. The mean curve for all the data showed an asymptotic increase in PC from 4.8 μmoles/kg at 0 time to 58.2 μmoles PC/kg at 5 hours. Subsequently, the PC pool size increased linearly (r=0.99) by only 1.9 μmoles/kg/hr. We interpret the initial release of ∿ 53 μmoles/kg PC to represent secretion of surfactant stores, and the slow subsequent increase to be the baseline secretory rate. 22 other lambs were sacrificed at 40 min, 1.5, or 3 hours after birth, and the actual PC pool size recovered by alveolar wash was consistent with the curve derived from the ^{3}H-NS data. The experiments document 1) the time course of release of surfactant stores by premature lambs with RDS, and 2) estimate the slow accumulation of de novo synthesized surfactant PC after birth.

1282 DEFICIENCY OF ALVEOLAR MACROPHAGES (AM) IN PRIMATES WITH HYALINE MEMBRANE DISEASE (HMD). R.F. Jacobs, C.B. Wilson, S. Palmer, D. Kessler, J. Murphy, G. van Belle, E. Chi, and W.A. Hodson, Dept. of Pediatrics, Univ. of Washington, Seattle, WA.

AM protect the lung from infection and are the principal lung scavengers of oxygen radicals and effete surfactant. AM are derived from blood monocytes that are attracted to the lung by unknown factors. We sought to determine the role of lung phospholipid (PL) in this process and the potential role of AM in lung protection and healing in HMD. Bronchopulmonary lavage was performed in a uniform manner on newborn, premature primates (M. nemestrina); 10 of these (gestational age; GA=141±7 days) could be classified as to the presence or absence of HMD. The number of AM recovered correlated positively with PL in the lavage fluid (PL wash) and absence of HMD ($p<0.01$), GA and postnatal age (PNA) ($p<0.05$) but did not correlate ($p>0.1$) with weight, PL content of lung, or lung dry weight. By multivariate analysis, presence of HMD correlated negatively in decreasing order of significance with GA, PL wash and AM; the number of AM correlated most positively with PL wash followed by absence of HMD. When data from 8 additional animals sacrificed at or within 15 min of birth were included in this analysis, number of AM correlated with PL wash and PNA ($p<0.01$). These data suggest that components of lung PL stimulate egress of monocytes into the lung to form AM; the deficiency of AM in severe HMD may predispose to lung damage and impede repair. Additional study of AM in this model may provide important data on the role of AM in the pathogenesis of HMD.

1283 SERIAL CREATINE PHOSPHOKINASE ISOENZYME CHANGES IN HEALTHY AND SICK NEWBORNS R. Jedeikin, R. Primhak, S.M. Makela, A. Shennan, P.R. Swyer, G. Ellis, R.D. Rowe, Div. of Pediatric Cardiology and Perinatal Medicine and Dept. of Biochemistry, Hospital for Sick Children, Toronto.

Creatine kinase (CK) and its isoenzymes were measured in cord and capillary blood from term newborn infants at 5-8 h, 24-33 h, and 72-100 h after birth. Babies born after uncomplicated labour and delivery, and with a normal hospital course, were classified as "normal" (n=45), those born after complicated labour and delivery with birth asphyxia "sick" (n=20). Mean CK activity (U/L) in cord blood from the healthy and sick groups was 185 (SD=73) and 568 (SD=1181) respectively. At 6 h, corresponding figures were 536 (SD=236) and 3878 (SD=7088). At 24 h, levels were 494 (SD=254) and 4504 (SD=9275) for the healthy and sick babies respectively. By 72 h, levels fell to 288 (SD=163) and 1020 (SD=1870). CK-MM isoenzyme followed a similar pattern. CK-MB isoenzyme increased after birth from a mean of 3 (SD=3) to 25 (SD=28) at 6 h in the healthy group and 14 (SD=28) to 296 (SD=610) in the sick group, and by 24 h had fallen to means of 18 (SD=14) and 152 (SD=331) respectively. By 72 h there was a further fall in both groups. CK-BB isoenzyme followed a similar pattern. The rapid rise and fall in CK-MB and CK-BB activity observed in the sick infants suggest that enzyme release (from the skeletal muscle, myocardium or brain) occurs as a consequence of some undefined injury before, during or shortly after birth.

1284 COMPUTED AXIAL TOMOGRAPHY (CT SCAN) IN FETAL ALCOHOL SYNDROME INFANTS (FAS). R.C. Jhaveri, W. Rosenfeld, C. Laqui-Pili, R. Giridharan, G. Hotson, S. Flicker, H.E. Evans, Department of Pediatrics and Radiology. Jewish Hospital & Medical Center/SUNY Downstate Medical Center. Brooklyn, NY

Alcohol consumption during pregnancy is a well known cause of multiorgan anomalies and developmental retardation in newborns. Absent corpus callosum in experimental animals exposed to ethanol has been demonstrated but the incidence of this and other CNS anomalies in humans is unknown. We performed CT scan in 20 infants with classic features of FAS during hospital stay. They included 9 males, 11 females with mean gestation age of 33.3 wks and mean birthweight of 2323 ± 48 gms.

Abnormalities were found in 3 of 20. Two female infants showed absence of corpus callosum and a third female had evidence of prominent cortical sulci suggestive of cortical atrophy. The 2 patients with absent corpus callosum had the most severe phenotypic expression of FAS in the group.

The 15% incidence of detectable CNS anomalies suggests that CT scan should be considered in clinical investigation of infants with FAS. The correlation of these findings with neurologic and developmental abnormalities will be determined by long term followup study.

●1285 EFFECTS OF SURFACTANT TREATMENTS ON CARDIAC OUTPUT AND LUNG FUNCTION IN LAMBS. Alan H. Jobe, Harris C. Jacobs, Machiko Ikegami, Sally J. Jones, UCLA School of Medicine, Harbor-UCLA Medical Center, Department of Pediatrics Torrance, CA.

14 lambs at 134-136 days gestational age were delivered by C-section and placed on infant ventilators. The settings were held constant at FiO_2 of 1.0, rate of 20/min, insp. time of 1 sec and PEEP of 2 cm H_2O. Peak inspiratory pressure (PIP) was varied to control pCO_2. At 5 hrs of age all lambs received 50 mg natural sheep surfactant (NS) lipid/kg by tracheal instillation. Cardiac output (CO) with regional distribution by microsphere injection, mean pulmonary artery pressure ($\overline{PA}$), mean aortic pressure ($\overline{Ao}$) and arterial blood gases (ABG) were all measured pre and 20 min post NS. There were 6 responders (R) and 8 non-responders (NR) to NS based on ABG changes. All values for R vs NR pre NS were different ($p<.01$) except $\overline{PA}$.

	pH	pO_2	pCO_2	$\overline{Ao}$	$\overline{PA}$	PIP	CO
R pre NS	7.16±.02	66±7	65±3	47±5	32±5	36±2	195±60
R post NS	7.29±.02*	209±47*	46±3	40±4	29±3	36±2	195±25
NR pre NS	7.35±.03	273±31	37±3	61±2	33±6	24±1	276±14
NR post NS	7.28±.03†	255±50	43±4†	57±2	35±6	25±1	247±14*

*p<.01, †p<.05 compared to pretreatment group

CO and regional flow in R did not change following NS. In NR the flow to the carcass and adrenals decreased while the flow to the GI tract increased. Other organ flows remained unchanged. Conclusions: 1) Only the lambs with severe RDS responded to NS. 2) Blood gas values deteriorated and CO fell in lambs with less severe RDS following NS.

1286 PREVALENCE OF ENAMEL HYPOPLASIA IN INCISORS OF LOW-BIRTHWEIGHT INFANTS. D.Johnsen, M.Hack, C.Krejci, A. Fanaroff. Dept. Ped., RB&C Hosp.,CWRU, Cleveland,O

The dental defects among recent very low birthweight graduates from neonatal intensive care are poorly documented. Dental examinations were completed on 44 very low birthweight infants mean BW 1.2 Kg, mean G.A.-28.8 weeks at age 20 to 36 months. Strikingly one or more hypoplastic or hypocalcified incisors were found in 22 (50%) of the children including enamel hypocalcification in 15 (34%) and hypoplasia in 8 (18%). Maxillary central incisors were involved in 19 (86%) of the 22 cases, maxillary lateral incisors in 5 (22%) and mandibular central incisors in 3 (14%) of the cases. Hypoplasia and hypocalcification had the same pattern and followed lines of enamel formation. The lesion was limited to the middle third of the incisal edge in 13 (60%) and followed a circular pattern in 14 (64%) involving always the middle third with one exception involving the cervical third.

No significant differences in the birth weight, gestation or Hobel antepartum, intrapartum and neonatal risk scores were found between infants with enamel hypoplasia and those without. The incidence of asphyxia, respiratory distress syndrome and jaundice did not differ between groups. Furthermore caloric intake during the first week, duration of suboptimal caloric intake (<80 cal/kgm/day) and growth during the prenatal and study period was similar. An association with hypoxia and hypercarbia was noted. ($p<.054$).

The role of early nutrition, blood gases and calcium dynamics in the etiology of this condition need to be further elucidated.

1287 MORBIDITY SCORE FOLLOWING ACTIVE RETINOPATHY OF PREMATURITY (ROP). SUMMATION OF OUTCOME IN FELLOW EYES L. Johnson, G. Quinn, Univ of Penn Med Sch. Pennsylvania & Children's Hospitals, Depts. Peds & Ophth, Phila. Pa.

A scoring system is presented for reporting ophthalmologic findings in fellow eyes of infants recalled for follow-up of active ROP after age 1 year. Visually significant differences in findings between eyes-no light perception (NLP) vs count fingers (CF), or CF vs high myopia correctable to 20/20 - is not uncommon following the more severe stages of retinopathy. For example, among infants with at least 3-plus active ROP in the nursery (prominent dilitation & tortuosity of vessels in the posterior pole with obvious intravitreal neovascularization in at least 2 quadrants) we found differences in long term visual morbidity of this magnitude or greater in 17% of 23 untreated infants and in 30% of infants in whom high dosage E Rx was initiated at 3-plus active disease. Considering visual outcome on the basis of summed findings in fellow eyes rather than on findings in either the best or worst eye allows for more accurate evaluation of risk factors, changes in medical management and usefulness of treatment regimes.

	Score		Score
Refraction/Vis. Acuity	0 - 3	Grade Cicatricial RLF	0 - 5
Myopia-None to Severe (Correctable to 20/20		Binocular Functions Anisometropia	
Vis. Acuity (corrected) 20/20 to 20/200	4 - 8	Amblyopia	0 - 3
Count Fingers to NLP		Strabismus	
		Total Score per eye	0 -13

Visual Morbidity Score = Sum of Findings in Fellow Eyes

●1288 VITAMIN E SUPPLEMENTATION & RETROLENTAL FIBROPLASIA (RLF) L. Johnson, G. Quinn, D. Schaffer, M. Mathis, C. Otis., Univ. of Penn Med. Sch. Pennsylvania and Children's Hospitals, Depts. Peds & Ophth., Philadelphia, Pa.

Progressive grade 3-plus active RLF (prominent tortuosity & dilitation of vessels of the posterior pole with obvious intravitreal vascularization in at least 2 quadrants - Schaffer/Quinn Classification) carries a bad visual prognosis. From 1968 to 75 7 of 9 such infants in our nurseries progressed to legal blindness (visual acuity (VA) 20/200) or worse.

High dosage E Rx (Im & oral-target serum E level 5-6mg%) was initiated at 3-plus active RLF in 10 infants born from 1976-78. Outcome at age 1 to 2 years was compared to that in 14 control infants born during the same time period who also had had progressive grade 3-plus disease documented by serial exams. Using a standardized scoring system for summing visual morbidity in fellow eyes, the incidence of bilateral legal blindness or worse was decreased from 71 to 40% in E Rx as compared to non E Rx infants & the finding of minimal to mild visual morbidity with zero to minimal cicatrix (Cic) was increased from 14 to 40%.

Vis. Morbidity Rank	Score	Control Babies	E Rx Babies	Clinical Findings
A-B	0- 5	0 %	10%	± Min Myopia ± Cic
C-D	6-11	14.3%	30%	High Myopia Gr 1-2 Cic
E-F	12-17	14.3%	20%	High Myopia Gr 2-3 Cic
G-H	18-22	7.2%	10%	Best Eye-VA 20/200
I	23-26	64.2%	30%	Best Eye-Light Perception
Mean Birth Wt.		1176 gm	1212 gm	p = <.02

1289 HOW GOOD IS CONTINUOUS WAVE (CW) DOPPLER SONOGRAPHY IN ESTIMATING DUCTUS ARTERIOSUS (PDA) SHUNTS? J. Karsdon R. Clyman, M. Heymann, D. Teitel, Dept. of Peds., Mt. Zion Hospital & Medical Center & University of CA, San Francisco.

CW Doppler sonography has been advocated as a non-invasive method for assessing the degree of left-to-right shunt through a PDA in premature infants (Serwer et al, J. Ped. 97:394, 1980). The ratio of reverse flow signal to forward flow signal (R/F) was used as an index of percentage of blood flowing down the descending aorta which subsequently flowed back up the aorta through the PDA. However, no correlation was made between the amount of PDA shunt and the Doppler ratios. We studied 7 preterm neonatal lambs with a CW Doppler unit (MedaSonics) while measuring the volume of blood flowing through their PDA. All lambs lay on their left side. A 5 mHz pencil probe was positioned to the left of the spine, next to the tip of the scapula, and above the diaphragm. The probe was oriented so that a maximally intense arterial velocity flow pattern was obtained free of low frequency artifacts. The velocity pattern was displayed as simultaneous tracings of flow towards the probe (F) and flow away from it (R). The area under each tracing was planimetered. Cardiac output and its distribution were measured by injecting radioactive microspheres into the left ventricle. 30 measurements of left-to-right PDA shunts ($\dot{Q}$ ductus/$\dot{Q}$ systemic) were compared with simultaneous measurements of R/F. $\dot{Q}$ ductus/Q systemic varied from 0 to 1.35. Although there was a significant relationship between R/F and the amount of left-to-right shunt ($p<.05$) there was only a weak correlation ($R=0.34$). Better means for evaluating PDA shunts still need to be developed.

1290 EFFICACY OF INTERMITTENT $TcPaO_2$ SAMPLING IN LESS THAN 1500 GM. NEONATES. Gerald Katzman, Malini Satish, Kathy Douglas. (Spon. by M. G. Robinson) Medical College of Ohio, The Toledo Hospital, Dept. of Ped., Toledo, Ohio.

2 groups of neonates with a birth weight of less than 1500 gm. were studied in order to determine the range of $TcPaO_2$ during selected time intervals after removal of umbilical artery catheters. Both groups demonstrated more hypoxemic than hyperoxemic episodes. Infants in room air (Group I) spent 4.9% of time in $TcPaO_2 > 80$ torr vs 10% in $TcPaO_2 < 50$ torr. Group II infants, who were in FiO_2 ranges between 0.23-0.49, had only 0.04% time in $TcPaO_2 > 80$ torr vs 21.5% in $TcPaO_2 < 50$ torr.

Group #I Total # of runs = 26; # of patients = 19						
	Time/pat $TcPaO_2$	$TcPaO_2$ Ranges 150-101	100-81	80-51	50-40	<40
Dur. in min. $\bar{x}$ ± S.D.	178±19	1.9±0.6	17±7	153±32	22±14	4.5±9.5
$\bar{x}$ % of time in each range	100	0.3	4.6	85	8	2
Group #II Total # of runs = 29; # of patients = 19						
	Time/pat $TcPaO_2$	$TcPaO_2$ Ranges 150-101	100-81	80-51	50-40	<40
Dur. in min. $\bar{x}$ ± S.D.	176±14	0	0.45±0.8	136±45	29±27	9.3±20
$\bar{x}$ % of time in each range	100	0	0.04	78.4	16.5	5

The percent of time that neonates managed with intermittent $TcPaO_2$ monitoring demonstrated hypoxemia is disturbing. 24-hour-a-day $TcPaO_2$ monitoring concomitant with rapid indicated adjustments in oxygen therapy certainly seems warranted from this study.

1291 COMPARATIVE ANALYSIS OF LOWER AND HIGHER STAGE RETROLENTAL FIBROPLASIA (RLF). Gerald Katzman, Malini Satish, Venkatesan Krishnan, Daniel Marcus, Jerald Bovino. (Spon. by M. G. Robinson) Medical College of Ohio, The Toledo Hospital, Dept. of Ped., Toledo, Ohio.

Fifty neonates were identified with RLF between 1/75 & 12/79. According to the Owens Classification, 39 neonates were lower stage (Stages I & II) and 11 neonates were higher stage (Stages III, IV, V). There was no significant difference in total duration of oxygen exposure nor of exposure to particular FiO_2 ranges between the lower and the higher stage RLF groups. Umbilical artery catheters were in place for similar durations in lower & higher stage groups. There was no significant difference in the time of exposure to any PaO_2 range above 50 in either group.

	LOWER STAGE		HIGHER STAGE		P Value
TABLE #1	$\bar{x}$	SD	$\bar{x}$	SD	t test
PaO_2<50 torr (Hrs.)	5.03	3.09	8.64	11.01	<.05
CBG<35 torr PaO_2 Hrs.	11.4	21.4	36.7	48.3	<.01
$PaCO_2$>65 torr Hrs.	0.7	1.4	3.5	4.89	<.05
$PaCO_2$ Peak (torr)	56.8	9.5	63.9	14.7	<.05
Gestation (Wks.)	30.5	2.8	28.6	2.05	<.05
# Apnea c Bagging	2.15	3.03	8.7	10.35	<.05
TABLE #2	YES	NO	YES	NO	X^2
Transfusion	37	2	11	0	<.05
Thrombocytopenia	2	37	3	8	<.05
PDA-LA/AO>1.3	9	30	6	5	<.05

Physiologically less stable neonates seem more susceptible to higher stage RLF. Hypoxia and hypercarbia may be more important determinants in causing severe RLF than hyperoxia.

1292 CHEMOTACTIC MIGRATION OF NEUTROPHILS (PMN) IN POST-PARTUM DIABETIC MOTHERS AND THEIR NEWBORNS. A.J. Khan, W. Rosenfeld, R. Jhaveri, M. Varghese, P. Khan and H.E. Evans, Dept of Ped. Jewish Hosp. Med Ctr/SUNY Downstate Medical Center Brooklyn, NY

PMN chemotaxis in post partum diabetic mothers (PPDM) and their infants has not been studied. 12 full term newborn infants of diabetic mothers (IDM) (age 24-72 hours), 12 full term normal newborn (NNB) (age 24-72 hours), 5 PPDM (mean age 35 year) and 5 post partum normal non diabetic mothers (PPNM) mothers were included. A modified Boyden's technique requiring 6-10 mL of blood was utilized for the mothers and a semimicro modification (requiring 1-2 mL) was used for the infants. PMNs placed in the upper compartment were tested against in turn 1) endotoxin activated serum (EAS) 2) E Coli bacterial factors (ECF), 3) Hank's solution placed in the lower compartment. Ratio of migrated to total cells was termed as chemotactic Index (CI) in first 2 and random migration (RM) in the third set. Mean (± 1SD) CI & RM were as follows (table) CI and RM of IDM were lower than NNB ($P<0.005$ in each instance). CI and RM of PPDM were lower than PPNM ($P<0.02$ in each instance). Chemotaxis is known to be defective in normal newborn infants. This defect in IDM is

	IDM	NNB	PPDM	PPDM
CI with EAS	37(25)	71(17)	35(11)	90(19)
CI with ECF	40(24)	68(17)	30(9)	86(19)
RM	18(10)	24(7)	13(3)	20(4.7)

exaggerated as compared with the defective status of normal newborn. Defective chemotaxis in the diabetic mothers & their newborn infants may contribute to their predisposition to sepsis.

1293 BREAST FEEDING AND EARLY NEONATAL UNCONJUGATED HYPERBILIRUBINEMIA. M. J. Khoury, R. H. Latham, J. S. Marks, M. M. Zack, R. Korhel, and J. R. Little. Centers for Disease Control, Atlanta, Ga., and St. John's Hospital, Jackson, Wy. (sponsored by G. P. Oakley).

Breast feeding has been associated with prolonged unconjugated hyperbilirubinemia (UHB) occurring after the first week of life but not earlier. We studied risk factors for UHB in neonates born in a Wyoming hospital between January 1979 and June 1981. After excluding cases with blood group incompatibility, we compared 80 cases (peak total bilirubin level ≥ 12.0 mg%) to 158 controls (< 12.0 mg% or unmeasured) randomly selected from the same months of birth as cases. Cases were more likely to be breast fed (odds ratio (OR)=15.6), have transient tachypnea after birth (OR =11.0), be premature (≤ 37 wks) (OR=4.2), or of borderline maturity (38-39 wks) (OR=3.3), and be delivered by elective C-section (OR=3.2). We used stepwise logistic regression to control for the interrelation of these and other factors occurring during labor and the early neonatal period. Only breast feeding (OR=17.7), transient tachypnea (OR=6.7), prematurity (≤ 37 wks) (OR=4.1), and borderline maturity (38-39 wks) (OR=3.0), remained as significant independent risk factors for UHB. Furthermore, breast feeding was a risk factor for early-onset (≤ 4 days of life) (OR=9.3) as well as late-onset (OR=13.0) UHB. Breast fed cases did not differ from breast fed controls with respect to labor medications, type of anesthesia, oxytocin infusion, birth weight, neonatal weight loss and fluid intake. This study shows that breast feeding is an independent risk factor for both early- and late-onset neonatal UHB.

1294 AUDITORY BRAIN STEM RESPONSES (ABR) IN SUDDEN INFANT DEATH SYNDROME (SIDS). COMPARISON OF SIBLINGS, NEAR-MISSES AND CONTROLS. Paul Kileny, Neil Finer Glenrose Hospital, Department of Audiology, Royal Alexandra Hospital, Department of Pediatrics, Edmonton, Alberta, Canada.

It has previously been suggested by Orlowsky, et al (Cleveland Clinic Quarterly, 1979) that the ABR was a potential screening device for infants at risk for SIDS. To confirm the validity of this statement, ABR's were recorded from 33 infants (age 4-16 wk) whose diagnostic category was unknown to the audiologist (11 siblings, 11 near-misses, 11 controls). Two siblings also had near-miss episodes. Monaural responses were obtained from all subjects to both 20 dB H.L. and 60 dB H.L. clicks. Statistical analysis (ANOVA, Cluster Analysis) revealed no significant differences in ABR response parameters between groups. The expected inverse relationship between age and ABR peak and interpeak latencies was present in the control group, but absent in both siblings and near-misses.

	BIRTH		PEAK & INTERPEAK LATENCIES, MSEC			
GROUP	WT.	GEST.	I - III	III - V	I - V	V
CONTROLS	3493	39.2	2.62±0.15	2.08±0.09	4.70±0.18	6.47±0.22
NEAR-MISS	3576	38.8	2.57±0.25	2.14±0.21	4.71±0.15	6.72±0.57
SIBLINGS	3508	38.4	2.69±0.15	2.16±0.21	4.86±0.31	6.67±0.29
NEAR-MISS & SIBLINGS	2260	35.5	2.50±0.03	2.22±0.08	4.72±0.11	6.80±0.33

In conclusion, the ABR is not a useful screening test for indicating infants at risk for SIDS. The lack of significant maturational effect seen in siblings and near-misses will require further confirmation by sequential longitudinal studies.

1295 COMPARISON OF VENTILATORY RESPONSES TO CHANGES IN END TIDAL PCO_2 ($PACO_2$) AND TRANSCUTANEOUS PCO_2 ($TcPCO_2$). Won Kim, Kristine McCulloch, Rama Bhat, Dharmapuri Vidyasagar. University of Illinois. Dept. of Pediatrics, Chicago, Illinois.

$PACO_2$ (Beckman LB-2), $TcPCO_2$ (Roche 634) and tidal volume were measured simultaneously during room air, 2% CO_2 and 4% CO_2 breathing in 14 healthy preterm infants on 17 occasions. Relationships of changes in minute ventilation (ΔV_E) with $\Delta TcPCO_2$ and $\Delta PACO_2$ were determined by linear regression analysis. The relationship of the CO_2 response slopes obtained using the two PCO_2 monitoring methods is described by the equation:

$TcPCO_2$ response slope = 18.25 + 0.52 x $PACO_2$ response slope ($r=0.60$ $p=0.01$).

The strength of linear association as estimated by regression coefficients was as good between $\Delta TcPCO_2$ and ΔV_E ($\bar{x}$ ± SD=0.72 ± 0.26) as between $\Delta PACO_2$ and ΔV_E ($\bar{x}$ ± SD=0.71 ± 0.22) and regression coefficients for the 17 pairs of CO_2 response slopes were highly correlated ($r=0.85$, $p=0.001$).

We conclude that while the actual CO_2 response slope values differ, ventilatory response testing may be done as accurately using transcutaneous PCO_2 monitoring as with the usual end tidal measurements.

1296 THE PERIPHERAL CIRCULATORY RESPONSE TO FEEDING IN GROWING PRETERM INFANTS. Mae H. Kim, Alice C. Yao, Adela C. Gatmaitan, Khaja Raziuddin, and Patricia E. Pierce, Department of Pediatrics, Downstate Medical Center, S.U.N.Y., Brooklyn NY

The effect of postnatal age on the peripheral circulatory response to feeding was investigated in 23 growing preterm infants:

GROUP	NUMBER	POST CONCEPTUAL AGE (WKS)	POST NATAL AGE (DAYS)	WEIGHT(G)
I	6	35-36	14-52	1460-2150
II	8	>39	23-101	1750-2850
III	9	37-38	14-56	1900-2310

Peripheral blood flow (PBF, calf) was measured by venous occlusion plethysmographic method before and after oral feeding of standard formula amounting 23±6 ml/kg. Postprandial PBF changes showed in Group I infants, a gradual increase from ½ to 2 hours, similar to that reported in ≤14 days preterm infants; in Group II, an immediate 20% reduction followed by 24% rise above prefeeding value accompanied by increased, then decreased peripheral vascular resistance respectively, similar to that of term infants and in Group III, variable responses similar either to Group I or II. The results indicate that the pattern of postprandial PBF changes of term infants is seen in growing preterm infants when their postconceptual age approaches term.

●1297 CEREBRAL ARTERIAL PULSATILE FLOW CHANGES IN NEONATAL POLYCYTHEMIA AND HYPERVISCOSITY. Harold W. Kolni, Henrietta S. Bada, Sheldon B. Korones, Charles W. Fitch, and Diana L. Ford (Spon. by John F. Griffith), University of Tennessee, Department of Pediatrics, Memphis, Tennessee.

The cerebral pulsatile flow changes in neonatal polycythemia and hyperviscosity were studied using Doppler ultrasound technique. From flow velocity patterns of the anterior cerebral arteries, right and left pulsatility indices (RPI and LPI) were calculated; a high PI indicating increased cerebrovascular resistance and a low PI, the opposite. Two groups of neonates were studied, a control (n=12) and a study group (n=7). Both groups were comparable as to birth weight and gestational age. The control had central hematocrit (HCT) <63% whereas the study group had HCT ≥63% and were treated with partial plasma exchange transfusion (PPET). The following table compares the HCT, viscosity (cps, shear rate 11.5 sec^{-1}), RPI and LPI values of the control group with the pre and post PPET values of the study group.

	Control	Pre Exchange	Post Exchange
Hematocrit	56 ± 4	67 ± 3.2	51.7 ± 3.8
Viscosity	10 ± 2	16 ± 5	7.4 ± 2
RPI	0.76 ± 0.11	0.92 ± 0.09	0.77 ± 0.09
LPI	0.76 ± 0.10	0.93 ± 0.08	0.77 ± 0.10

All pre PPET measurements were significantly higher than post PPET and control values ($p<.01$). No statistical difference was observed between control and post PPET values. We conclude that alterations in cerebral hemodynamics occur in polycythemia and hyperviscosity as indicated by increased PI values, and may be a critical factor in determination of the need for PPET.

1298 HIGH VS LOW FREQUENCY VENTILATION IN THE PREMATURE BABOON WITH RDS. T Kuehl, K Meredith, N Ackerman, L Minnick, R Stoddard, J Hilliard, M Escobedo, J Coalson, D Null, J Robotham*, R deLemos. Southwest Foundation for Research and Education, Wilford Hall USAF Medical Center, University of Texas Health Science Center, Department of Pediatrics, San Antonio, Texas

The potential role of HFV in the care of newborns with RDS is unclear. Based on previous data which showed that both RDS and BPD could be produced in the baboon, we ventilated nine immature animals with RDS alternately for two hour periods with one of two modes of HFV (5 Hz with a pneumatic oscillator or 15 Hz via a mechanical device) and standard IPPV. Blood gases at an F_IO_2 1:0 were optimized by adjusting mean airway pressure and oscillatory amplitude during HFV.

Blood gases and mean airway pressures were statistically similar during all treatment periods. P_aO_2 was highest in the animals ventilated at 15 Hz. All survived the experimental period. No treatment related differences in lung pathology were noted.

	N	P_aO_2	P_aCO_2	MAP		N	P_aO_2	P_aCO_2	MAP
IPPV	4	123	36	16	IPPV	5	114	40	17
HFV5	4	114	36	15	HFV15	5	153	33	15

These preliminary studies suggest that HFV may be an acceptable alternative in the management of primates with RDS and will provide a tool for investigation of the etiology of BPD. However, attempts to ventilate premature baboons for 24 hours with HFV have thus far resulted in late cardiopulmonary deterioration in 2/3 animals.

1299 PERINATAL FACTORS RELATED TO SURVIVAL IN INBORN INFANTS ≤ 800G AT BIRTH. Savitri P. Kumar, Endla K. Anday, Linda M. Sacks, Steven G. Gabbe, and Maria Delivoria-Papadopoulos, Univ. of PA., Depts. of Pediatrics and Obstetrics-Gynecology, Philadelphia, PA.

In the recent past there has been a steady increase in survival of infants ≤ 800g. To determine the perinatal factors related to survival, 34 inborn infants ≤ 800g at birth at the Hospital of the Univ. of PA. delivered between Jan.1980-Sept.1981 were studied. Fifteen infants (44%) survived beyond the 1st wk of life. Maternal obstetrical complications between survivors (Gr I) and non-survivors (Gr II) were similar except for a significant difference among survivors in the incidence of preeclampsia ($p < .025$), prenatal dexamethasone ($p < .001$), and C-section mode of delivery ($p < .025$). Mean birth weight + SEM between Gr I and Gr II was 705 ± 24g and 634 ± 20g ($p < .025$) respectively. Mean gestational age of Gr I was 27 ± .4wks and Gr II was 23 ± .4wks ($p < .001$). The 1 and 5 min Apgar scores between the two groups were 4.5 ± .6 and 1.4 ± .1 ($p < .001$) respectively. Twelve of 15 survivors (80%) were female while 12 of 19 non-survivors (63%) were male ($p<.025$). Ten of 15 infants (70%) were small for gestational age (SGA) in Gr I while none of the infants from Gr II were SGA ($p<.005$).

Although gestational maturity is one of the most important factors affecting survival at differing birth weights, these data indicate that at the extreme low limits of birth weight, infant maturity is most critical to survival. Optimal perinatal management to prevent premature delivery and perinatal asphyxia in this group of infants cannot be overemphasized.

1300 MEDICAL AND DEVELOPMENTAL OUTCOME IN <1500 GRAM INBORN SURVIVORS, 1979-80. Catherine Lam, Beverly L. Koops, (Spon. by Frederick C. Battaglia), Department of Pediatrics, University of Colorado School of Medicine, University Hospital, Denver.

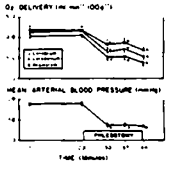
A follow-up study was done on 85 < 1500 gram inborn survivors at University Hospital between 1979-80. The mean age of follow-up was 16 months corrected age. The overall outcome shows that normal growth was achieved in 80%. Twenty-four percent had bronchopulmonary dysplasia (BPD), 14% having prolonged home oxygen dependency. Germinal matrix hemorrhage/intraventricular hemorrhage (GMH/IVH) occurred in 25%. Initial muscle tone problems were present in 42% and 18% had residual major neurologic sequelae. Developmental assessment was normal in 72%. Speech defects occurred in 11%, behavioral problems in 12%, ocular defects in 9% and mild conductive hearing loss in 4%. There were 3 infant deaths.

The overall outcome was found to be related to the number of days of ventilation ($p<.025$) and to the presence of BPD ($p<.005$), but GMH/IVH showed no significant effect on these results.

A comparison of the morbidity of infants with birth weights <800, 801-1000, 1001-1300 and 1301-1500 grams was made. With decreasing birth weights, there were longer median durations of hospital stay, oxygen and ventilation therapies. In the smallest groups, there were lower five minute Apgar scores ($p<.025$), higher incidence of hyaline membrane disease ($p<.005$), apnea ($p<.025$) and BPD ($p<.005$). However, no significant difference was noted in the neurologic and developmental outcome between these groups of children.

1301 REGIONAL BRAIN BLOOD FLOW AND O_2 DELIVERY DURING HEMORRHAGIC HYPOTENSION IN THE PIGLET. Abbot R. Laptook, Barbara S. Stonestreet, and William Oh. Brown Univ., Women & Infants Hosp., Dept. of Ped., Providence, RI

We have previously shown regional differences in brain blood flow (BBF) reduction when hemorrhagic hypotension was induced in spontaneously breathing newborn piglets. However, in that study both mean arterial blood pressure (MABP) and $PaCO_2$ were lowered and both correlated with the reduction in BBF. To examine the effect of hypotension alone, 8 piglets were studied with controlled ventilation. BBF was measured by microspheres and hypotension was produced by phlebotomy. Hypotension with normocapnia produced a significant reduction in BBF similar to our previous data when the piglets were hypocapnic. In addition, different regional blood flow responses occurred during hypotension. As shown in the graph, blood flow to the cerebrum (C), brain stem (BS), and cerebellum (CB) decreased during the initial phase of hypotension but returned to normal for BS and partly for CB. O_2 delivery decreased in all regions during hypotension but more for C and CB than for BS (*indicates $p<.05$ from control). The data indicates that during hypotension, hypocapnia does not have an additive effect on reduction of BBF and that hypotension produced differential reduction in blood flow and O_2 delivery to the various regions of the brain providing a more protective effect on the vital areas such as CB and BS.



1302 NORTH CAROLINA PERINATAL TELECOMMUNICATIONS NETWORK: ONE YEAR'S EXPERIENCE. Edward E. Lawson, James S. Bostick, and Henry S. Hsiao. University of North Carolina, Department of Pediatrics, Chapel Hill, NC.

Transport of newborns and high-risk mothers is often delayed due to lack of readily available information regarding neonatal facilities at regional perinatal centers. We have developed a minicomputer based telecommunications network to provide current data regarding perinatal bed availability. Data is automatically collected, analyzed, and disseminated back to each of the state's nine NICUs every two hours. This design enables referring physicians to access the current data without changing their established referral patterns. During the months July-October 1981, there were an average of 354 polls/month/center. 98% of all computer initiated polls were completed, and <4% of the polls resulted in erroneous data. After one year of operation the following results have been obtained: 1)Bed availability was restricted at 7 or more of the 9 centers 41% of the time. 2) The system reduces the number of physician calls, and therefore the time, to locate an available bed for a patient needing transport(neonatal - with system <5% required 3 or more calls, without system 31% required 3-9 calls; obstetric - with system 10% required 3 or more calls, without system 31% required 3-8 calls: $p<.0005$ for both). 3)This network operates on a much smaller budget (<$25,000/yr) than comparable 24 hour manual telephone systems which provide similar services. We conclude that a computer telecommunications system can provide a reliable, cost-effective mechanism for efficient allocation of limited perinatal resources. The collected data also provides a reliable base for future perinatal planning.

1303 RETROGRADE EMBOLIZATION RISK WITH ARTERIAL CANNULAE IN THE NEWBORN INFANT. Bruce R. Lewis, Jonathon M. Whitfield, Frances Padilla, and Reginald Washington. (Spon. L. Joseph Butterfield) Depts. of Perinatology & Cardiology The Children's Hospital, Denver, Colorado.

Retrograde embolization into the cerebral circulation from temporal artery cannulae has been suspected in the newborn. To establish if this phenomenon could occur during routine flushing of other arterial lines [umbilical at vertebral level L^4 (UAC), radial (RAC), posterior tibial (PTC)] , a saline contrast real time echocardiographic study was undertaken in 12 newborns < 14 days old. Birth wts. ranged 590-3280g (median 1010g). Contrast was looked for in the aortic arch proximal to the left common carotid artery. A positive (+ve) contrast echo (CE) was established by blind review by cardiologist. All babies had normal BP and did not have PDAs when studied. A flush rate (FR) approximating (c.) 1cc/5secs. by hand was used.

RESULTS:

		no.	
RAC	+ve CE at arch	3/4	(-ve infant 3280g)
UAC	+ve CE at arch	5/6	(-ve infant 1400g)
PTC	+ve CE at arch	0/2	(both < 1200 g)

Negative CE was achieved in 2 babies studied to date (RACs; < 1000 g) by decreasing the FR to c. 1cc/10secs.

These preliminary data suggest the potential for embolization to cerebral circulation when flushing RACs or low UACs in low birth wt. neonates at rates of c. 1cc/5 secs. A safe flush rate awaits determination.

● **1304** NEONATAL ISOIMMUNE NEUTROPENIA David H. Levine, Prema Madyastha, Theodosia R. Wade, and Abner H. Levkoff. (Spon. by Milton Westphal) Medical University of South Carolina, Departments of Pediatrics and Laboratory Medicine, Charleston, South Carolina.

Isoimmune neutropenia has been previously considered an uncommon disorder in neonates. Identification of several specific neutrophil antigens and availability of corresponding antisera have stimulated a search for additional antigens and for documentation of the true incidence of isoimmune neutropenia. All infants born during a six-month period were screened for neutropenia in the first two days of life. Those with initial and persisting neutropenia were evaluated for the presence of isoimmune disease. Maternal sera were tested against paternal neutrophils by EDTA microagglutination and indirect immunofluorescence, and confirmed against normal donors. Of 1465 infants born during this period, 16 met criteria and were evaluated. All but one of these neutropenic infants had been admitted to the special care nurseries. Isoimmune neutropenia was confirmed in 3 of the 1465, representing 2/1000 live births and 1.5% of special care nursery admissions during that period. Two of these infants had suspected or proven infection. They represent 16% of infants with suspect/proven sepsis and neutropenia born during this period. Isoimmune neutropenia appears to be a not uncommon entity, particularly among infants admitted to a special care nursery. It should be considered as a cause of the neutropenia frequently associated with neonatal sepsis, as it may be a predisposing factor.

1305 IMPROVED LONGEVITY OF RADIAL ARTERY CANNULATION IN THE NEWBORN INFANT. Bruce R. Lewis and Adrian Trenholme. (Spon. L. Joseph Butterfield). Paediatric Department, National Women's Hospital, Auckland, New Zealand.

In previous reports, radial artery cannulae (RACs) have not generally been noted for their longevity of function. We report our experience with 32 consecutively placed RACs in 25 newborns. Birth wts ranged 680-3760g (median 1300g) and gestational ages 25-41 weeks (median 29). Age at placement ranged 1.5-597 hours (hr) (median 121.5). Cannulae were placed percutaneously and remained in situ until no longer required, malfunctioned or complication dictated removal. A 22 guage Venflon (Viggo) Teflon cannula was used. All were continuously infused with 1/2 Normal saline/water with 2 units heparin/ml at 1ml/hr and flushed with 1ml heparinized saline after blood sampling.

Longevity: cannula life ranged 12-787hr, 19 (59%) functioning beyond 1 week, 13 (40%) beyond 2 weeks, 6 (18%) beyond 3 weeks and 2 (6%) beyond 4 weeks. Number of blood samples drawn from RACs ranged 4-199 (median 75). Temporary impairment of distal perfusion occurred in 2 cases; recovery followed RAC removal.

Possible reasons for improved longevity of RACs which warrant further study include:

1. Cannula type.
2. Meticulous attention to immobilization of cannula.
3. Elevation of forearm throughout life of cannula.
4. Absence of dextrose from infusate and flush solution.

1306 UMBILICAL ARTERIAL CATHETERIZATION(UAC):A 3 YEAR RETROSPECTIVE REVIEW IN A REGIONAL CENTER. Anita Lim, Eugene Kim, Excelsis Antonio, Ilana W. Zarafu, (Spon. Franklin C. Behrle) College of Med. and Dent. of N.J.-N.J.Med. School, Newark Beth Israel Med. Center, Dept. of Ped. Newark, N.J. 07112

Records of 455 Newborns(NB) who had UAC in the Newborn Special Care Unit from '77-'79 were reviewed. Umbilical arterial lines (UAL) were used for blood sampling, intravenous fluid administration(except hyperalimentation)and medications. Size 3.5F endhole polyvinyl chloride catheters were used in NB <2000gms. Heparin was not used. Placement was confirmed by x-ray. In 445 the UAL was at D_7-D_8 level and in 10 it was at L3-L4. 82 NB expired without evidence of UAL complications (COM), hence, they were excluded.

The incidence of COM in survivors was 37%(137/373). Catheters remained in place for 1-576 hours (hrs.); mean duration was 74 hrs. in the group with COM and 58 hrs. in those without. This difference is significant. The incidence of COM, 54%(74/137) in NB <1500gms and 46%(63/137) in NB >1500 was similar. The most common COM were: clotting in 59%(67/137) and blanching in 46%(61/137). Bleeding, weak pulse, leaking, periumbilical erythema, kinking and accidental dislodgement, each occurred in <2% of the cases. 234 UAL tips were cultured, 10%(24) were positive. Organisms isolated were S.epidermidis 42%, E.coli, S.aureus and α streptococcus 13% each. Enterococcus, Pseudomonas and Enterobacter accounted for the rest.

Heparin in the UAL had been discontinued prior to this study because small NB frequently demonstrated bleeding problems. The high frequency of clotting(49%) in our review suggests the need for a control trial with heparin. In 1978 we began routine use of transcutaneous oxygen monitoring, despite it's liberal use, there has been no change in the incidence of UAC in infants <1500 gms.

1307 DEFORMABILITY OF RED BLOOD CELLS IN NEWBORN INFANTS WITH POLYCYTHEMIC DISORDERS. Otwin Linderkamp, Herbert J. Meiselman, Paul Y.K. Wu. Univ. of So. Calif. Sch. of Med., Depts. Physiol. and Biophys. and Peds., Los Angeles.

Neonatal polycythemia can produce life-threatening impairment of the circulation as a result of high viscosity which increases nonlinearly with increasing hematocrit. The hematocrit-viscosity relationship becomes steeper when the deformability of red blood cells (RBC) is decreased. To test whether neonatal disorders frequently associated with polycythemia also impair RBC deformability, we studied 45 newborn infants with various disorders and 10 normal neonates. Blood viscosity was measured using a cone-plate viscometer, RBC deformability was determined by direct microscopic observation of RBC at shear stresses of 2.5 to 500 dyn/cm^2 in a counter rotating Rheoscope. The deformability index (D), which increases with increasing deformation, is calculated from width (W) and length (L) of the elongated RBC: D=L-W/L+W. At a shear stress of 500 dyn/cm^2, D was as follows: 10 normal newborn infants: 0.59±0.04; 10 with uncomplicated polycythemia: 0.58±0.05; 10 with intrauterine asphyxia: 0.56±0.06: 10 growth retarded infants: 0.54±0.06; 10 infants of diabetic mothers (IDM): 0.53±0.04; 5 with necrotizing enterocolitis (NEC): 0.42±0.06. Thus, D was slightly decreased ($P<0.05$) in IDM and markedly reduced ($P<0.001$) in infants with NEC. Hematocrit-viscosity relationships were similar in all groups with the exception of infants with NEC who showed a markedly steeper curve. Our results show that most of the diseases frequently associated with polycythemia do not significantly affect RBC deformability. In NEC, RBC rigidity may contribute to disturbed microcirculation.

● 1308 SUPRA-BRAINSTEM INHIBITION OF RESPIRATION DURING CAROTID SINUS NERVE STIMULATION IN PIGLETS. Walker A. Long and Edward E. Lawson. University of North Carolina, Department of Pediatrics, Chapel Hill, NC

We have recently shown that the biphasic response to hypoxia in the newborn must be due to a central neural mechanism (Pediat. Res. 15:668, 1981). We hypothesized that feedback from a supra-brainstem inhibitory center (SBIC) could be such a mechanism. To test this hypothesis we used a piglet model in which the chemical feedback loop was opened by paralysis, vagotomy, and servocontrolled ventilation at constant CO_2 on 100% FiO_2. Phrenic neural activity was used as the index of respiratory output(RO). Hypoxia was simulated by carotid sinus nerve (CSN) electrical stimulation. We compared the changes in RO during one minute CSN stimuli in two groups of piglets (<10d age), one group following midcollicular decerebration(MCD), and the other with the brains remaining intact.

	0-10s	10-20s	20-30s	30-40s	40-50s	50-60s	N
MCD	56±25	83±7	80±3	84±4*	81±8*	85±5 *	4
Intact	74±8	85±5	87±6	54±7	56±7	44±10	10

units=% range of control to max stimulated RO; ±SE; *p<.05 T-test

Since decerebration resulted in a sustained increase in RO during CSN stimulation, we conclude that CSN stimulation in the intact young animals activated a SBIC which, in turn, depressed respiratory drive. We speculate that this SBIC is responsible for the transient respiratory response to actual hypoxia observed in newborns. Furthermore, this mechanism may be responsible for much of the relative depression of breathing during fetal life. Other stimuli, independent of the CSN, may also activate the SBIC.

1309 SURVIVAL OF THE VERY LOW BIRTH WEIGHT INFANT: DEPENDENCE ON OPTIMAL INTRAPARTUM AND NEONATAL CARE. Lula O. Lubchenco, L. Joseph Butterfield, Beverly L. Koops, Virginia D. Black, Edward Goldson, Catherine Manchester, Departments of Pediatrics and Perinatology, University of Colorado Health Sciences Center and Denver Children's Hospital, Denver.

Data from UCHSC indicated that inborn infants weighing 600-700 grams at birth survived only when all obstetric and neonatal factors were optimal.

A collaborative study between Denver Children's Hospital (DCH), University Hospital (UH) and 5 metropolitan Denver hospitals (MDH) with Level I nurseries supports this hypothesis.

From 1/1/75 to 12/31/78, 297 infants weighing <1500 grams were born in the 5 MDH; 393 infants in UH. One hundred nine of these infants weighed 500-700 grams; 62 were born in the 5 MDH while 47 were born in UH.

The fetal death rate was 50% in MDH and 36% in UH (p=NS). It is not known how many of the fetal deaths occurred during the intrapartum period.

There were 31 liveborn infants in MDH and 30 liveborn in UH. All 31 from MDH died within 24 hours, including the 11 transported to DCH. Eight of the 30 liveborn infants at UH survived (p<.005). Furthermore, there were 6 late neonatal deaths (after 24 hours) versus 0 in MDH population (p<.005).

Follow-up of the 8 survivors at 1 year showed 3 to be normal, 2 with moderate visual handicap and 2 with developmental delays. One died at 6 months of medical and neurologic problems.

1310 PLASMA PROSTAGLANDINS AND THROMBOXANES IN INFANTS WITH PERSISTENT FETAL CIRCULATION (PFC) AND SEPSIS. V. E. LUNYONG AND ZVI FRIEDMAN. Dept. of Ped., Baylor College of Medicine, Houston, Texas.

Prostaglandins (PGs), prostacyclin (PGI_2) and thromboxane A_2 (TxA_2) are derived from the arachidonic acid cascade via the cycloxygenase enzyme. We previously reported that human fetal and neonatal lungs are a major site for synthesis, release and degradation of PGs, PGI_2 and TxA_2. PGs, PGI_2 and TxA_2 exert physiological effect on the smooth muscle of blood vessels and the tracheobronchial tree. TxA_2 is a potent vasoconstrictor compound. Thus, it may play a role in the pathophysiology of pulmonary hypertension and PFC. We determined serially by radioimmunoassay the plasma levels for PGs, PGI_2 and TxB_2 (the stable metabolite of TxA_2) obtained from three term infants. Patient 1 had meconium aspiration syndrome (MAS) and PFC and expired on day 14. Patient 2 had group B streptococcal (GBS) sepsis, pneumonia and PFC. Patient 3 had GBS and pneumonia but not PFC. Patients 2 and 3 recovered. The following TxB_2 results were obtained (pg/ml):

Patient	Day 1	Day 3	Day 5	Day 10
1. MAS + PFC	1988	2688	1391	724
2. GBS + PFC	948	769	592	287
3. GBS only	319	190	225	110

The study demonstrates 1) plasma level of TxB_2 is elevated during the acute phase of MAS and GBS sepsis 2) higher plasma levels of TxB_2 are seen in the infants with PFC 3) plasma level of TxB_2 is correlated with the clinical course of the disease. 4) changes observed with PGs and PGI_2 were not as conclusive as TxB_2, 5) circulating TxA_2 may play a role in the persistent of perinatal pulmonary hypertension.

1311 PROSTACYCLIN (PGI_2) AND THROMBOXANE (Tx) IN NEONATES WITH HYALINE MEMBRANE DISEASE (HMD) AND PATENT DUCTUS ARTERIOSUS (PDA). V.E. LUNYONG, H. SMITH, P. BERKOWITZ AND ZVI FRIEDMAN. Dept. of Ped., Baylor College of Medicine, Houston, TX

Prostacyclin(PGI_2) and thromboxane A_2 (TxA_2) exert physiological effect on the smooth muscle of blood vessels and the tracheobronchial tree; PGI_2 dilates and TxA_2 constricts. The lungs are a major site for synthesis and release of PGI_2 and TxA_2, and degradation of TxA_2. We previously reported the association between PGE, PGF and HMD and PDA. Altered PGI_2 and TxA_2 functions may also contribute to the pathophysiology of HMD. Three infants with HMD were studied by serial analysis of their plasma for PGI_2 and TxA_2 (measured as their stable metabolites 6-keto $PGF_{1\alpha}$ and TxB_2, respectively) by radioimmunoassay. Gestational age and birth weight were 33±1 weeks and 1967±147 gm, respectively. One infant developed PDA on days 5-8 of life. The following results (mean±SD) were obtained (pg/ml).

	Days: 1-2	3	4	7-10	
6-keto $PGF_{1\alpha}$	3679±565	2158±794	1382±396	737±122	*1167
TxB_2	480±147	267±99	332±93	212±11	* 231

*Results from infant with PDA.

The study demonstrates: (1) plasma PGI_2 and TxA_2 are elevated in HMD. (2) upon recovery from HMD there is a progressive fall in plasma PGI_2 and TxA_2. (3) Higher plasma level of PGI_2 may contribute to PDA.

●1312 EFFECT OF CHEST AND ABDOMEN UNCOUPLING ON VENTILATION AND WORK OF BREATHING IN THE NEWBORN INFANT DURING SLEEP. Jorge Luz, Augusto Winter, Don Cates, Michael Moore, and Henrique Rigatto. Dept. of Pediatrics, University of Manitoba, Winnipeg, Canada.

To determine the effect of chest/abdomen uncoupling on lung inflation and diaphragmatic work we studied 6 term infants (BW 3.5±0.5 kg; GA 39±1 wk) during sleep. After a control period in quiet (Q) or active (A) sleep, infants rebreathed 3% CO_2 plus 40% O_2 from a bag for 2.5 minutes. We measured $\dot{V}_E$, V_T, f, P_ACO_2, work of lung inflation (W_L), work of the diaphragm (W_D), CO_2 response, ECoG, EOG and heart rate. We measured lung volume = A x Abdomen + C x Chest + B to partition $\dot{V}_E$ into chest and abdominal components and be able to calculate W_L and W_D. To assess the pure effect of distortion on the work of breathing we fixed f for breaths in and out of phase. Results:

	CONTROL				CO_2 REBREATHING			
	IN		OUT		IN		OUT	
	W_L(g.cm/ml)	W_D	W_L	W_D	W_L	W_D	W_L	W_D
Q	2.1±0.6	2.4±0.8	3.3±0.1	4.3±0.5	4.8±2	4.8±2	4.3±2	5.1±2
A	3.0±0.3	3.2±0.4	2.8±0.4	3.6±0.6	5.5±1	5.7±1	5.1±1	6.2±1

Average slope of CO_2 response was .055 L/min/kg (in phase) and .062 (out) in quiet sleep and .074 (in) and .079 (out) in active sleep. These results suggest: 1) If length of breath is fixed, $\dot{V}_E$ is the same with and without distortion; 2) The respiratory apparatus pays 19 to 30% extra work to maintain ventilation if chest and abdomen are uncoupled; 3) Chest and abdominal uncoupling does not reduce the ventilatory response to CO_2.

1313 EVALUATION OF NEUTROPHIL FUNCTION USING IMMUNOBEADS IN NEONATES AND CRITICALLY ILL PEDIATRIC PATIENTS J. Carlos Maggi, Alan Loren, and Craig L. Anderson, Spon. by Lewis E. Gibson, Department of Pediatrics , Loyola University Stritch School of Medicine, Maywood, IL 60153

Introduction: An improved assay for the simultaneous assessment of phagocytic uptake (Immunobeads R) and metabolic integrity (NBT dye reduction) was used to evaluate neutrophil function in critically ill pediatric patients, neonates, one year old children and adults. The assay evaluates both phagocytic and and killing function simultaneously, allowing more sensitivity in the detection of neutrophil dysfunction.

Methods: Approximately 6 ml of blood were obtained from 20 patients of each group. The assay was prepared by suspension of immunobeads (polyacrylamide beads coated with known quantities of rabbit anti-human IgG antibody) in NBT solution. The neutrophils were isolated by density gradient and mixed with the assay solution. A totally functional neutrophil (TFN) was defined as a cell able to ingest Immunobeads and reduce NBT. Results were expressed as the number of TFN per 100 neutrophils seen.(Mean ± SD)

Results: A significant neutrophil dysfunction in full term unstressed neonates (TFN: 70.6 ± 6.5) and a subtle hyperfunction in critically ill children after surgery or trauma (TFN: 87.1 ± 3.2) was detected when compared with normal adults (TFN: 81 ± 7.5) and normal one year old children (TFN: 80.8 ± 3.4) ($p< 0.01$ by chi square analysis). Preliminary results show a more pronounced neutrophil dysfunction in stressed premature newborns as well as septic critically ill children.

1314 COLLOID OSMOTIC PRESSURE IN THE NEONATE. Mark C. Mammel, Dana E. Johnson, Theodore R. Thompson (Spon. by Stephen J. Boros), University of Minnesota, Department of Pediatrics, Minneapolis, MN

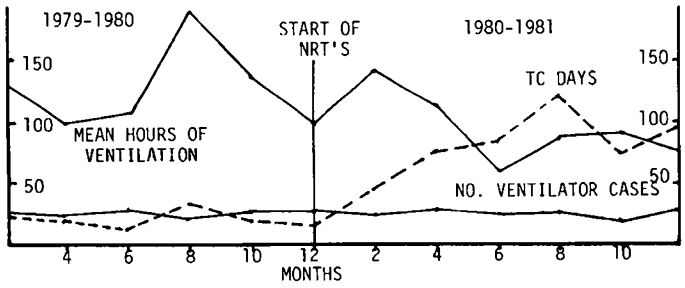
The use of colloid osmotic pressure (COP) in the newborn has been limited by a lack of normal values and questions about the meaning of values obtained. What are normal values? Does mode of delivery affect values obtained? Is COP a useful predictor of outcome? We studied 125 term infants, 40 preterm, and 9 post-term (Table). COP in vaginally delivered infants was higher than those delivered by C-section ($p < 0.01$). Cord blood COP and the lowest COP measured during hospitalization were lower in sick infants than in well infants ($p < 0.001$). COP measured in infants who died was lower than that measured in either sick or well infants ($p < 0.001$).

	Normal Term Infants		Sick Infants	Infants Who Died
	C/S	Vag	Lowest	Lowest
COP + SD (mm Hg)	17.8 + 1.7*	19.3 ± 2.98	13.29 + 3.1†	9.56 + 2.1†
	*$p < 0.01$		†$p < 0.001$	†$p < 0.001$
n	12	101	48	9

Low values of COP identify an extremely high-risk population of infants. Using a COP value of 11 or less as an indicator of mortality, the test has a sensitivity of 89%, specificity of 97%, and a predictive value of 62%. We conclude that COP varies both with mode of delivery and state of health. Very low values of COP reflect a high mortality group.

1315 DECREASED LENGTH OF MECHANICAL VENTILATION (MV) IN NEONATES WITH USE OF NEONATAL RESPIRATORY THERAPISTS (NRT'S). Frank L. Mannino, Robert J. Kopotic (Spon. by Louis Gluck), Univ of Calif, San Diego, Dept Peds, La Jolla.

A well trained group of NRT's was developed in an NICU where previous respiratory therapy was sporadic. The NRT's were full-time in the NICU, enacted physician ordered ventilator changes & maintained ventilation equipment. There was an increase & improvement of quality in ventilator, transcutaneous (TC) & blood gas monitoring. A significant drop in mean MV time per patient ventilated occurred concurrent with the presence of NRT's (126±40 hr to 94±31 hr; $p<0.05$). The number of patients requiring MV and the general nursery population remained constant. Use of TC blood gas monitoring significantly increased. Well trained NRT's improve ventilatory care and can decrease the length of MV in neonates.



1316 INTRINSIC FACTOR (IF) SECRETION AS AN INDICATOR OF PARIETAL CELL (PC) FUNCTION IN THE NEWBORN. Lucyndia Marino, Bruce Bacon, John Hines, Thomas Halpin (Spons. by William Speck), Case Western Reserve University, Rainbow Babies & Childrens Hospital and Cleveland Metropolitan General Hospital, Cleveland, Ohio.

To evaluate neonatal PC function, gastric aspirates were obtained at birth in 19 term infants and collected for 1 hr in 11 premature (P) and 15 full-term (FT) infants between 24-72 hrs of age. IF was determined by a competitive-binding assay. IF was detected in 16/19 infants at birth, $\bar{x}$=5.9 ng/ml, (range .8-15). Two groups of FT infants were identified and significantly different in HCl production and postnatal age.

	#	$\bar{x}$ age hrs	[H+] mEq/hr	[H+] mEq/kg/hr	[IF] ng/hr	Nutrition
FT_1	7	41.5	.0300	.0100	30.6	PO
FT_2	8	35.5	.0018	.0008	5.4	PO
P	11	46.6	.0074	.0032	23.5	IV

Student T-Test Comparison (p values shown)

	[H+] mEq/hr	[H+] mEq/kg/hr	[IF] ng/hr
FT_1 vs FT_2	.001	.01	.02
FT_1 vs P	.05	.10	.10

Above data show that 1) PC function is present in utero; 2) there is an abrupt increase in PC secretion with postnatal age; 3) IF production is not related to PC mass, as P infants with less PC mass have the same capacity to produce IF as FT infants; 4) P infants produce acid similar to FT when expressed on a mg/kg/hr basis, and 5) secretory mechanisms for IF and HCl respond to extrauterine stimuli not related to enteral feeding.

1317 TRANSCUTANEOUS OXYGEN(tcO_2) AND BLOOD PRESSURE (BP) MONITORING OF NEONATES DURING DUCTUS ARTERIOSUS (DA) LIGATION. Terry A. Marshall, Foster Marshall, P. Prithvi Reddy, (Spon. by John Kattwinkel), Univ. of S. C. Medical School, Dept. of Pediatrics, Columbia, S. C.

The tcO_2 monitor and a BP monitor were used on 13 neonates to examine physiologic changes during DA ligation. Simultaneous tcO_2 and arterial blood gas measurements were recorded frequently throughout each operation and arterial BP was measured continuously.

There was close correspondence between PaO_2 and tcO_2 ($r=.96$). All infants required increases in inspired oxygen and ventilation to correct abnormal values when the left lung was deflated(table, s=seconds). A significant increase of BP occurred 10 seconds after DA ligation(mean systolic BP=17.9mmHg±9.5, $p<.001$). The post-DA ligation BP returned to the pre-operative BP 5 minutes to 22 days later. Heart rate decreased($p<.001$)10 seconds after ligation (meanΔHR=-6.2bpm±5.1). In 5 neonates, gradual closure of the DA over 40-75 seconds resulted in a gradual increase in BP. Intraventricular hemorrhage(IVH) was confirmed in 2 patients following surgery.

MeanΔ tcO2 (mmHg) During Surgery for DA Ligation		
30s post lung deflation	30s post DA ligation	150s post lung inflation
-20.2±8.3($p<.001$)	-17.0±11.4($p<.001$)	44.6±31.3($p<.001$)

tcO_2 closure results in a decrease in tcO_2 which improves following left lung expansion. Probably by eliminating a low resistance circuit, ligation of the DA results in an abrupt increase in BP, which may be related to the pathogenesis of IVH. We suggest that the DA should be closed gradually to allow a more gradual increase in BP.

●1318 ABNORMAL PATTERNS OF CEREBRAL FLOW IN INFANTS WITH A LARGE PATENT DUCTUS ARTERIOSUS. Christopher G. Martin, A. Rebecca Snider, Joyce L. Peabody, June P. Brady. Children's Hospital and Cardiovascular Research Institute, University of California, Department of Pediatrics, San Francisco

To determine whether there are significant alterations in cerebral blood flow patterns in infants with patent ductus arteriosus (PDA), we performed range-gated pulsed-Doppler examinations of the aorta and cerebral arteries in 20 infants. Ten infants had a PDA (mean birthweight = 1210gm, mean gestational age = 29.5 wks) and ten control infants did not (mean birthweight = 2050gm, mean gestational age = 33 wks). The pulsatility index, PI = (peak systolic frequency minus trough diastolic frequency)/peak systolic frequency, was calculated.

Seven infants with a large PDA had retrograde diastolic flow in the descending aorta (DAo). This pattern was not seen after PDA closure. In the cerebral arteries in the 7 infants with a large PDA, diastolic flow was retrograde in 3 and decreased or absent in 4 (PI = 0.97 ± 0.13; mean ± SD). After PDA closure, cerebral diastolic flow was antegrade in all 7 infants (PI = 0.73 ± 0.04). In the 10 control infants and 3 infants with a small PDA, there was no diastolic backflow in DAo. Flow in the cerebral arteries was antegrade throughout diastole and PI was significantly lower (0.75 for controls and 0.73 for small PDA, $p<0.005$ vs. large PDA).

We conclude that a large PDA can cause abnormal flow patterns in the DAo and cerebral arteries. These flow patterns may predispose these infants to CNS ischemia or intraventricular hemorrhage.

1319 GLYCEROL KINASE: DEVELOPMENTAL BIOCHEMISTRY IN MAN. Edward R.B. McCabe, William K. Seltzer, Renea Hill and David Sadava (Spon. by Donough O'Brien). University of Colorado School of Medicine, Departments of Pediatrics, and Biochemistry, Biophysics and Genetics, Denver.

At birth the human is 16% fat, the human fetus acquiring nearly 2 g fat/g nonfat dry weight in late gestation with fat deposition representing approximately 90% of the caloric accretion at term (Sparks et al, Biol Neonate 38:113, 1980). Glycerol kinase (GK) phosphorylates glycerol for utilization and reutilization in triglyceride synthesis and might be expected to be active in such a system. Previous workers had shown this enzyme to be active in liver of human neonates shortly after birth, though animal studies suggested activities of this enzyme in fetal liver to be quite low. Preliminary results of GK activity are reported from 7 liver samples: 6 from stillborns ranging in gestational age from 22-40 weeks and one from a neonate of 37 weeks gestation dying within 20 hours of life. All of these samples contained GK activity, similar to child and adult values in specific activity ("fetal" 10-315 pmol/min·mg protein, no gestational age correlation; 3-4 y.o. 165-236 pmol/min·mg; 77 y.o. 699 pmol/min·mg) and in apparent Km for glycerol (107±21 μM, n=5; 2m.o. infants, range 30-64 μM; 58 y.o. 145 μM). Distribution of GK activity in 10,000 g supernatant and pellet differed markedly between fetal and adult liver samples, 52% and 94% being soluble, respectively. Term human placenta contained low activity (5.7 pmol/min·mg) distributed similar to adult liver. The presence of GK in placenta and fetal liver suggests a role for this enzyme in the major accretion of fat in the human fetus.

●1320 TIMING AND ETIOLOGY OF NEONATAL INTRACRANIAL HEMORRHAGE. Marilyn M. McDonald, Beverly L. Koops, Mary Anne Guggenheim, Carol M. Rumack, Michael L. Johnson, and Wm. E. Hathaway. University of Colorado School of Medicine, Departments of Pediatrics and Radiology, Denver.

Fifty infants (<33 weeks gestation) were followed prospectively from birth to evaluate the temporal relationships of various clinical factors to the onset and progression of intracranial hemorrhage (ICH) in an inborn population given maximal support. ICH was diagnosed and followed with bedside ultrasound every 8 hours. The incidence of severe ICH was 30% and of any ICH was 40% with onset from <2 hours to 8 days of age. There were significantly more episodes of ICH in babies born vaginally as compared with Caesarian section (x^2 <.02) with a trend toward longer labors in babies who developed ICH (p <.1).

The occurrence or progression of severe ICH correlated with: (1) perinatal asphyxia (Apgar score <5, 5 minutes), (2) premature rupture of membranes and premature labor, (3) fluctuations of BP greater than 100%, (4) initial infant hypocoagulability and maternal bleeding. No relationship was seen between onset or progression of ICH and pH, paO_2, $paCO_2$, infant sex, ventilation, patent ductus arteriosus or pneumothorax. Use of colloid infusions to treat hypotension or transfusions of red cells to replace blood sampling volumes was carefully monitored and found not to relate to the onset or timing of ICH.

In this study of intensively supported inborn infants (<33 weeks gestation) the occurrence and course of ICH was influenced more by factors related to prenatal stress than specifics of nursery care.

1321 ELECTROACOUSTIC IMPEDANCE MEASURES OF THE TYMPANIC MEMBRANE IN HIGH RISK INFANTS IN THE NICU. David L. McPherson and David Hicks (Spon. by Robert F. Huxtable) Univ. of California, Irvine, Dept. of Peds., Coll. of Medicine, Irvine, CA.

The purpose of this study was to define electroacoustic impedance changes of the tympanic membrane in the postnatal period in a NICU. A series of 120 infants were studied to determine 1) the incidence of middle ear effusion and 2) the developmental aspects of the middle ear using acoustic impedance of the tympanic membrane. Measurements were completed following feeding of the infant and during the infant's normal sleep period. Results demonstrated that either a normal type A curve or "W" pattern was observed in the neonate. As the infant's chronological age increased the "W" pattern transitioned into a normal type A curve. No infants beyond 56 weeks were seen with a "W" pattern. Likewise, the amplitude of the response, reflecting an increase in impedance, was observed to increase as a function of conceptual age. Abnormal tympanograms were obtained in 38% of all infants in the NICU. Those at highest risk for middle ear effusions were those on ventilators for more than 36 hours, and not treated with antibiotics. Those infants on antibiotics, usually to rule out sepsis, had a much lower incidence of middle ear dysfunction (12%). It is our opinion, based on the results of this study that the use of tympanometry in a NICU is beneficial in identifying and following those infants that have middle ear dysfunction with a high risk for hearing loss secondary to the pathology. In addition, it helps identify those infants that need to be followed for medical management of hearing problems.

1322 NON-HOMOGENEOUS REDISTRIBUTION OF BLOOD FLOW AFTER VASODILATOR THERAPY IN NEWBORN SEPTIC SHOCK: AN UNRECOGNIZED HAZARD. William L. Meadow & Paul J. Meus (Spon. by K-S Lee). U. of Chicago Dept of Pediatrics and Michael Reese Hospital Departments of Surgery and Cardiac Surgery, Chicago, IL

Morbidity in shock results from both systemic and regional hypoperfusion. We correlated the time course and magnitude of changes in total body cardiac output(CO) and regional mesenteric blood flow(QMES) in an animal model of neonatal septic shock.

Newborn piglets (n=6) were intubated, paralyzed, anaesthetized, and ventilated. CO and QMES were monitored by flow probes. Septic shock was induced by continuous infusion of Group B Strep (GBS). When CO had fallen by 30% after GBS, tolazoline (TZ), a vasodilator, was given by i.v. bolus at doses between 2 - 25 mg/kg.

During GBS infusion, CO and QMES fell with identical magnitude and time course. When CO fell to 70 ± 3% of pre-GBS value, QMES was 69 ± 3%(n.s.). In these septic animals, TZ produced a sustained, dose-related rise in CO (14/14 trials, p<0.01 vs placebo). In contrast, between 2-25 mg/kg, no simple dose relationship was apparent for the effect of TZ on QMES in sepsis. TZ caused a fall in QMES in 8/14 trials (p<0.05 vs. CO effect) while TZ caused a sustained rise in QMES in only 2/14 trials.

Conclusions: 1. In the normotensive, hypoperfused phase of GBS septic shock, the fall of CO and QMES were directly correlated, both temporally and quantitatively. No proportion of blood flow was redistributed either towards or away from the mesenteric circulation during GBS infusion. 2. After TZ in sepsis, CO was uniformly improved, but QMES was not. QMES often decreases despite improvement in CO after TZ administration in sepsis.

●1323 UTILITY OF CENTRAL VENOUS OXYGEN SATURATION AS AN INDEX OF CARDIAC OUTPUT IN NEWBORN SEPTIC SHOCK. William L. Meadow & Paul J. Meus, (Spon. by K-S Lee), U. of Chicago Department of Pediatrics and Michael Reese Hospital Departments of Surgery and Cardiac Surgery, Chicago IL

Direct determinations of cardiac output (CO) in ill newborn infants are frequently desired but seldom performed. We investigated central venous oxygen saturation (Sat_vO_2) as an index of cardiac output in an animal model of neonatal Group B Strep septic shock.

Newborn piglets (n=6) were intubated, paralyzed, anaesthetized, and ventilated with 50% O_2/50% N_2O. After a control period, GBS sepsis was induced by i.v. infusion of live organisms @ 0.75-4.0 $x10^7$ org/kg/min. Cardiac output was determined by pulmonary artery flow probe. Paired arterial (aorta) and venous (pulmonary artery) blood samples (n=49,range 6-11/exp, x=8.2) were obtained to determine Sat_aO_2, Sat_vO_2, blood pH, and base excess (BE).

During GBS infusion, CO fell to 39 ± 7% (S.E.) of control, while Sat_vO_2 fell from 64 ± 4% to 24 ± 3%, pH fell from 7.49 ±.01 to 7.14 ±.06, and BE rose from -.95 ± .90 to -16.5 ± 2.9 (all p<0.01). Sat_aO_2 remained constant at 97±2% during GBS infusion.

For each of the 6 experiments, a plot of $(CO)^{-1}$ vs. Sat_vO_2 was first-order, linear (r range .903 to .976, all p<0.01). No significant tendency was observed for $(CO)^{-1}$ vs. Sat_vO_2 to deviate from linear even at low CO, low pH, or high BE.

Conclusion: In newborn septic shock, over a wide range of CO, pH, and BE, changes in $(CO)^{-1}$ are accurately and linearly reflected by changes in Sat_vO_2. This observation may be useful in neonatal clinical contexts where changes in CO are of concern.

1324 PRESCHOOL FOLLOW-UP OF INFANTS TREATED WITH INDOMETHACIN OR SURGICAL LIGATION. Thurman A. Merritt, Charlotte L. White, Ronald W. Coen, Louis Gluck, Univ. of California, San Diego, Department of Pediatrics, La Jolla.

Forty-three infants with patent ductus arteriosus (PDA) treated with indomethacin (INDO) and 36 infants with PDA undergoing ligation have been followed into their preschool years. Seventy-two percent completed preschool clinic assessments, 3 infants died (2.7%), and the remainder moved or were lost to follow-up. No significant differences in growth, except for lighter male infants at 18 months, was found for length, weight, or head circumference at 36 months. No differences in visual or auditory function was evident between the two groups; 4 of 36 infants undergoing ligation developed retrolental fibroplasia, and none treated with INDO has this complication. Analysis of the latest Bayely Scale of Infant Development revealed no significant difference between the number of infants scoring ± 1, 2, or 3 standard deviations of the mean or in the unscorable category. Analysis of scores on the Peabody Picture Vocabulary Test demonstrated no significant differences between the INDO or ligated infants. An overall clinical assessment of all infants reveals 7/43 INDO and 6/36 ligated infants having minor or major neurodevelopmental delay. At 36 months; no significant differences were found in clinical, visual, auditory or developmental outcome in infants with PDAs treated with INDO or surgical ligation. INDO treatment in preterm infants for PDA does not have selective adverse effects on long term outcome compared to infants having surgical PDA closure.

1325 EFFECT OF DIETARY AMINO ACID IMBALANCE IN PREGNANT RATS ON PLACENTAL & FETAL BRAIN PROTEIN Jack Metcoff, Timothy Cole, Peter Lunn, Sohair Salem. University of Oklahoma Health Sciences Center, Oklahoma City, OK and Dunn Nutrition Laboratory, MRC, Cambridge, England.

36 rats, from day 1 of pregnancy, were fed a complete basal diet of 6% casein plus the amino acids (AA) MET, THR, equimolar mixtures of 4.5% SER, GLY & ALA, & 5% ILE, LEU, VAL, PHE, TYR & HIS, with a protein equivalence of ~15g/100g, i.e.: marginally protein restricted (MPR). On day 3, B continued on the basal MPR diet, C (control) received an equicaloric diet supplemented with 14% casein, and E (MPR with AA imbalance) got the basal diet with the THR supplement omitted. The protein contents of pup placenta & brain & the relation of the maternal plasma AA levels to fetal & placental growth were compared. E pup brains & placentas <B <C. The number of pups/litter was E>B>C. The total amount of protein in the placentas, brains & litter size were correlated. Adjusting for maternal & litter size (by multiple regression) the protein content in placentas of C>B, but E=B; for the brains E <B, but C=B. When adjusted for maternal prepregnant weight, weight gain to term & length, the difference in (Δ) pup brain weights E vs. B were related to a Δ the maternal plasma levels of VAL, PRO, TYR, GLY & ASP, combined. The larger brains of C vs. B were partially accounted for by Δ maternal plasma levels of the combination ILE, MET, LYS, LEU & GLY. With dietary protein restriction giving larger litters, each pup & placenta get less protein; but the concentration in the brain is not reduced. With AA imbalance, both protein concentration & content of the pup brains is reduced. Thus, dietary AA imbalance with MPR during pregnancy alters the maternal plasma AA pattern, which is associated with a smaller pup brain containing less protein.

1326 THE EFFECT OF DELIVERY METHOD ON NEONATAL pH IN VERY LOW BIRTH WEIGHT (VLBW) INFANTS. William H. Michaels, Joseph V. Collea, John J. Schruefer, Michael Harbison, K.N. Sivasubramanian. (Spon. P.L. Calcagno.) Georgetown Univ. Med. Ctr, Washington,D.C.

Two hundred and twenty-four observations of at least one determination of neonatal pH were reviewed retrospectively based on: 1) admission to intensive care nursery; 2)< 36 weeks of gestational age (GA); 3) and/or < 2500 gms. The relationship of the first neonatal pH to the method of delivery, presentation, labor, gestational age and birth weight were analyzed. Ninety vertex presentations were delivered vaginally (VV), 12 breech presentations were delivered vaginally (VB) and 122 were delivered by cesarean section (CS). The entire population's mean GA 33.4 wks; $\bar{X}$ birth weight 1850 gms; $\bar{X}$ pH 7.23; $\bar{X}$ pCO_2 38.7 torr. The status of labor was not significantly different ($p < 0.7$) among the groups.

METHOD OF DELIVERY	N	pH
CS	122	7.23±0.10
VB*	12	6.90±0.33*
VV	90	7.10±0.14*

B.W.(gms)	N.	pH
1000*	30	7.13*
1001-1500	66	7.25
2001-2500	50	7.21

$p < 0.05$ - pH analyzed as H+ ion concentration.

Conclusions: 1) The VLBW infants delivered vaginally were significantly more acidotic than the rest of the infants; 2) The VLBW breeches (VB) delivered vaginally were significantly more acidotic than those delivered by CS or VV ($p < 0.05$).

1327 TIMING OF MATERNAL TRANSPORT IN PREMATURE LABOR: William H. Michaels, Joseph V. Collea, John J. Schruefer, Michael Harbison and Kolinjavadi N. Sivasubramanian. (Spon. P.L. Calcagno.) Georgetown University Medical Center, Washington, D.C.

The delivery records of 208 infants delivered vaginally were reviewed based on 1) Admission to intensive care nursery; 2) Birth weight (B.W.)< 2500 gms. and/or; 3) < 36 weeks of gestation to determine the relationship between B.W. and the length of second stage of labor. There was a significant difference in the length of stage II between premature primigravidas and premature multigravida nulliparas (P_0) and term primigravidas. According to the literature, the $\bar{X}$ duration of Stage II at term was 57 mins.for primigravidas.

B.W.	N P_0	STAGE II ($\bar{X}$ Min.)
500-1000	11	13.4*
1001-1500	13	15.5*
1501-2000	23	25.7
2001-2500	63	34.0

*$P < 0.05$

Conclusions: 1) The length of stage II was significantly shorter ($P < 0.05$) for mothers delivering infants < 1500 gms; 2) once active labor has started, maternal transport is not feasible; 3) And maternal transfer should be completed prior to the active phase of labor.

1328 PERINATAL OUTREACH EDUCATION PROGRAM (POEP) AND ANTENATAL TRANSPORTS: IMPACT ON NICU ADMISSIONS, MORBIDITY AND MORTALITY. Houchang Modanlou, Wendy Dorchester, Ruth Redmann, Neonatal-Perinatal Medicine, Miller Children's Hospital, Long Beach, University of California, Irvine.

Admissions to NICU, morbidity and mortality patterns were analyzed for a period of 2 years(1975-76)prior and 2 years(1979-80) following 4 years of POEP to 12 primary and 2 Level II hospitals. There were 877 antenatal transports in 1979-80 but none in 1975-76. There were 1176 NICU admissions in 1975-76, 563(47%) inborn, 613 (52%)transports. In 1979-80 there were 1545 NICU admissions with 1004(65%)inborn and 541(35%)transports. Half of the inborn (511) were delivered to antenatal transports.The birthweight(BW)distributions changed significantly between the 2 periods. In 1975-76 14% of the inborn had BW≤1500gm with 28% in 1979-80($p<.01$). This increase was entirely due to antenatal transports with 216 (42%) of these weighing ≤1500gm. Also the percent of low birthweight (LBW) neonatal transports decreased by 10%(54%[331]vs 44%[241],$p<0.01$ between the 2 periods. Despite a 16% increase in inborn admissions of LBW there was only 5% increase in the incidence of RDS. In 1975-76 there were 151 NICU deaths(13% mortality)compared with 145(9%) in 1979-80; $p<.001$. Mortality for BW≤1500gm & BW≤1000gm were 24% & 47% respectively in 1979-80 while in 1975-76 were 34% & 63%,$p<.01$. Fifty-six percent of deaths in 1979-80 were inborn compared with 36% in 1975-76; $p<.001$. However, if antenatal transports are excluded the rate is 21%, significantly lower($p<.05$)than 1975-76. There was a decreasing trend in NICU deaths from severe perinatal asphyxia. Many factors contribute to this improvement in perinatal outcome. POEP and antenatal transfers may play a major role.

1329 LARGE FOR GESTATIONAL AGE (LGA) NEONATES: ANTHROPOMETRIC REASONS FOR SHOULDER DYSTOCIA (SD). Houchang D. Modanlou and Glen Komatsu, Division of Neonatal-Perinatal Medicine, Miller Children's Hospital of Long Beach, University of California, Irvine.

Anthropometric measurements were carried out in 202 LGA infants with birth weights (BW) ≥4001gm, in 100 control with BW 2501-4000 gm and in 27 infants of diabetic mothers (IDM).Ten LGA infants had SD. Compared to control, LGA infants had higher length, head (HC), chest (CC) and shoulder circumferences (SC), shoulder-head (S-HCD) and chest-head circumference differences (C-HCD) ($p<0.001$).Comparison between 10 LGA infants with SD and 130 vaginally delivered LGA infants without SD showed that the HC was similar but there was significant differences in CC, SC ($p<0.005$), S-HCD and C-HCD (4.8±2.1 vs 3.3±1.8cm; $p<.025$ and 1.6±2.2 vs 0.2±1.8cm; $p<.025$, respectively). Such a difference was not seen when LGA infants with SD were compared to 30 LGA infants delivered by primary cesarean section as a result of failure to progress in labor. Comparison of 11 IDM with BW ≥4001gm to 202 LGA infants showed that in spite of a lower gestational age, IDM had larger SC and S-HCD ($p<.001$). Similar comparison between 16 IDM with BW ≤4000gm to the 100 control infants showed that IDM had significantly lower HC ($p<.005$) but higher S-HCD ($p<.001$). This study shows that the anthropometric disproportions of S-HCD of 4.8cm and C-HCD of 1.6cm in LGA fetus indicate a high probability of SD. These anthropometric disproportions are more pronounced in IDM irrespective of their weight. In suspected fetal macrosomia and in diabetic pregnancies, antenatal evaluation, by ultrasound, for fetal anthropometric disproportions should be done for selection of the appropriate route of delivery.

1330 SIGNIFICANCE OF MEAN AIRWAY PRESSURE (MAP) DURING ASSISTED VENTILATION (AV): CORRELATION WITH ALVEOLAR RUPTURE (AR), INTRAVENTRICULAR HEMORRHAGE (IVH) AND BRONCHOPULMONARY DYSPLASIA (BPD) IN VERY LOW BIRTH WEIGHT (VLBW) INFANTS. Houchang Modanlou, Don Owings, Tom Ciszek, Neonatal-Perinatal Medicine, Miller Children's Hospital, Long Beach, CA.

Alveolar rupture, IVH and BPD are common in VLBW infants with RDS requiring AV. A prospective study in 32 VLBW infants with severe RDS requiring AV before the first 4 hours of life, with continuous monitoring of MAP and ultrasound examination of the head during the first 48 hours was carried out.Their mean birth weight and gestational age were 1096±301gm and 28.8±1.9wks. Eleven developed AR at the mean age of 18.5±17.4hrs. The use of antenatal steroid, birth weight, radiographic severity of RDS and the age AV was initiated were similar in 11 with and 21 infants without AR. During the 1st and 2nd 24 hours of AV, the highest positive end expiratory pressure (PEEP), duration of positive pressure (DPP), rate, flow and FiO2 were similar but there were significant differences in peak inspiratory pressure (PIP), 31.4±7.3 vs 25.8±7.9 cmH20 and MAP 14.1±5.4 vs 9.2±3.4cmH20; $p<.005$. The incidence of Grade III and IV IVH was 55% and 22% respectively. Six of 7 (86%) infants with AR who survived the neonatal period developed BPD while only 2 of 17 (12%) without AR developed BPD ($p<.01$).MAP, as a composite of all pressures transmitted to the airways increases transpulmonary pressure which in turn impairs cephalic venous return leading to IVH by cephalic venous distention & hypertension. MAP may be modified by changes in flow, PIP, PEEP, DPP and rate. Whatever the modality of AV, one should try to provide it with the lowest possible MAP and PIP.

●1331 PHARMACOKINETICS OF TOLAZOLINE (TZ) IN NEONATES WITH PERSISTENT FETAL CIRCULATION (PFC). Pierre Monin, Paul Vert, Paolo Morselli. (Spon. by William Oh). Maternite Universitaire, Department of Pediatrics, Nancy and LERS Synthelabo, Paris, FRANCE.

In 19 patients (BW : 2153±1079 g, GA : 33.7±5.1 wks) treated for PFC, we studied the kinetics and pharmacodynamic profile of TZ. When indicated an IV bolus of TZ of 2 $mg.kg^{-1}$ was given followed by a maintenance dose of 2 mg/kg/hr. Plasma levels of TZ were measured by HPLC on 0.5 ml of blood at 10.30 mn, 1,3,6,12 hrs and q. 12 hrs after the onset of treatment. Changes in PaO_2 mmHg were evaluated with 90 mn and 6 hrs by $tcPO_2$ or on blood samples.

TZ plasma levels rise during the first 12 hrs with a plateau and a large individual dispersion (5 to 20 µg/ml).

t(mn-hrs):	10	30	1 hrs	3	6	12	24
TZ($\bar{x}$±1SD): ($\mu g.ml^{-1}$):	4.61 ±2.32	5.93 ±3.68	7.65 ±6.69	8.65 ±5.18	11.11 ±5.19	12.43 ±6.34	12.98 ±11.23

Except for one case (33 h) the elimination half-life (t1/2β) was between 2.5 and 10.1 hrs (7.0±2.8 hrs, n=8), ΔPaO_2 (38±12 mmHg within 90 mn and 38±24 within 6 hrs) occur only when blood pH before injection was >7.18 (n=10). When present, ΔPaO_2 was unpredictable and no correlation was found between $AaDO_2$ and TZ levels. Usually ΔPaO_2 occurs early after the onset of treatment suggesting a pharmacodynamic effect for lower levels than those observed at 10 or 30 mn. These results suggest that the pharmacodynamic effect of TZ on pulmonary vessels and/or myocardium does not occur in acidemic patients. In optimal acid-base status a lower dose could be proposed. According to the long t1/2β, the opportunity of a continuous infusion is questionable.

1332 RETINOL BINDING PROTEIN(RBP) LEVELS IN PREMATURE INFANTS:AFFECT OF NUTRIENT INTAKE. Sharon R. Moskowitz, Gilberto R. Pereira,Louisa Heaf, Alan Spitzer, Jon Amsel, John B. Watkins. Univ. of Pa. Sch. of Med., Dept. of Peds., Children's Hospital of Phila., Philadelphia, PA.

Normal serum RBP levels require protein for synthesis and adequate hepatic Vit.A stores for secretion of Vit.A-RBP complex. Since preterm infants may have inadequate hepatic reserves of Vit.A or loss through inefficient enterohepatic circulation and poor absorption, RBP levels were determined by radial immunodiffusion in 38 preterm and 24 full term cord-maternal pairs and in 14 preterm AGA infants (880-1600g, 27-33 weeks gestation) followed until discharge(n=14). Changes in RBP levels were compared to intake of protein, calories, Vit.A, zinc, to changes in length, weight, head and arm circumference, and to serum prealbumin(PA) values. Cord RBP, mean ± SD (mg/dl), in infants born≤30 weeks (n=11) was 1.6±0.45 compared to 1.9±0.38 in 31-34 weeks (n=13) ($p<.025$), and 2.3±0.79 in full term (n=24)($p<.01$). Maternal RBP was similar at all gestational ages, 3.9±1.0. In infants studied serially, when protein intake was ≤2g/Kg, RBP was lower than with >2g/Kg, 1.8±0.6 compared to 2.4±0.98 ($p<.005$), irrespective of gestational age. Also, with ≤100 Kcal/Kg intake, RBP was lower than with >100 Kcal/Kg, 1.9±0.8 vs 2.5±0.98 ($p<.0005$). RBP correlated poorly with intake of Vit.A supplements, oral or IV and zinc. PA:RBP molar ratios were variable with no relationship to nutritional treatment. Conclusions: Serum RBP levels increase with fetal age unrelated to maternal levels. After birth, low RBP levels are consistent with low protein and caloric intakes. However, low RBP irrespective of recommended intakes of Vit.A, protein and calories, with normal serum PA, is suggestive of poor Vit.A status in the growing premature infant.

1333 OPHTHALMOLOGIC FINDINGS AT 3 YEARS IN LOW BIRTH WEIGHT INFANTS WEIGHING ≤ 1500 GRAMS AT BIRTH. Z.D. Najak,J.A. Gammon, and A.W. Brann, Jr., Emory University School of Medicine, Atlanta, Georgia.

In order to assess visual function,sick preterm infants weighing ≤1500grams(gm)at birth are followed.This is a prospectively followed group(Gp)comprising those of birth weight ≤1000gm, Gp.A (1976-78 births);Gp.B were >1000-1500gm at birth(1978 births).The mean gestational age of Gp.A was 29 weeks and of Gp.B was 31weeks Abnormalities were detected in 17/51(33%)of Gp.A,and in 16/58(28%) of Gp.B.Total blindness secondary to retinopathy of prematurity (ROP)occurred in 4(8%)children from Gp.A and in 2(3.5%)children from Gp.B.Blindness in these 5 children was recognized at the time of initial eye examination(at discharge)or within 6 months after discharge.4 additional infants have significant visual impairment:3 are myopic and 1 has moderate ROP.All the ophthalmologic findings are summarized below:

	Gp.A(n=51)	Gp.B(n=58)
ROP:(I)Blind	4	2
(II)Grade III-IV	0	1
(III)Grade I-II	4	5
Vision impaired(myopia)	2	1
Strabismus	7	6
with intraventricular hemorrhage	3	4
with neurologic deficits/IQ retardation	3	3
Nystagmus	2	1

Our data suggests that:(1)Besides ROP,there are other major visual problems in this high risk group;(2)Strabismus in this population may often imply underlying central nervous system dysfunction.

● 1334 EFFECT OF VARIOUS RESUSCITATIVE FLUIDS ON BLOOD PREFUSING THE BRAIN. L. Dennis Nalle, Stephen M. Golden, William M. Heroman, Errol R. Alden (Spon. by Gerald W. Fischer) Uniformed Services University of the Health Sciences, Department of Pediatrics, Bethesda, MD 20814.

Intraventricular hemorrhage may be precipitated by sudden changes in arterial pressure and plasma osmolality. Yet the sickest newborns are subjected to a variety of fluids during resuscitation. Therefore, we investigated changes in carotid artery blood in chronically catheterized newborn lambs during infusion (2-3 min) of commonly used resuscitative fluids. Fluids were infused into the descending aorta and inferior venacava to simulate umbilical artery and venous infusion.

	ΔNa	ΔOSM	ΔOncotic Press.	ΔHCT	ΔMAP
$NaHCO_3$ (.9mEq/ml;2mEq/kg)	+5.7	+8.6	-1.7	-1.1	+8.3
$NaHCO_3$ (.5mEq/ml;2mEq/kg)	+3.3	+4.3	-1.9	-2	+4
$D_{10}W$	10cc/kg -11.7	+7.9	-1.9	-2.9	+10
D25	4cc/kg -7.2	+16.9	-2.0	-2	+6.7
Blood	5cc/kg				+12.9

mean Δ; all $p < .01$

Significant changes in mean carotid artery blood pressure (MAP), osmolality and oncotic pressure occur with infusion of commonly used resuscitative fluids. Whole blood infusion caused a 3X greater increase in MAP than diluted $NaHCO_3$ infusion. Maximum electrolyte and osmolal changes occurred during the infusion, and persisted over 20 minutes. These changes may contribute to the incidence of IVH in the newborn.

1335 AMNIOTIC FLUID (AF) MICROVISCOSITY STUDIES IN DIABETIC PREGNANCY: RELATION TO PHOSPHOLIPID COMPOSITION. N. Neufeld, L. Corbo, S. Melmed, G. Braunstein (Intr. by B. Kagan). Departments of Pediatrics and Medicine, Cedars-Sinai Medical Center, UCLA School of Medicine Los Angeles, CA.

Microviscosity (MV) of AF, assessed by fluorescence polarization (P) measurements correlates with surface-tension lowering properties and is a predictor of respiratory distress syndrome (RDS) (Stark et al. J. Pediat. 96:301, 1980). We measured MV of AF obtained from control (C) and alloxan diabetic (D) pregnant rabbits on day 27 and compared these results to both L/S ratios and fetal lung phosphatidyl glycerol (PG, mg/gm tissue). P was measured at 25°C following incubation of AF with 2,4, diphenyl 1,3,5 hexatriene (DPH). Both C (n=27) and D (n=14) had comparably immature (>.310) P values (.352±.008 vs .335±.007 NS), although L/S (3.53±.05 vs 2.56±.23, $p<0.001$) and PG (.38±.04 vs .25±.01 mg/gm tissue $p<0.01$) were dissimilar reflecting relative immaturity of D. Treatment of mothers with 3,5 dimethyl, 3' isopropyl thyronine (DIMIT) (0.5 mg/kg), a fetal-active thyromimetic agent known to accelerate lung maturity, resulted in significant lowering of MV in both C (.245±.014, n=15, $p<0.001$ vs C) and D (.312±.005, n=9, $p<0.005$ vs D). DIMIT treated D showed significant elevations in L/S (3.57±.224, $p<0.01$ vs D) and PG (.360±.03, $p<0.01$ vs D). In contrast, treatment of D mothers with betamethasone (0.2 mg/kg x 2 d.) was associated with worsening maternal diabetes and resulted in marked elevation of MV (.384±0.1, n=11, $p<0.001$ vs D) as well as lowering of L/S (2.13±.03, $p<0.001$) and PG (.130±.03, $p<0.01$).

Conclusion: In diabetic pregnancy, MV correlates with fetal pulmonary PG and thus predicts the likelihood of RDS with greater accuracy than L/S.

1336 AUDITORY BRAINSTEM RESPONSE (ABR): EXPERIENCE WITH TERM ASPHYXIATED INFANTS. Sarvesh K. Nigam,Janet Purn, Ilana W. Zarafu. (Spon. Franklin C. Behrle) College of Med. and Dent. of N.J.-N.J. Med. School,Newark Beth Israel Medical Center (NBIMC),Dept. of Ped. Newark, N.J. 07112

Between 6/79 and 10/81 584 neonates admitted to the Newborn Special Care Unit at NBIMC were evaluated with ABR: 90(15.4%) of these had abnormal findings upon initial evaluation. There were 359 preterm infants,60(16.7%) of these had abnormal ABR. Thirty out of 225 term infants (13.3%) had abnormal initial ABR findings. Sixteen of 30(53%) occurred in infants with a variety of diagnoses,none predominant. Fourteen of 30(46.6%) had perinatal asphyxia with a mean 1 minute Apgar Score of 2.7 and a mean 5 minute Apgar Score of 4.9. Ten of 14(71.4%) required assisted ventilation. Four of 14(28.5%) expired.

The initial ABR was completed between 2 hours-168 hours postnatally with a mean age of 54.5 hours. The following abnormalities were noted: auditory sensory deficit (threshold > 50 dbHL) 9/14(65%),3 of these were profound losses,only 1 of the 3 survived. Prolongation of interpeak interval (wave I-V > 5.5ms) was present in 7/14(50%). Unlike our ABR experience in infants with intracranial hemorrhage, none of the asphyxiated infants showed the absence of any of the major ABR components.

Follow-up of the survivors shows 2/10(20%) with moderate/severe bilateral sensorineural hearing loss and 1/10(10%) with moderate unilateral loss. 7/10(70%) were normal audiologically. Term babies with severe asphyxia demonstrate transient,major ABR abnormalities. They are also at high risk for permanent sensorineural hearing loss, 3/10(30%).

● 1337 LUNG LAVAGE OF NEWBORNS WITH RESPIRATORY DISTRESS SYNDROME(RDS): PROLONGED NEUTROPHIL(PMN) INFLUX IS ASSOCIATED WITH BRONCHOPULMONARY DYSPLASIA(BPD). Bruce E. Ogden, Shirley A. Murphy, George C. Sanders, and John D. Johnson, University of New Mexico School of Medicine, Department of Pediatrics, Albuquerque, NM, and Los Alamos National Laboratories, Los Alamos, NM.

To determine if lung inflammation plays a role in the development of BPD, serial bronchoalveolar lavage (BAL) was performed in 23 infants with RDS, 11 who developed BPD, and 11 without lung disease. The 24 hr. BAL showed no difference in absolute alveolar macrophage (AM) or PMN counts between control, RDS, or BPD groups. Peak PMN influxes, occuring at 96 hrs., were higher in RDS(99±25) than in BPD(20±8)($p<.02$). Values represent mean±SEM x 10^{-5}. At 1 week, as RDS infants recovered, their BAL PMN counts returned to normal(5±2). In contrast, 1 week BPD BAL PMN counts were higher(35±7) than RDS($p<.02$); PMN counts remained elevated while AM counts were decreased for up to 6 weeks. There were no significant differences in BAL values of albumin, IgG, and LDH between BPD and RDS groups at any time point. However, BAL alpha-1-antitrypsin was significantly higher in RDS (2.0±0.6 mg/dl) in contrast to BPD (.6±0.2) at 96 hours ($p<.05$). BAL elastase levels in RDS peaked at 96 hours (302±187)and returned to baseline by one week (36±3) whereas prolonged elevation of the elastase levels occurred in BPD peaking at 2 weeks (470±406) and not returning to baseline (45±8) until 4 weeks. It is likely that the prolonged pulmonary inflammatory responses in BPD play a role in the pathogenesis of the chronic lung disease.

●1338 NEWBORN INTENSIVE CARE AND NEONATAL MORTALITY IN A TOTAL POPULATION. Nigel Paneth, John L. Kiely, Sylvan Wallenstein, Michele Marcus, Jean Pakter, Mervyn Susser. Columbia Univ. College of Physicians & Surgeons, Depts. of Public Health, Pediatrics and Sergievsky Ctr. and New York City Dept of Health. (spon. by David Rush)

We examined neonatal mortality by level of hospital care in the 13,560 LBW singletons (501-2250g) born in NYC in 1976-1978.

The neonatal mortality rate (adjusted for race, sex, BW, and GA) for infants born at Level 3 hospitals, 128.5/1000 live births, was significantly lower ($p < .001$) than the mortality rates for infants born at either Level 2 (168.1/1000), or Level 1 (163.0/1000) units. Although there was no net difference in mortality between Level 1 and Level 2 units, infants weighing less than 1250g did significantly better at Level 1 than Level 2 hospitals, whereas for those weighing more than 1250g the reverse was true.

On a 5-level scale of care (with Levels 2 and 3 each divided into upper and lower divisions) a linear gradient of mortality was found for singletons weighing 1251-2250g. Adjusted mortality rates, per 1000 live births, for the 5 levels, from highest to lowest scoring hospitals, were 45.3, 51.3, 64.8, 75.5 and 75.4 (X^2 for linear trend = 21.47, $p < .001$).

The association of hospital level with mortality could not be accounted for by maternal age, parity, race, education, economic resources, or marital status, or by extent of prenatal care or medical complications of pregnancy. We conclude that newborn intensive care lowers mortality in LBW infants and that a substantial number of LBW infants in NYC are at higher risk of mortality through lack of immediate access to such care.

1339 TRANSCUTANEOUS BILIRUBINOMETRY CAN BE USED DURING PHOTOTHERAPY. Marykay Pasnick and Jerold F. Lucey, Dept. of Pediatrics, Univ. of VT, Burlington 05405.

One hundred and sixty-three transcutaneous bilirubin determinations were performed on 103 term and preterm infants both with and without phototherapy. Correlation coefficients in infants not receiving phototherapy were .926 in the group with birth weights less than 1500 grams and .824 for infants with a birth weight greater than or equal to 1500 grams ($p < .001$). Correlations were slightly less in infants under phototherapy but remained significant with $p < .001$. Slope and Y intercept of the calculated regression lines differed according to birth weight but were not greatly affected by the use of phototherapy provided a patched area of skin on the forehead protected from light was used. Previous investigators have found similar correlations, but the linear regression lines calculated from our data do not coincide well with these previous reports. This suggests that correlations may need to be determined separately for each instrument and the hospital laboratory's method for doing serum bilirubin. The transcutaneous bilirubinometer (Minolta) is an effective, non-invasive device for assessing jaundice in the newborn period in both term and preterm infants. The use of phototherapy does not markedly affect results if the area of skin tested is carefully protected from light exposure.

1340 ROLE OF A LEVEL II NURSERY, OUTCOME & COST Daksha Patel, Richard Nachman, Leela Selvam, Columbus-Cuneo Cabrini Medical Center (Spon. by Carl Hunt, Children's Memorial Hospital, Chicago, Illinois)

The purpose of the study is to present an expanded role of a community hospital in the care of sick neonates. One year's statistics from Columbus Hospital, who delivers 1500 neonates per year, is presented. The diagnoses of patients managed in a community hospital, the percentage of patients requiring transport to a tertiary care center, the cost of running the unit, the staffing needs, perinatal mortality and the cost to the patient are presented. One-hundred and fifty-one charts of sick neonates admitted to the Intensive Care Nursery were reviewed and the Billing Department computed charges on the sick patients. Perinatal mortality was 14 per 1000 live births, there were 10 maternal and 13 neonatal transports per 1511 deliveries. Ten percent of the neonates were admitted to the ICU. Thirty percent of the ICU babies had RDS and 16% required ventilator care. Total hospital charges on 120 neonates for 1546 days were $380,037. The charge per day was $245. The hospital collected 70% of the charges. A 2.5 million dollar budget was presented for the projected 1600 deliveries in 1982. The tertiary care center provided space for ongoing resuscitation training, consultation services and training of the respiratory therapists. The obstetricians and neonatologists from the community hospital participated in perinatal conferences at the tertiary care center. Conclusion: With strong support from the tertiary care center, the community hospital provided a high quality of care to the sick neonates at a reasonable cost. This can be used to expand the role of level II nurseries.

1341 YAWNING BEHAVIOR IN NEONATES Daksha Patel, Howard Weiss, Leela Selvam, Columbus-Cuneo-Cabrini Medical Center (Spon. by Carl Hunt, Children's Memorial Hospital, Chicago, Illinois)

Yawning, a homeostatic reflex, is an indicator of neuro-physiological well being in an adult. In order to understand the significance in the neonate, 25 normal term neonates and 25 admitted to the Intensive Care Nursery were continuously observed for yawning episodes. The time of the appearance of the first yawn was correlated with the other parameters of physiological well being. In two premature neonates with prolonged hospitalization, daily frequency of yawning was correlated with separate episodes of acute illnesses. Yawning behavior was studied in a pair of discordent twins and a hypopituitary dwarf. Yawning was present in neonates of all gestations. The mean age in hours when the first yawn appeared in the normal neonates was 16±13 hours compared to the sick neonates, where the mean age was 85±56 hours.

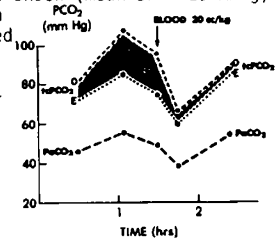
Category	Presence of Yawning in the First 48 Hours	
	Present	Absent
Normal	22	3
Sick	7	18

Chi square P = .001

There was a significant positive correlation between ages in hours at the time of the first feeding and the ages in hours when the first yawn appeared in the 23 sick neonates (P=.02). The daily frequency diminished during the episodes of acute illness in those with prolonged hospitalizations. The first yawn appeared on the 6th day in the growth retarded second twin and in the hypopituitary dwarf. Conclusion: In newborn infants, the presence of yawning indicates recovery phase & physidogical well being.

1342 DOES SHOCK AFFECT THE TRANSCUTANEOUS-ARTERIAL P_{CO_2} GRADIENT? Joyce L. Peabody and Janet R. Emery (Spon. by June P. Brady). Children's Hosp. and Cardiovasc. Research Institute Univ. of Ca., Dept. of Ped., San Francisco.

To find out whether shock affects the reliability of the transcutaneous P_{CO_2} electrode, we compared the transcutaneous versus arterial P_{CO_2} (tcP_{CO_2} vs P_aCO_2) in 31 sick infants on 93 occasions. In 27 studies of 4 infants, arterial blood pressure (BP) was more than 2 S.D. below normal. Three infants were studied again after correction of their hypotension (n = 9). TcP_{CO_2} was measured with a Radiometer TCM20 at 43°C. In 66 paired measurements from infants not in shock, $tcP_{CO_2} = 1.4\ P_aCO_2 + 4$, similar to previous reports. However, this was not true for infants in shock ($tcP_{CO_2} = 1.6\ P_aCO_2 + 7$); the $tcP_{CO_2} - P_aCO_2$ gradient was significantly higher by analysis of covariance ($p < .001$). After correction of hypotension, the gradient was not significantly different from the normotensive infants. The figure shows the $tcP_{CO_2} - P_aCO_2$ gradient in a 1310 gm infant in shock (mean BP = 29 mmHg). After administration of blood, the mean BP was 42 mmHg and the gradient narrowed to that observed in normotensive infants. The observed (O) and expected (E) tcP_{CO_2} (calculated from the regression line of normotensive infants) and the P_aCO_2 are shown.



We conclude that the gradient for transcutaneous and arterial P_{CO_2} is much greater in infants in shock and decreases when shock is corrected.

1343 CAN NEONATAL GLUCOSE HOMEOSTASIS BE ACCURATELY MONITORED BY RAPID BEDSIDE QUANTITATIVE METHODS? Robert H. Perelman, Gary R. Gutcher, Michael J. Engle, Michael J. MacDonald, (Spon. by Richard D. Zachman), University of Wisconsin, Dept. of Pediatrics, Madison, WI.

As a fundamental aspect of newborn care, the rapid assessment of glucose homeostasis is most often accomplished by a glucose oxidase/peroxidase chromagen test strip method, either alone or with a reflectance colorimeter. The precision of these techniques has been established, but few studies have determined accuracy in a clinical intensive care setting. Consequently, we performed the following study: During the time of routine heelstick blood sampling, intensive care nurses collected 90 complete study sets for glucose analysis from 43 neonates. Dextrostix, Ames Meter, Chemstrip bG and Stat Tek Meter determinations were performed immediately according to manufacturers' instructions. Concurrent determination of blood glucose by a Beckman Glucose Analyzer II served as a standard for comparison. There was no significant difference in estimation of true blood glucose among the rapid methods tested.

	Regression Line Intercept	Slope	95% confidence interval at 60 mg/dl	Correlation to true glucose
Ames Dextrostix	26.3	0.50	31-89	0.689
Ames System Meter	24.4	0.58	35-85	0.774
Chemstrip bG	23.5	0.62	36-84	0.790
Stat Tek Meter	20.8	0.75	35-85	0.774

As indicated in the above table, the marked variability of results suggests only modest accuracy in estimating whole blood glucose when employed in the routine neonatal clinical setting.

1344 DIASTOLIC BLOOD PRESSURE: A SENSITIVE INDICATOR OF SIGNIFICANT PATENT DUCTUS ARTERIOSUS IN THE ≤1200 g INFANT. B. Perelmuter, I. Ratner, W. Toews, and J.M. Whitfield (Spon. by L.J. Butterfield), Dept. of Perinatology, The Children's Hospital, Denver, Colorado.

A prospective study of infants ≤1200 g requiring mechanical ventilation for hyaline membrane disease (HMD) was undertaken to determine if blood pressure (BP) correlated with hemodynamically significant PDA. Daily echocardiograms were performed during the first week of life. BP measurements obtained through the umbilical artery line were used to calculate daily average diastolic and systolic BP. A PDA was significant if (1) an echocardiogram showed a structurally normal heart, LA/Ao≥1.3 with evidence of left ventricular overload and (2) one or more clinical signs of a PDA were present. Thirty-four infants were studied and 17 developed a significant PDA requiring ligation in the first week of life. The PDA and non-PDA babies were comparable in all respects, including severity of HMD and fluid management. Average diastolic blood pressure (ADBP) is shown in the Table in mmHg (±1 S.D.):

Day	1	2	3	4	5	
PDA	25±3.3	26±3.9†	24±3.5†	23±2.7†	24±3.6†	†p<.005
Non-PDA	26±4.3	30±3.4†	34±5.8†	35±5.5†	36±6.0†	

By the third day of life an ADBP <28mmHg identified 13 of 14 infants with significant PDA (3 ligated by day 3) whereas 16 of 17 with insignificant PDA had ADBP >28mmHg. We conclude that ADBP can be used as a sensitive and continuous objective indicator of hemodynamically significant PDA in the ≤1200 g infant.

1345 CEREBRAL BLOOD FLOW VELOCITY (CBFV) IN RELATION TO INTRAVENTRICULAR HEMORRHAGE (IVH) IN THE PRETERM INFANT. Jeffrey M. Perlman and Joseph J. Volpe, Wash. Univ. Sch. Med., St. Louis Children's Hosp., St. Louis, MO 63110.

The Doppler technique can be used at the anterior fontanel to measure CBFV in the anterior cerebral arteries (ACA). CBFV is measured from the systolic (S) and diastolic (D) amplitudes of flow. A pulsatility index (PI) is calculated (S-D/S) and is inversely related to CBFV. It has been reported that this technique is reliable in the diagnosis of IVH. Thus, markedly elevated PI was described at the time of IVH. We undertook this prospective study to assess the relationship of IVH to CBFV in the ACA.

One hundred infants with birthweight <1500 gms were studied from birth to day 7 of life. Daily ultrasound scans were utilized for the diagnosis of IVH. Thirty-two infants developed IVH. (Infants with subependymal hemorrhage only and/or equivocal IVH were excluded.) The relationship of IVH to mean PI for the 32 infants is shown in the Table.

	DAYS			
	1	2	3	4
No. with IVH	15	7	8	2
PI (mean ± SE)	.57 ± 0.12	.55 ± 0.14	.57 ± 0.10	.61 ± 0.09

No discernible change in PI occurred at the time of or following IVH, despite the fact that the lesions were severe in 50% of the cases and progressed after the initial diagnosis in 20%.

These data demonstrate no consistent effect of IVH on CBFV in the ACA. We conclude that CBFV in the ACA is not likely to be affected by IVH and that the noninvasive Doppler technique for measurement of CBFV is not reliable for the diagnosis of IVH.

● **1346** THE EFFECTS OF ORAL SUCTIONING (OS) AND ENDOTRACHEAL SUCTIONING (ES) ON CEREBRAL BLOOD FLOW VELOCITY (CBFV) AND INTRACRANIAL PRESSURE (ICP) IN THE PRETERM INFANT. Jeffrey M. Perlman and Joseph J. Volpe, Wash. Univ. Sch. Med., St. Louis Children's Hospital, St. Louis, MO 63110

Although OS and ES are performed routinely in neonatal care, their deleterious effects are not entirely known. CBFV in the anterial cerebral arteries can be measured in the newborn with a transcutaneous Doppler technique. From the systolic (S) and diastolic (D) amplitudes of flow, a pulsatility index (PI) is calculated (S-D/S) and is inversely related to CBFV. ICP can be measured noninvasively with a fiber-optic sensor placed over the anterior fontanel. This study examined the effects of OS and ES on CBFV, mean blood pressure (MBP) and ICP.

Fifteen infants of <1500 gm were studied at rest and during OS and ES. In each case, CBFV, MBP and ICP increased markedly with OS and ES and returned to baseline following these procedures. Table 1 shows the values obtained in a typical case, and table 2, the mean changes in PI, MBP and ICP for all cases ($p<0.0001$).

TABLE 1

	PI	MBP(mmHg)	ICP(cmH_2O)
Rest	.63	38	7
OS	.54	47	11
ES	.50	51	12

TABLE 2

	ΔPI(↓)	ΔBP(↑)	ΔICP(↑)
OS	.09±.01	7.2±1.4	7.3±1.0
ES	.12±.06	7.5±1.2	8.0±1.1

These data indicate that OS and ES are associated with an abrupt increase in CBFV, presumably a direct effect of the increase in MBP (because of impaired autoregulation) and reflected in an increase in ICP. In the preterm infant these repeated increases in flow velocity could be important in the pathogenesis of IVH.

1347 NEURODEVELOPMENTAL OUTCOME OF INFANTS WITH NEONATAL APNEA AND AMINOPHYLLINE THERAPY. Ivette Pena, Maureen E. Sims, Joan E. Hodgman and Annabel Teberg. Univ. of So. Calif. Sch. of Med., Dept. Peds., LAC-USC Med. Ctr. L.A., CA.

There is very little available information about the sequelae of apneic spells in the preterm infants, especially if aminophylline therapy has been used. Seventeen infants with birthweights ranging from 27 weeks to 34 weeks were evaluated. Apnea was defined as cessation of respiration equal or greater than 20 secs. It was classified as severe if more than 50 episodes of apnea occurred during their neonatal hospitalization and moderate to mild if 50 or less episodes occurred. Nine infants had severe apnea and 8 had moderate to mild. Three of the infants with severe apnea needed ventilatory assistance. The remaining 14 infants were included in a controlled study of which seven were treated with aminophylline. A neurodevelopmental evaluation was done at 40 weeks corrected chronological age. The three infants that needed ventilatory assistance were abnormals. Of the seven that were treated with aminophylline two were suspect neurologically. One infant of the group that didn't receive aminophylline was abnormal. These infants belong to the severe apnea group. The infants from the moderate to mild apnea group were normals. Although based on a small number of patients these results suggest that the outcome for the infants with apnea is related to the frequency of the episodes and need for assisted ventilation. The use of aminophylline does not appear to influence the outcome.

● **1348** BILIRUBIN TOXICITY WITHOUT CNS STAINING. Harold Perl, Amarjit Nijjar, Hakuyo Ebara, Kwang-sun Lee and Lawrence M. Gartner. Albert Einstein Coll. Med., Bronx, & Univ. of Chicago Pritzker Sch. Med., Dept. Pediatr., Chicago.

"Kernicterus", yellow staining of basal ganglia of the brain, has evolved to include its clinical manifestations as well. Newborn rabbits of less than 48 hours of age were studied. Gr. I and II were subjected to hypoxia (FiO_2 0.1) for 1 hour and then total anoxia until last gasp and then resuscitated. Gr. II was then injected intravenously with 80-120 mg/kg of bilirubin in water at pH 12. Gr. III was injected with bilirubin without prior hypoxia. Gr. IV was injected with buffer at pH 12. Gr. V was unmanipulated. Those injected with bilirubin developed the classical clinical pictures of kernicterus including jaundice, high pitched cry, irritability, seizures and opisthotonus. Proceeding hypoxia did not appear to be a significant factor in development of bilirubin CNS toxicity.

Group	n	Irrit.	Cry	Jaundice	Lethargy	Seizure	Opisthot.
I	7	0	0	0	7	2	0
II	6	6	2	6	0	4#	6*
III	70	9	0	64	9	21#	41*
IV	61	0	0	0	2	2	3
V	5	0	0	0	0	0	0

* & #: differences, both $p>0.05$.

Upon postmortem examination of the brains, none showed any gross yellow staining. On histologic examination some yellow pigment was noted within the capillary spaces but none in the brain parenchyma. These observations suggest that bilirubin neurotoxicity occurs independent of gross staining of the brain.

● **1349** EFFECT OF HYPOXEMIA ON RECOVERY FROM OXYGEN INDUCED RETINOPATHY IN THE KITTEN MODEL. Dale L. Phelps and Arthur L. Rosenbaum, UCLA School of Medicine, Center for the Health Sciences, Depts. of Pediatrics and Ophthalmology, Los Angeles

Infants who develop cicatricial retinopathy of prematurity often have spent prolonged periods in supplemental oxygen. We hypothesize that the marginal hypoxemia experienced by these infants (FiO_2 usually adjusted to pO_2 goals of 40 to 70, occasionally 80 torr) could adversely affect their retinopathy.

Five litters of kittens were exposed to 80% FiO_2 on the 3rd day of life for 65 hrs to induce a standard retinal vascular injury. Each litter was randomly divided such that ½ recovered in room air (21% O_2) and the other ½ recovered in 13% FiO_2. At four weeks of age India Ink injected retinal flat mounts were prepared from both eyes and the retinopathy scored on a scale of 0 to 13.

The arterial pO_2 of 4 kittens in 13% O_2 was 34 ± 8 torr. The kittens recovered in 13% O_2 did not gain weight as well as their litter mates (250 ± 63g vs 308 ± 50g at 4 wks M ± SD). In all 5 litters, the mean retinal scores of the room air recovered kittens were less (better) than the mean scores of the littermate hypoxic recovered kittens, (paired t test, differences 5.2 ± 2.1, $p<0.01$). Cicatricial retinopathy was not observed in these animals. Carbon dioxide levels in all incubators were less than 0.5%.

These data further support the general hypothesis that vascular retinopathies develop in response to peripheral retinal ischemia. These findings specifically demonstrate that arterial hypoxemia results in a more severe vasoproliferative retinopathy following hyperoxic injury.

1350 LASER NEPHELOMETER AND LATEX DETERMINATIONS OF ACUTE PHASE PROTEINS IN NEONATAL SEPSIS. Alistair G.S. Philip and Rosemary Tucker, Northwestern University and Evanston Hospital Depts. of Pediatrics, Evanston, Illinois.

Several proteins categorized as acute phase reactants have been proposed as helpful in the diagnosis and management of neonatal infection (particularly sepsis). Levels of haptoglobin (Hp), α_1 acid glycoprotein (AGP), immunoglobulin M, transferrin, fibrinogen (F) and C-reactive protein (CRP) were determined using a laser nephelometer. There were no apparent differences between serum and plasma levels on 50 paired samples of cord blood (except F). Determinations of all 6 proteins were possible on a plasma sample of 45 µl and available within 90 min. In 4 babies with acute bacterial infection (3 sepsis, 1 peritonitis) followed serially, the most responsive protein was CRP. It rose briskly and fell within 3 days of starting antibiotics. The levels of AGP and Hp rose somewhat less acutely and dropped more slowly during antibiotic treatment. In one baby with asymptomatic bacteremia, there was no acute phase response over 3 days. Ten other infants with early respiratory difficulty, in whom infection was suspected, had negative blood cultures and normal levels of proteins over several days.

Using serial dilutions and 25 µl samples, a range of semiquantitative values from 0.8 to 12.8 mg/dl for CRP and from 10.0 to 400 mg/dl for Hp was available using latex reagents. These latex values gave good correlations with laser determinations and were available in 25 and 40 minutes respectively; the tests are simpler and cheaper. We conclude that these techniques may be useful, not only in early diagnosis but also in the subsequent management of infants with proven or suspected neonatal infection.

1351 COMPARATIVE UTILIZATION OF PARENTERAL AND ENTERAL FEEDINGS IN THE PREMATURE INFANT WITH NECROTIZING ENTEROCOLITIS (NEC).
Mitchell B. Porten, Gilberto R. Pereira, Moritz M. Ziegler. (Spon. by W.W. Fox). Depts. of Peds. & Surg., Nutrition Support Service, Children's Hospital of Philadelphia, and Univ. of Pa. Sch. of Med., Phila., PA.

The optimal transition from parenteral (PN) to enteral (EN) feeding in the premature infant with NEC remains undefined. To examine the differential utilization of calories during this period, 35 premature infants were divided into 3 groups: surgically treated NEC (S-NEC, n=8), medically treated NEC (M-NEC, n=14), and infants free of gastrointestinal disease (NORM, n=13). All groups were of comparable gest. age (mean ± SEM= 30±1 wks for each group) and wt. at initiation of total parenteral nutrition (TPN) (S-NEC= 1.30 ± 0.16, M-NEC= 1.30 ± 0.11, NORM= 1.22 ± 0.16 kg). During the TPN period, wt. gain was directly related to caloric intake for all groups. However, during the transitional period, S-NEC patients were found to have a decreased utilization of enteral cals. as reflected in wt. gain. Despite comparable caloric intake, when transitional feedings were predominantly enteral (>50% of total cals.), less wt. gain was observed than when such feedings were predominantly parenteral (> 50% of total cals.) - 6.9 vs. 17.6 gm/100 cal/kg/day ($p < .05$). This differential wt. gain was unrelated to fluid intake (EN >50%=154 ± 5 vs. PN> 50%= 136 ± 6 ml/kg, $p < .05$). EN and PN caloric predominance was not found to be differentially related to wt. gain in either the M-NEC (13.2 vs. 19.5 gm/100 cal/kg/day, pNS) or the NORM group (18.6 vs. 15.1 gm/100 cal/kg/day, pNS). The apparent intolerance to the enteral component of transitional feedings was accentuated in S-NEC patients with cholestasis (0.26 vs. 21.3 gm/100 cal/kg/day, $p<.10$); a more gradual weaning from PN to EN feeding is warranted in those S-NEC patients with cholestasis.

1352 EFFECT OF PERINATAL ASPHYXIA ON SERUM CPK ISOENZYMES AND CPK(CSF), LDH(CSF) ISOENZYMES AND GOT(CSF)CHANGES. Kanamarlapudi Rao, Narasingrao Pampati, James Shelly, Spons. by Ronald Poland. Pontiac General Hospital, Division of Neonatology, Department of Pediatrics, Pontiac, Mich.

A prospective study of 8 term babies with perinatal asphyxia with Apgar score less than 7 at 5 minutes, more than 36 weeks, AGA were studied within 4 hours after birth. A serum CPK estimation and CSF estimations of CPK isoenzymes, LDH(CSF), GOT(CSF) estimations were done within 4 hours after birth. All the CSF were studied by COBAS method and different fractions of isoenzymes were identified and measured. The following conclusions:

A. This data suggests the perinatal asphyxia with acidosis results in release of CPK into the circulation as well as into the CSF.

B. CPK changes correlated well to the 1st minute Apgar. Did not correlate to the type of delivery.

C. Elevated serum CPK and CSF elevated enzymes may indicate poor prognosis for survival.

D. The elevation such as GOT(CSF), CPK(CSF) brain band, LDH 1,2 and 3 (CSF) is a sign of severe neurological involvement in the neonatal period. Presence of CPK brain band (CSF) was associated with neurological abnormalities at discharge examination.

E. Enzyme detection in the CSF depends on release from the tissues and transport in the CSF, may be controlled by other factors.

F. The long term prognosis cannot be established.

●1353 HUMAN MILK vs FORMULA: INFLUENCE ON ENERGY METABOLISM AND THE COMPONENTS OF WEIGHT GAIN IN PRETERM INFANTS. Brian Reichman, Philippe Chessex, Gaston Verellen, Guy Putet, John Smith, Tibor Heim, Paul Swyer. Dept Paeds, Med Eng, U of Toronto, Res Inst, Hosp for Sick Children, Toronto.

We compared the influence of feeding formula(F)& own mothers' milk(OMM)on the oxidation(OXID)& accretion(ACCR)of energy, fat & protein in very low birthweight(<1300g)growing preterm infants. 22 studies in F fed & 15 studies in OMM fed infants were done combining macronutrient balance, continuous open circuit indirect calorimetry & anthropometry. The clinical & growth parameters & volume of feeds retained(F: 180±4; OMM: 172±4ml/kg.d)were similar in the two groups.

RESULTS:

(M ± SE)	Energy(kcal/kg.d)	Protein(g/kg.d)	Fat(g/kg.d)
Intake	148.6±4 *	111±4	3.2 ±0.1	3.02±0.1	7.5±0.1 *	4.74±0.3
Losses	18.2±1 †	11±2	0.55±0.05	0.37±0.01	1.5±0.1 †	0.86±0.2
OXID	62.6±1 *	56±1	0.73±0.03	0.68±0.07	0.6±0.3 †	1.63±0.3
ACCR	67.8±3 *	44±4	1.92±0.1	1.97±0.1	5.4±0.3 *	2.25±0.5

* $p < 0.001$ † $p < 0.025$

The proportional fat content of the daily wt gain was higher in the F fed infants(33% vs 16%; $p < 0.005$)but protein content was similar(12% vs 13%). The higher energy storage in the F fed infants (4.3 vs 3.1kcal/g wt gain; $p < 0.001$)reflects the different composition of the wt gain. The accretion of energy, fat & protein correlated with their respective metabolisable intakes in both groups (r ranges from 0.81 to 0.98; $p < 0.001$)suggesting that accretion rates & hence composition of wt gain can be manipulated by changes in energy & macronutrient intake & can be defined by our investigatory methods.

1354 RELATIONSHIP OF PROSPECTIVE DIABETIC CONTROL IN PREGNANCY TO NEONATAL CARDIOMYOPATHY. Mark Reller, Richard Meyer, Colleen Braun, Reginald C. Tsang, University of Cincinnati, Department of Pediatrics

Infants of diabetic mothers (IDM) have an increased incidence of hypertrophic cardiomyopathy (HC) with an increase in thickness of left (LV) and right (RV) ventricular walls and interventricular septum (IVS); and persistent pulmonary hypertension (PPH). We hypothesized that prospective diabetic control during pregnancy would reduce the incidence of HC and severity of PPH. Three groups of IDMs were studied. Mothers of Group 1 IDMs had prospective diabetic control from 1st trimester. Group 2 had prospective control from 2nd or 3rd trimester. Group 3 were outborn neonatal referrals in the same period (diabetic control unknown). Echocardiography was used to measure ventricular wall thickness and RV systolic time interval ratio (STI), which correlates with pulmonary artery pressure. Mean±SD vs controls.

	Control	Group 1	Group 2	Group 3
Birth Wt	3804±404	3426±510 (ns)	3571±782 (ns)	4013±1120 (ns)
Mean LV	.30±.09	.33±.07 (ns)	.38±.06 (ns)	.45±.15 p<.01
Mean IVS	.37±.06	.40±.08 (ns)	.42±.06 (ns)	.58±.18 p<.01
Mean RV	.30±.03	.30±.08 (ns)	.33±.07 (ns)	.40±.20 (ns)
Number With Thickened Walls/Total	0/12	10/59 (ns)	8/27 p<.05	27/49 p<.01
STI ratio	.29±.04	.29±.05 (ns)	.37±.04 p<.01	.37±.14 p<.05

Thus, early prospective diabetic control during pregnancy may reduce the incidence of hypertrophic cardiomyopathy and the increased pulmonary arterial pressure seen in IDM.

1355 CAUSES OF ELEVATED PULMONARY RESISTANCE (R_p) IN ACUTE HEMORRHAGIC PULMONARY EDEMA. Peter Richardson, (Spon. by L. Glasgow). Department of Pediatrics, University of Utah School of Medicine, Salt Lake City, Utah.

Two factors that may cause increased R_p in pulmonary edema are: 1) decreased airway lumen due to decreased functional residual capacity (FRC) and 2) fluid in the airways. We investigated the contribution of these two factors on R_p at different levels of PEEP. Control measurements of R_p and FRC were made in 20 cats at 10 different PEEPs from -8 to +10 cm H_2O then repeated, at positive PEEPs only from 0 to 10 cm H_2O, after inducing pulmonary edema (alloxan, 75 mg/kg). Negative pressures were used to induce atelectasis in the healthy lung and to give estimates of the effects of decreased FRC on R_p. Negative PEEP of -8 cm H_2O caused R_p to increase from 29.5 ± 3.9 cm H_2O/ℓ/sec (mean ± SE), measured at 0 PEEP (ZEEP), to 84.1 ± 13.1 cm H_2O/ℓ/sec and caused FRC to decrease from 24.2 ± 1.4 ml/kg to 8.3 ± 1.1 ml/kg. Pulmonary edema caused R_p to increase to 81.1 ± 19.7 cm H_2O/ℓ/sec and FRC to decrease to 15.0 ± 1.8 ml/kg; 23% of the R_p increase was attributed to the FRC decrease. Increases in PEEP caused significant decreases in R_p (edema) only at levels of 2, 4 and 6 cm H_2O. Further PEEP increases did not cause significant changes in R_p (edema), and R_p (control) remained relatively constant throughout the positive PEEP range. FRC (edema) returned to normal at a PEEP of 4 cm H_2O. Contributions of decreased FRC to R_p at 2, 4, and 6 cm H_2O were 24, 19 and 3%. We conclude that 1) pulmonary edema causes large increases in R_p, 2) one-fourth of the R_p increase is due to FRC loss and 3) increases in PEEP which return FRC to normal cause sharp decreases in R_p.

1356 EFFECT OF SLEEP ON PHASIC AND "TONIC" DIAPHRAGMATIC EMG IN PRETERM INFANTS. Henrique Rigatto, Francisco Reis, Don Cates and Leanne Horvath. Dept. of Pediatrics, University of Manitoba, Winnipeg, Canada.

To determine the effects of sleep on diaphragmatic EMG we studied 10 infants (BW 1.6 to 2.1 kg; GA<37 wks). We measured surface (D_S) and esophageal (D_E) diaphragmatic EMG, $\dot{V}_E$, V_T, f, Ti and Te. D_S and D_E were analyzed for integrated electrical activity (EMG_i), total (TPA) and expiratory (EPA) phasic activity, EPA/TPA and presence of "tonic" activity. As expected, $\dot{V}_E$ increased from non-REM to REM sleep (0.385 to 0.414 L/min, p<.05) due to an increase in f (30 to 35, p<.05). This change in ventilation was associated with decreased EMG_i (18.7 vs 12.2 uV, p<.05) decreased TPA (1.25 vs 0.71 sec, p<.001), decreased EPA (0.67 vs 0.21 sec, p<.002), decreased EPA/TPA (0.51 vs 0.27, p<.001) and decreased "tonic activity" (51 to 5%, p<.01) of D_S. Similar changes were observed in D_E, except that tonic activity was never observed. TPA_E was shorter than TPA_S (1.06 vs 1.25 sec, p<.06) due to a decrease in EPA (0.48 vs 0.67, p<.002). We suggest: 1) Decrease in TPA from non-REM to REM sleep, with increased EPA/TPA indicates loss of breaking mechanism during expiration; 2) Longer EPA in D_S than in D_E implies that diaphragm does not behave like a single muscle; 3) The absence of tonus in D_E indicates that "tonic" activity recorded via surface electrodes (D_S) may represent postural chest muscles rather than diaphragmatic tonus. (Supported by Medical Research Council of Canada, MA 4980).

1357 REGIONAL VARIATIONS IN BILIRUBIN ABSORPTION WITHIN THE SMALL INTESTINE. David A. Roberson, Kwang-sun Lee and Lawrence M. Gartner. The University of Chicago, Pritzker School of Medicine, Department of Pediatrics, Chicago Illinois.

The enterohepatic recirculation of bilirubin (BR) may contribute to neonatal jaundice. In an attempt to better understand the physiology of intestinal bile pigment transport prior to developmental studies, regional variations in unconjugated BR absorption were examined in 32 adult male Sprague-Dawley rats.

Sections of the small intestine were ligated in vivo, and the isolated segments infused with a single bolus of 1mg unconjugated BR in 5cc phosphate buffer pH 8.6. Controls received buffer alone. The rate and amount of BR absorption was calculated as the net change in amount BR excreted in bile above the pre-infusion endogenous excretion, over the first five hours following gut BR infusion.

Cumulative	Control n=6	Duodenum n=6	Proximal Jejunum n=6	Distal Jejunum n=7	Ileum n=7
1 hr.	.002±.005#	.105±.028*	.045±.015*	.021±.024	.041±.015*
2 hr.	.007±.006	.176±.044*	.047±.024	.032±.033	.060±.027
5 hr.	-.018±.019	.270±.101*	.030±.038	.010±.072	.080±.079

#=net change in mg BR excreted above endogenous rate (M±SEM)
*=statistically significant from control

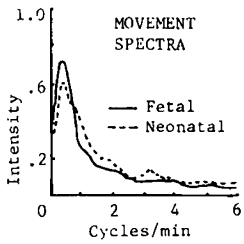
These data indicate that the duodenum is the major site of unconjugated BR absorption. The proximal jejunum and ileum absorb BR at a lower but significant rate, only during the first post-infusion hour. The distal jejunum failed to absorb BR at a significant rate throughout the entire five hour period.

● 1358 CONTROL OF RESPIRATORY ACTIVITY OF AN UPPER AIRWAY DILATING MUSCLE (GENIOGLOSSUS) IN INFANTS. John L. Roberts, William R. Reed, Oommen P. Mathew, Bradley T. Thach. Washington University School of Medicine, Dept. of Pediatrics, St. Louis, Missouri 63110.

No documentation of respiratory related activity in the genioglossus (GG) muscle is available in infants although studies in animals and adult man suggest that respiratory activity of the GG is essential for upper airway (AW) patency. Therefore we studied the GG electromyogram (EMG) and its response to various respiratory stimuli in 3 infants (age: 1-3 mos.) with Pierre Robin Syndrome who had a prior history of obstructive apnea. EMG was recorded using fine wire electrodes placed perorally into the GG muscle. Tonic activity with phasic inspiratory bursts, similar to that seen previously in animals and adults, was recorded in all babies. This activity increased with increased (3-5%) inspired CO_2 (15 of 16 trials) indicating chemoreceptor modulation. To test the GG response to lung and/or AW stretch receptors, we intermittently occluded the nasal AW at end-expiration. The phasic EMG of the first occluded breath increased, similar to the response found in animals, in 100 of 129 trials. When nasal occlusion was maintained the tonic and phasic EMG of subsequent breaths progressively increased (111 of 115 trials). Also, the phasic EMG increased markedly with sighs, and was greater during nasal than during mouth breathing. There were no complications of the EMG technique. The present data provide evidence in infants for respiratory related GG activity and its modulation by chemoreceptors and stretch receptors. Supported by NIH RO1HD10993-05 and Am. Lung Assoc.

● 1359 NEONATAL MOTOR RHYTHMS EXIST IN THE FETUS. S. Robertson, L. Dierker, Y. Sorokin, M. Rosen (Spon. by M. Klaus), Dept. Ped. (Rainbow Babies & Childrens Hosp), Obstet.(Cleveland Metro. Gen. Hosp.), CWRU, Cleveland, OH.

The brain of the mature neonate provides rhythmic control of numerous behavioral and physiological processes (eg sleep, respiration). We recently found another newborn rhythm: regular fluctuations in body movement. To determine if similar periodicity exists in utero, we studied 11 healthy fetuses in the last 2 weeks of gestation (subsequently delivered AGA at 39-42 wks). Spontaneous fetal movement (FM) was detected by pressure transducers on the mother's abdomen. The analog record was digitized in 5 sec intervals during 20-40 min ($\bar{x}$=30, SD=8) of fetal activity free of major artifacts. Tests revealed significant temporal patterns (p<.001) in each fetus. The dominant rhythms in FM, isolated with spectral analysis, ranged from .24-.60 cycles/min ($\bar{x}$=.37, SD=.11), too fast to be due to changes in sleep state. The mean spectral density function (relative intensity of FM rhythms between 0-6 cycles/min) is shown. Similar findings in the fetus and neonate suggest the periodicity in spontaneous movement is intrinsic. Whether it reflects an autonomous CNS rhythm controlling motor output or arousal, or is linked to another process, is not known. Analysis of movement spectra may reveal neurobehavioral changes in the fetus before other signs of distress are detectable.



1360 INCREASED EXTRACELLULAR WATER VOLUME ASSOCIATED WITH NEONATAL HYPONATREMIA. Jorge Rojas, Petaiah Mohan, Kathy K. Davidson and Robert B. Cotton. Vanderbilt University Medical School, Departments of Pediatrics and OB-GYN, Nashville, Tennessee.

Extracellular water volume (Bromide Space) (BR) was measured in thirty consecutive inborn premature infants within one hour after birth. The infants were divided into two groups, those with serum sodium (NA) < 135 (n=16) and > 135 meq/L (n=14). There were no significant differences in birth weight, gestational age, length or head circumference between the groups. Total BR and BR normalized to length (L), head circumference (HC) and gestational age (GA) are shown in the table. All BR values were significantly higher in the hyponatremic group.

	Total BR (ml)	BR/L (ml/cm)	BR/HC (ml/cm)	BR/GA (ml/week)
NA > 135	536±131	13.8±2.7	19.5±4.1	17.6±3.9
NA < 135	666±179*	16.8±3.1*	23.3±4.6*	21.4±4.5*

*p < 0.05 Mean±SD

Although complete maternal fluid data were not available in all cases, a significant (p < 0.05) number of mothers of hyponatremic infants were given intravenous fluids prior to admission (60% as opposed to 13%).

These data demonstrate that hyponatremia in premature infants at birth is associated with an increase in extracellular water volume. We postulate that this excess water is acquired before birth and it may be related to maternal fluid therapy.

1361 INCREASED INCIDENCE OF NEONATAL AIR LEAK (AL) ASSOCIATED WITH NEONATAL HYPONATREMIA. Jorge Rojas, Petaiah Mohan, Kathy K. Davidson and Robert B. Cotton. Vanderbilt University Medical School, Departments of Pediatrics and OB-GYN, Nashville, Tennessee.

Twenty consecutive inborn infants with Hyaline Membrane Disease (HMD) requiring mechanical ventilation & birth weight < 1250g were followed prospectively for factors associated with AL (pneumothorax, interstitial air dissection). The incidence of AL was 60% (12/20). There were no differences in respirator settings, oxygen requirement or arterial blood gases between the AL group & the group without AL. Birth weight, gestational age, initial pH & base excess were also similar. Only the initial serum sodium (NA) concentration was found to be significantly different: 132.9±3.4 in the AL group & 137.7±3.0 in the no AL group. When the infants were separated into those with NA <135 & >135, 100% of the infants with hyponatremia developed AL as opposed to 16% with a normal NA. We then investigated whether hyponatremia was related to fluid therapy during labor. A review of maternal charts revealed that fluid volumes as great as 4250 ml were administered during the last 6 hours prior to delivery. Lowest NA concentrations were found in infants whose mothers received the largest volumes of fluid. There was no difference in maternal NA between the 2 groups at the time of admission. Those infants with AL had greater urine output in the first 72 hrs of life than those without AL. Since all infants were kept in radiant warmers, and since the amount of IV fluids, hours under phototherapy and use of diuretics was similar for both groups, it is estimated that the AL infants had an average of 77 ml/kg greater water volume at birth. We postulate that the acquisition of a fluid load intrapartum may increase the risk of AL in small infants with HMD.

●1362 SEX AND FETAL LUNG MATURATION. EFFECTS OF ESTROGEN IN THE FETAL RABBIT. Seamus A. Rooney, Arlette Brehier, Linda D. Ingleson and Patricia A. Parks. Yale Univ. School of Med., Dept. of Pediatrics, New Haven, Connecticut.

17β-Estradiol (E) accelerates fetal lung maturation in the rabbit. There are also reports that female fetal lungs mature earlier than those of males. To determine if the E effect was sex dependent we administered E (2.2 µg/kg) or vehicle to pregnant does on day 26 of gestation and delivered the fetuses on day 27. Fetal sex was determined by visual inspection of the gonads and confirmed by histology. E decreased fetal lung glycogen from 143±5 µg/mg protein (mean ± SE) to 35±18 in males and from 150±10 to 28±11 in females. The E effect on glycogen depletion was dependent on gestational age. E had little effect on glycogen at 22-25 days but reduced it to 13-24% of the control level at 26-27 days. E increased fetal lung cholinephosphate cytidylyltransferase (CYT) activity by 83% from 341±39 pmol/min/mg protein to 626±74 in males and by 87% from 385±22 to 722±162 in females. These data show that the effects of E are the same in both sexes. The effect of E was also examined in vitro and compared with the effect of dexamethasone (D). Explants of 25-day fetal rabbit lung were cultured for 48 h with and without 10^{-5}M E, 10^{-8}M D and D+E. E increased CYT by 39% from 344±10 pmol/min/mg protein to 477±30, D increased it by 41% to 484±34 and E+D increased it by 42% to 490±46. Thus, the effects of E and D are similar and are not additive. Addition of 1.1 mM phosphatidylglycerol to the assay mixture increased CYT activity to 2.2 nmol/min/mg and abolished the effects of E and D. E and D may stimulate existing CYT rather than increase its amount. Supported by NIH grant HD-10192.

● 1363 REDUCTION OF CEREBRAL BLOOD FLOW (CBF) IN LOW BIRTH WEIGHT (LBW) INFANTS AFTER AMINOPHYLLINE ADMINISTRATION. Ted S. Rosenkrantz and William Oh. Brown Univ., Women and Infants Hospital, Dept. of Pediatrics, Providence, RI.

Aminophylline (A) administration is known to cause decreased CBF in adults while its effect on the CBF of LBW infants is generally unknown. We used continuous waveform Doppler ultrasonography to study blood velocity in the anterior cerebral arteries (ACA) of 6 spontaneously breathing LBW infants with apnea of prematurity prior (PRE) to and at 1 and 2 hours after the intravenous administration of a 5 mg/kg loading dose of A. Mean arterial blood pressure (BP), heart rate (HR), respiratory rate (RR), Peak Systolic Velocity (PSV), Pulsatility Index (PI) and Area Under the Velocity Curve (AUTC) were measured. The Doppler tracings were coded for analysis to avoid bias. In vitro studies with a pulsatile pump showed that AUTC reflects blood flow (correlation coefficient = 0.99). Data (M±SD) are shown below:

Time	BP (mmHg)	HR (per/min)	RR (per/min)	PSV (cm/sec)	PI	AUTC (u/min)@
PRE	53±6	141±10	52±8	18.2±4.4	.66±.07	2411±459
1 hr POST	50±12	149±11*	57±9	14.2±2.8*	.68±.05	1901±329*
2 hr POST	50±7	152±6*	58±10	15.4±3.4*	.68±.04	2003±424*

@Planimeter units; *p<.05 compared to control values

The data indicate that A administration results in an increase of the HR and RR with a decrease in blood flow through the ACA. Thus the systemic and cerebral circulation of LBW infants respond in a manner similar to adults. Whether this reduction in CBF is due to hyperpnea and secondary hypocapnia or direct drug effect is unclear and is currently under investigation.

● 1364 CEREBRAL BLOOD FLOW (CBF) AND CEREBRAL VASCULAR RESISTANCE (CVR) IN POLYCYTHEMIC AND HYPERVISCOUS (PCH) INFANTS FOLLOWING PARTIAL EXCHANGE TRANSFUSION (PET). Ted Rosenkrantz and William Oh. Brown University, Women and Infants Hospital, Department of Pediatrics, Providence, RI

The central nervous system manifestations of PCH in the newborn have been attributed to increased CVR and decreased CBF. To examine this we used continuous waveform Doppler ultrasonography to study blood velocity in the anterior cerebral arteries in 11 PCH infants before (PRE) and after (POST) PET. For comparison, 7 control infants (C) matched for birth weight, gestation, and postnatal age were also studied. Velocity tracings were evaluated for Peak Systolic Velocity (PSV), Pulsatility Index (PI), and Area Under the Velocity Curve (AUTC). In vitro studies with a pulsatile pump showed that AUTC correlates with blood flow (r=.99). Venous Hct, viscosity, velocity, heart rate (HR), respiratory rate and blood pressure were measured prior to PET and 4-6 hours afterward. Data (M±SD) are shown below:

	Hct (%)	Viscosity*	PSV(cm/sec)	PI	AUTC(u/min)@
PCH-PRE	68.1±3.6×	10.4±2.1×	11.1±2.8×	.71±.17×	1565±578×
PCH-POST	52.3±3.0	6.2±0.6	15.2±3.4	.62±.07	2186±519
C - PRE	51.1±3.2	6.6±0.6	16.0±3.2	.57±.05	2395±496
C - POST	- not done -		16.4±2.4	.58±.05	2423±420

*Centipoise at shear rate of 45sec^{-1}; @Planimeter units; ×p<.05 compared to PCH-POST and both C periods.

HR increased in PCH infants after PET (p<.05). The data indicate that PCH infants have decreased CBF and increased CVR in the cerebral circulation which improve after PET. These findings may account for the neurologic symptoms observed in PCH infants.

1365 ENZYMATIC AND IMMUNOLOGIC QUANTITATION OF ERYTHROCYTE SUPEROXIDE DISMUTASE (SOD) IN ADULTS AND NEONATES OF DIFFERENT GESTATIONAL AGES. Louise S. Saik, Hui-Lung Hsieh, William H. Baricos and Emmanuel Shapira. Tulane Univ. Sch. of Med. The Hayward Genetics Center. Depts. of Biochem., Peds. and Path. New Orleans.

The SOD isoenzyme system is the major protective mechanism against oxygen toxicity. It has been suggested that premature infant susceptibility to oxygen therapy might reflect decreased lung SOD activity.

In the present study, human erythrocyte SOD 1 was purified and specific antiserum was raised in rabbits. SOD 1 from adults and from newborns were shown to be indistinguishable in their immunological and electrophoretic properties. Erythrocyte SOD 1 was quantitated in blood specimens from adults and in cord blood specimens from neonates of different gestational ages using both an immunologic and an activity assay. The mean values of SOD concentration and SOD activity for adults and for newborns of average size for gestational age (AGA) showed no significant difference. Adult red cells contained 28.0± 8.34 SOD units/mg Hgb while AGA neonate red cells had 28.5± 8.29 SOD units/mg Hgb. Immunological quantitation by single radial immunodiffusion revealed 0.69± 0.074 µg SOD/mg Hgb in adults and 0.70± 0.144 µg SOD/mg Hgb in the AGA neonates. However, the SOD concentrations from both small for gestational age (SGA) and large for gestational age (LGA) neonates were significantly lower than those of the AGA babies and the adults (SGA: 0.567± 0.236 µg SOD/mg Hgb, $p < 0.05$; LGA: 0.59± 0.156 µg SOD/mg Hgb, $p < 0.05$). Supported in part by grants from The March of Dimes and The Schleider Foundation.

1366 VITAMIN D METABOLITE LEVELS IN RESPONSE TO EARLY NEONATAL HYPOCALCEMIA IN PRETERM INFANTS. Bernard L. Salle, Francis H. Glorieux, Edgard E. Delvin and Louis David. Hôp. E. Herriot, Neonatal Dept., Lyon, France and McGill Univ., Shriners Hosp., Genetics Unit, Montréal, Québec, Canada.

We have shown that after 5 days of life, vitamin D metabolite levels are high in vitamin D supplemented preterm infants (J. Pediat. 99,640, 1981). The present study aimed at assessing the onset of this rise immediately after birth. Fourteen subjects (31-35 w; 1100-2200 g) were studied from birth to 96 h of age. All were infused with 10% glucose, fed with pool banked human milk and received 60 mcg/d of vitamin D_3. No interfering pathological conditions were observed. Serum calcium decreased rapidly to reach a nadir at 48 h (1.8 ± 0.1 mmol/l, $p < 0.01$) and remained low at 4 days (1.9 ± 0.1 mmol/l). No significant change in serum phosphorus was observed. Serum iPTH response was maximum at 24 h (140 ±25 ml/Eq/l) and remained higher than the normal range during the 4 days of study. Serum 25-OHD increased regularly (cord: 10 ±1 ng/ml; 24 h: 15 ±3, n.s.; 48 h: 23 ± 6, $p < 0.05$; 96 h: 29 ± 5 ng/ml ($p < 0.001$)). Serum 1,25-$(OH)_2$D levels increased steadily during the whole study (cord: 39 ± 5 pg/ml; 24 h: 58 ± 14 ($p < 0.025$); 48 h: 73 ± 12 ($p < 0.001$); 96 h: 143 ± 23 ($p < 0.001$) and correlated after birth with 25-OHD levels ($n = 34$, $r = 0.77$, $p < 0.0005$). We concluded that: 1) all infants were somewhat D depleted and became hypocalcemic with an appropriate PTH response; 2) the maturation of the vitamin D synthetic pathway was achieved at 31 w of gestation and responded quickly to hypocalcemia and PTH secretion; 3) limited availability of 25-OHD appeared to interfere with 1,25-$(OH)_2$D synthesis.

All values are mean ± SEM

1367 FOLLOW-UP OF GRADE III AND IV IVH WITH AND WITHOUT VP SHUNT. Ponthenkandath Sasidharan, Evangelina Marquez, Edgar Dizon (Spon. by R. L. Schreiner). Porter Memorial Hospital, Valparaiso, Indiana.

We evaluated the developmental outcome of infants with severe IVH and hydrocephalus (H) with and without a ventriculo-peritoneal shunt (VP-S). Fifteen infants with Grade III or IV IVH were monitored by weekly ultrasound for ventricular size. Progressive severe ventriculomegaly necessitated VP-S in 8 of the 15 babies. The mean birth weight of the 8 infants with VP-S was 990 (range 680-1540) gm; of the 7 without VP-S, 1360 (range 800-2120) gm.

Follow-up evaluation was performed for all infants using the Bayley Scales of Infant Development. Developmental Quotient (DQ) ≥86 were considered normal; 75-85, suspicious; and <75, abnormal. Mean age of follow-up was 6.3 (range 2-11) months corrected for prematurity for the VP-S group and 9 (range 4 1/2-15 1/2) months for the non VP-S group. Among the VP-S infants 2 had a normal DQ, 2 suspicious, and 4 abnormal. The mean DQ for VP-S infants was 75. Among the non VP-S infants 6 had a normal DQ and 1 suspicious. The mean DQ for the non VP-S infants was 101 ($p < .002$).

These very preliminary follow-up data suggest that the outcome of infants requiring VP-S after a major IVH is poor. Whether the poor outcome is secondary to brain damage already present at the time of VP-S or whether the outcome could be improved by earlier VP-S is not known.

1368 PLASMA CATECHOLAMINES AND HYPOXANTHINE (HX) LEVELS IN NORMAL AND DISTRESSED NEWBORN BABIES. Ola D. Saugstad M. Ziegler, Bruce Kessel, Brian Saunders, Louis Gluck. Univ. of Calif. San Diego, Depts. of Pediatrics, Medicine, Reproductive Medicine, La Jolla, Calif; Kaiser Foundation Hospital Dept. of Pediatrics.

Plasma catecholamines and HX levels were determined by radioenzymatic assay and a P_{O_2} method respectively in hypoxic and normal neonates. Norepinephrine (NE) was elevated 4.7 times ($p < 0.0025$), epinephrine (E) 2.0 times ($p<0.05$), and HX 2.2 times ($p<0.005$) in hypoxic vs. non-hypoxic term neonates. E is released in response to hypoxia as demonstrated by the positive correlation of E and HX: lgE = 0.0197 x HX+1.98, r=0.45 ($p<0.05$). HX level was elevated and dopamine (DA) synthesis diminished in hypoxia illustrated by the negative correlation of DA and HX: lgDA= 2.34-0.041 x HX, r=0.65 ($p<0.01$); this synthesis reduction is probably because the rate limiting enzyme tyrosine hydroxylase is O_2 dependent.

Prematures with RDS had NE and E values similar to those in venous cord plasma of normal term infants, but DA was lower, near the limit of detection of the assay ($p<0.005$). Infants given continuous DA infusion had DA levels 35-400 times greater than those found in venous umbilical cord blood but NE and E were not elevated. This illustrates that DA does not metabolize further to NE and E under such treatment.

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●1369 PENICILLIN PROPHYLAXIS AGAINST NEONATAL GROUP B STREPTOCOCCAL (GBS) INFECTION--IS IT SAFE? V. Schauf, M. Tolpin, K. Ghaey, C. Anderson, M. Rathi, A. Ismail, D. Woo, K. Nelson, Depts. of Pediatrics and Preventive Medicine, U. of Ill.; Pediatrics and Obstetrics, Loyola, Christ, and University of Chicago Hospitals; Chicago.

Although penicillin (PEN) prophylaxis is effective in term infants against GBS infection, its safety is unknown. Hence, the role of PEN prophylaxis for the general population remains to be determined. In a randomized double-blind trial, 2873 babies received 100,000 U aqueous PEN G or placebo IM immediately after birth. The babies were observed for reaction to the injection, and for GBS and other bacterial infections during the neonatal period.There were no differences between the groups in reaction to the injection and no excess infections in the PEN group. Follow-up of 1390 subjects during the first year of life showed no differences between the groups in total or febrile illnesses, respiratory infections, hospitalizations, allergies, or drug reactions. Among 91 subjects subsequently treated with a penicillin drug, there were no significant PEN reactions and no increase in PEN related rashes in infants receiving PEN prophylaxis. In infants of carrier mothers, GBS isolation at birth was the same in PEN (48%) and placebo (46%) groups. However, at time of discharge, PEN had reduced GBS colonization to 7% while the placebo group was 42% ($p=0.053$). In contrast to the PEN effect on GBS colonization, no other differences in flora were detected between the 2 groups. Our demonstration that penicillin reduces GBS colonization without selecting an abnormal flora, increasing infections, or increasing PEN allergy suggests that widespread PEN prophylaxis in the neonate is likely to be safe and is worthy of further study.

1370 EFFECTS OF CHRONIC VENTILATION WITH POSITIVE END EXPIRATORY PRESSURE (PEEP): A MULTIPLE COMPARTMENT ANALYSIS OF THE CANINE LUNG SURFACTANT SYSTEM. Joseph Schulman and George W. Brumley, Duke University Medical Center, Div. of Perinatal Medicine, Dept. of Pediatrics, Durham, N.C.

Young (6 mo.) beagle males were ventilated chronically under light morphine sedation and succinylcholine paralysis. The animals were hydrated, turned and suctioned and arterial blood gases checked every 4 hrs. for 72 hrs. Controls (4) were maintained at 0 cm H_2O and test animals (3) at 4 cm H_2O PEEP. After 72 hrs. 100 µCi (^{14}C) palmitate was injected into a femoral vein and five 0.5 gm biopsies were obtained from the right lungs at 30 min. intervals. A sixth biopsy was taken from the left lung terminally. Pleural air was evacuated between biopsies. Histologic samples of lung specimens fixed at 20 cm H_2O pressure revealed no specific findings and wet wt/dry wt. ratios revealed no evidence of edema. A lamellar body (LB) fraction was derived from each lung biopsy using centrifugation of 1 M sucrose homogenates under a 0.2 to 0.8 M sucrose density gradient. LB disaturated phosphatidylcholine (DSPC) was used as a surfactant marker. (^{14}C) palmitate DSPC specific activity decay curves in control and PEEP lungs and lavage fluid were not different and pressure-volume relationships were comparable in both groups. During the lung biopsy period lungs treated with PEEP retained more LB DSPC per gm of lung than did controls ($p<0.025$). These data suggest that PEEP has a sparing effect on LB DSPC and, thus, the pulmonary surfactant.

1371 ELEVATED T_3 IN SUDDEN INFANT DEATH SYNDROME (SIDS) & NON-SIDS: A MARKER OF PREVIOUS HEALTH. E.Schwarz, L.Hillman, F.Chasalow, M.Erickson, R.Hillman and M.Yuan. Wash Univ, St Louis Child Hosp, Dept of Ped, St Louis

A recent study (J Ped 99:758) has suggested elevation of T_3 plays a role in the pathophysiology of SIDs. To further evaluate this we measured T_3, reverse T_3 (rT_3), T_4, free thyroxine (fT_4), & TSH in 62 SIDS and 30 control infants (DC) autopsied by the medical examiner. Our data and the published data showed T_4 and fT_4 to be lower in the DC group suggesting abnormal thyroid function due to severe illness prior to death. We thus formed group DC-1 (n=16) by excluding all infants with markedly depressed T_4, fT_4, or markedly elevated rT_3. The 14 excluded infants formed DC-2. 15 hospitalized infants without chronic disease were live controls (LC). Mean T_3 was higher in SIDS than in DC, DC-2, and LC but was similar to DC-1. T_3 was >1.9 in 69% SIDS, 37% DC, 63% DC-1, 7% DC-2, and 0% LC. In SIDS, elevation of T_3 was not associated with petechiae, infection, prematurity, age, or time until autopsy. Thus elevation of postmortem T_3 is a non-specific, though unexplained, finding. The normal TSH, T_4, fT_4, and rT_3 in SIDS and DC-1 suggests normal central and peripheral thyroid function prior to death.

	ADULT NORMAL	SIDS	DC	DC-1	DC-2	LC
T_3(ng/ml)	(.5-1.9)	2.5*	1.7	2.4*	.91	1.1
rT_3(ng/ml)	(.08-.35)	.79	1.0	.73	1.3†	.80
T_4(µg/dl)	(3.7-9.7)	8.6	6.2†	8.4	4.2†	9.2
fT_4(ng/dl)	(.68-1.8)	1.1	.84†	1.1	.60†	1.0
TSH(µu/ml)	(<10)	6.6	6.9	6.8	6.6	4.9

*P<.05 compared to LC, DC, DC-2, †P<.05 compared to SIDS, DC-1,LC

1372 ADVERSE EFFECTS OF DELAYED CLOSURE OF DUCTUS ARTERIOSUS (DCDA) IN VERY LOW BIRTH WEIGHT (VLBW) INFANTS. Bijan Siassi, Pedro Arce, Ruben Ackerman, Luis Cabal. Univ. of So. CA. Sch. of Med., LAC/USC Med. Ctr., Dept. Ped., LA.

Detection of DCDA and its influence on early clinical course of VLBW infants remains controversial. In order to further clarify this problem, 29 randomly selected premature infants with birth weights of 740 to 1500 grams and gestations of 25 to 34 weeks were studied. An aortogram was performed in each infant during 24 to 48 hours of age and revealed an open DA in 9 and closed DA in 20. Clinical evaluation including measurement of heart rate, respiratory rate, FiO_2, intraarterial blood pressure (ABP), right atrial pressure (RAP) and an M-mode echocardiogram were obtained at 8, 24, 48 and 72 hours of life in each infant. Echocardiograms were analysed for LA, LV, aortic sizes and LA/AA; RV and LV systolic time intervals; and LV shortening fraction, ejection fraction, VCF and stroke volume. From this study it was concluded that 1)Standard M-mode echocardiogram does not detect PDA in premature infants during the first 4 days of life. 2)DCDA was associated with the following adverse cardiopulmonary effects:A)FiO_2 requirement >60%, 50% and 40% respectively at <24, 24-48 and >48 hours of life. B)Diastolic BP <25 mmHg. C)RAP a-wave >5 mmHg beyond 24 hr. D)RPEP/RVET >0.35 after 24 hr. Furthermore, since the calculated LV outputs were similar in the two groups of infants, it was postulated that the LV functions at near maximal capacity in VLBW infants during the immediate neonatal period, thus presence of L to R shunt through DA results in hyperdynamic pulmonary hypertention and decreased systemic blood flow.

1373 CIRCULATORY SHOCK IN NEWBORN INFANTS-AN ECHOCARDIOGRAPHIC STUDY. Bijan Siassi, Pedro Arce, Ruben Ackerman, Guillermo Young, Luis Cabal. University of Southern California School of Medicine, LAC/USC Medical Center, Department of Pediatrics, Los Angeles.

Circulatory shock (CS) was detected in presence of hypotension and oliguria in 13 neonates during the first week of life (BW: 740 to 4270 g.; G.A.:25 to 42 w.). Serial M-mode echocardiograms were obtained in each infant and were compared with control values obtained in 40 healthy neonates (BW:710 to 4560 g.; G.A.:25 to 42w.). Echocardiograms were analysed for LA, LV and aortic sizes; RV and LV systolic time intervals; LV shortening fraction, ejection fraction and VCF; aortic ejection area (AEA) and LV stroke volume (LVSV). AEA and LVSV were decreased in 11 and 9 infants with CS respectively, whereas there were no significant differences in the other echocardiographic measurements. Infants with CS were further subdivided into 7 neonates with increased LA size (Group A) and 6 infants with normal or decreased LA size (Group B). LV systolic time intervals were abnormal only in Group A infants. Conclusion: Neonates in CS can be: 1-identified by use of M-mode echocardiogram, 2-classified into two groups:A-Neonates with primary LV failure, B-Neonates with decreased venous return to LA in association with normal or decreased LV function.

1374 EFFECTS OF PGD_2 ON THE FETAL CIRCULATION OF THE LAMB Eleftherios Sideris, Kazuoki Yokochi, Thomas VanHelder, Flavio Coceani, Peter M.Olley (Sponsored by Henry Levison) Hospital for Sick Children, Department of Cardiology, Toronto, CANADA.

The circulatory effects of Prostaglandin (PG)D_2 were studied in 16 fetal lambs using radionuclide microspheres (MICS) and in 2 newborn lambs by angiography. PGD_2 infusions of 50 ng/kg/min up to 10000 ng/kg/min were tested before and after pretreatment with 0.2 mg/kg indomethacin (INDO). Bolus injections of 2 µg/kg were also tested in the fetus. In the fetus there was a dose response increase (r=0.81) of the pulmonary flow (PF) with a threshold of 500 ng/kg/min before INDO. After INDO the threshold was 50 ng/kg/min but the dose response curve was not linear. The INDO induced main pulmonary artery-aorta gradient (MPA-AO) was abolished with a dose of 500 ng/kg/min of PGD_2 or higher. Pulmonary vasodilation occurred up to 10000 ng/kg/min. PF returned to INDO levels in 15' and (MPA-AO) reappeared in 30 min. Both cardiac output and right ventricular output increased significantly before INDO while they did not change when PGD_2 was given after INDO. Systemic pressure was unaffected. Bolus injections had similar effects to infusions. No action of PGD_2 on the closed neonatal ductus could be shown in 2 neonates angiographically. We conclude: (1)PGD_2 is a potent pulmonary vasodilator in the fetus with little systemic effect (2)Pulmonary action is potentiated by INDO pretreatment (3)Although (MPA-AO) is abolished with high doses of PGD_2 in the fetus, significant direct action on the ductus is unlikely. PGD_2 could be useful in treating persistent pulmonary hypertension.

1375 EFFECTS OF SALT LOADING ON THE RENIN-ANGIOTENSIN CONTROL OF NEWBORN BLOOD PRESSURE. Sharon R. Siegel, Department of Pediatrics, UCLA Hospital and Clinics, Los Angeles, California.

The high renin-angiotensin system (RAS) levels in the newborn serve to maintain basal blood pressure (BP) The effects of salt loading on the RAS control of basal BP and sensitivity to angiotensin II (A-II) were studied in the newborn lamb. In Exper. 1, 6 twin lambs were given NaCl (10 mEq/kg/day) for 5 days; saralasin (sar) (10 ug/kg/min) was infused for 60 min in all 12 lambs. In Exper. 2, 6 newborn lambs were infused with NaCl (10 mEq/kg in 20 ml/kg 5% D/W) over 60 min., followed by serial 15 min doses of A-II (0.025 to 0.25 ug/kg/min) in all 12. Mean aortic BP was monitored and plasma renin activity (PRA) measured. In Exper. 1, (sar) increased PRA and caused a 10 mm drop in mean aortic BP in the control lamb; chronic salt loading suppressed the high basal RAS levels ($p<.01$), and inhibited the PRA and hypotensive response to (sar) ($p<.01$). In Exper 2, acute volume expansion decreased PRA from 22.1 ± 2.1 ng/ml/hr (M and SEM) to 10.8 ± 2.1 ($p<.05$). A-II(0.025 ug/kg/min) caused no BP change in the control newborn lamb, and increased BP 15 mm Hg in the volume expanded lamb; (0.25 ug/kg/min) increased BP 30 mm Hg in the control lamb and 40 mm Hg in the volume expanded lamb. In conclusion: Salt loading: 1) inhibits the increase in PRA and the hypotensive response to (sar); and 2) increases the pressor responsiveness to A-II.

1376 THE IMPACT OF INTRAVENTRICULAR HEMORRHAGE ON SURVIVAL IN LOW BIRTH WEIGHT INFANTS. Maureen E. Sims, Susan B. Turkel, Marta E. Guttenberg, Paul Y. K. Wu, University of Southern California School of Medicine, Los Angeles County-University of Southern California Medical Center, Departments of Pediatrics and Pathology, Los Angeles.

Intraventricular hemorrhage (IVH) in premature infants is usually accepted as a major contributor to mortality. Previous studies relied on data from small numbers of very low birth weight, mainly outborn infants. To determine the influence of IVH on survival at various birth weights in a totally inborn population, we performed cranial ultrasound scans and/or postmortem examinations in 180 successive liveborn infants with birth weights of 620-2250 gm over a six month period. An ATL ultrasound sector scanner was used 1-4 times during the first week of life and weekly thereafter until discharge or death. The infants were divided into six groups according to birth weight. Results:

Group	I	II	III	IV	V	VI
Weight: gm	620-999	1000-1249	1250-1499	1500-1749	1750-1999	2000-2250
Number	23	25	26	41	25	40
Deaths	15 (65%)	7 (28%)	3 (12%)	4 (10%)	2 (8%)	2 (5%)
Total IVH	7 (30%)	9 (36%)	2 (8%)	4 (10%)	3 (12%)	1 (2.5%)
IVH deaths	6 (86%)	3 (33%)	1 (50%)	2 (50%)	0	0

The severity of hemorrhage did not correlate with birth weight, gestational age or survival in any group. Assisted ventilation correlated with IVH in groups I-IV. Asymptomatic infants with IVH were more common in groups IV-VI. In group I, IVH occurred primarily in AGA infants, most of whom died. In no group did IVH cause the majority of deaths. Based on a large number of inborn infants, we found a lower incidence of IVH than usually reported in outborn or combined populations. IVH is a significant cause of mortality, but its impact on survival decreases with increasing birth weight.

● 1377 DEVELOPMENTAL CHANGES IN THE EFFECT OF PROSTAGLANDIN D_2 ON THE PULMONARY CIRCULATION IN THE NEWBORN LAMB. Scott J. Soifer, Frederick C. Morin, David C. Kaslow, & Michael A. Heymann, Univ. of Calif., S.F., Dept of Pediatrics and Cardiovascular Research Institute, San Francisco, California.

Prostaglandin D_2 (PGD_2) lowers pulmonary artery (PA) pressure without changing aortic (AO) pressure in newborn lambs with induced PA hypertension. We investigated the effect of PGD_2 on the circulation in 4 lambs studied in the first 3 days of life and in 3 other lambs studied sequentially from 1 to 22 days of age. Under local anesthesia PA thermodilution, AO and venous catheters were placed to measure AO, right atrial, PA, PA wedge pressures and cardiac output (CO). All lambs spontaneously breathed a mixture of air and N_2 to induce PA hypertension. We infused intravenously PGD_2 at doses of 1 to 25 ug/kg/min. During the first 3 days of life, 5 ug/kg/min produced a 33 ± 4% SE fall in PA pressure, a 11 ± 4% increase in AO pressure and a 9.7 ± 2.5% increase in CO. By 10 days of age, there was only a 15 ± 5% fall in PA pressure, while changes in AO pressure and CO were similar to those seen in the first 3 days. At this dose, pulmonary vascular resistance (PVR) fell more than systemic vascular resistance at all ages. PVR fell 40 ± 3% during the first 3 days of life and only 26 ± 2 % after 10 days. At 25 ug/kg/min PGD_2 produced pulmonary vasodilation in the first 3 days but became a vasoconstrictor with increasing age. The specificity of PGD_2 for the pulmonary circulation and the attenuation of its vasodilating properties during the first weeks of life suggests that PGD_2 may be important in the regulation of PVR and pulmonary blood flow during the perinatal period.

1378 FOLLOW-UP OF INFANTS WEIGHING LESS THAN 1750 GRAMS WITH AND WITHOUT INTRAVENTRICULAR HEMORRHAGE. Yolande F. Smith, Mary K. Davitt, Anita M. Sostek, David C. McCullough, Edward G. Grant, Kolinjavadi N. Sivasubramanian. Georgetown Univ. Med. Center, Washington, D.C. (Spon. by P.L. Calcagno.)

Intraventricular Hemorrhage (IVH) was assessed serially by portable cranial sonography on 64 of 77 infants weighing ≤1750 grams at birth admitted to the Intensive Care Nursery. Hemorrhage was graded by a modified Papile classification Grades I & II (Minor)-Grades III & IV (Major). 33 of the 47 surviving infants studied were fully assessed quarterly using the Bayley scales of motor (PDI) and mental (MDI) development, and standard neurological and auditory examinations. Mean age at latest follow-up was 13.6 months (8-21m). 3 (9.1%) of the infants followed were shunted for hydrocephalus. Hypertonia was evident in 48%, hypotonia in 12%; hearing was normal in 90%. Bayley scores were corrected for gestational age.

Sonograms	Total	PDI≥80	MDI≥80	PDI <80	MDI<80
Normal	13	11	12	2	1
Minor IVH	5	4	4	1	1
Major IVH	15	6	10	9	5

The data show that at 13 months 1) 80% of premature infants with minor grades of IVH have normal mental and motor development; 2) infants with major hemorrhages have a 66% chance of normal motor development; 3) Caution must be used in assessing prognosis in infants with major IVH.

1379 PROGRESSION OF INTRAVENTRICULAR HEMORRHAGE (IVH) IN PREMATURE INFANTS. Yolande F. Smith, Kolinjavadi N. Sivasubramanian, Mary K. Davitt, Edward G. Grant, David C. McCullough. Dept of Pediatrics, Radiology, Georgetown U. Med. Ctr, Washington,D.C. (spon. by P.L. Calcagno.)

Serial portable cranial sonograms were done on 64 of 77 infants weighing less than 1750 grams at birth admitted to the Intensive Care Nursery. IVH was graded according to Papile's classification. Of 51 infants studied who survived more than 5 days, 27 (53%) had stable sonographic findings; 2 (4%) infants had regression of IVH to a lower grade or normal, and 22 (43%) progressed to a higher grade between days 5 and 7.

		GRADE IVH			
Sonogram	Normal	I	II	III	IV
<3 days	16	8	16	6	5
≥5 days Stable	15	1	2	4	5
≥5 days Progression	1	6	13	2	0

IVH occurs most frequently in the first 3 days of life in premature infants. However, 43% of the infants in our group had worsening of their hemorrhage by the 7th day of life. Follow-up sonograms should be done in sick premature infants if the initial study is done before the 5th day of life.

● 1380 THERAPEUTIC VALUE OF TERBUTALINE IN BRONCHOPULMONARY DYSPLASIA. Richard Sosulski, Soraya Abbasi, William W. Fox. Univ. of Pa. Sch. of Med., Div. of Neonatology, Children's Hospital of Philadelphia & Pennsylvania Hospital, Philadelphia, PA.

Bronchopulmonary dysplasia (BPD) is a significant problem in neonates requiring long-term mechanical ventilation. The clinical effect of terbutaline sulfate, a selective beta-2 adrenergic agonist was studied in 7 ventilator dependent infants with BPD (Wt.=2.45 ± .32 SEM kg, Age=12.6 ± 3.2 wks). Lung compliance (C_L), inspiratory resistance (R_I), expiratory resistance (R_E), total work of breathing (WOB), respiratory frequency (f), inspiratory/expiratory time (I/E), and arterial blood gases (ABG) were obtained prior to and at 30' and 60' following the subcutaneous injection of 5 ug/kg of terbutaline. Heart rate and respiratory rate were continuously monitored. Baseline $PaCO_2$= 52± 5 mmHg and PaO_2= 56 ± 4 mmHg. There was a significant ($p < .001$) improvement in C_L from baseline (2.16 ± .23 ml/cmH_2O) at 30' (2.94 ± .24 ml/cmH_2O) and 60' (3.05 ± .26 ml/cmH_2O. A 41% decrease in R_E at 60' (79.3 ± 22.4 cm H_2O/l/sec) and a 31% decrease in R_E at 30' (93.0 ± 24.0 cmH_2O/l/sec) from baseline (135.4 ± 42.4 cmH_2O/l/sec) was seen. An increase in the I/E occurred in all patients at 30' and 60' ($p < .05$, $p < .025$). Clinical improvement (decreased wheezing and improved air exchange) was noted in 5/7 infants. $PaCO_2$ was decreased in 4/6 patients at 60'. Heart rate increased transiently by 16% (147 ± 7 beats/min vs. 171 ± 3 beats/min, $p < .01$) during the study period. There was no significant change in WOB, R_I, or f. Subcutaneous terbutaline improves pulmonary function and clinical condition in ventilator dependent infants with BPD. The expiratory phase is most affected as indicated by increased I/E and trend toward decreased R_E.

1381 RESPIRATORY WATER LOSS IN INTUBATED PREMATURE INFANTS RECOVERING FROM RESPIRATORY DISTRESS SYNDROME (RDS). Richard Sosulski, Stephen Baumgart. (Spon. by W.W. Fox). Univ. of Pa. Sch. of Med., and Dept. of Peds., Children's Hospital of Philadelphia, Philadelphia, PA.

Changes in respiratory water loss may significantly affect fluid balance in the critically ill premature infant with RDS. The effect of breathing warm humidified air on insensible water loss (IWL) was studied in six premature infants receiving endotracheal CPAP for RDS (gestational age 33 ± 1 SEM wks and weight of 1.55 ± .18 kg). Infants nursed under servocontrolled radiant warmers were studied for two consecutive one hour periods, pre- and post-extubation. Intubated endotracheal airway temperature was 31.5 ± .5°C and airway humidity was rated at 100%. IWL (continuously monitored with a Potter scale in thermal equilibrium), radiant warmer power delivery (measured with wattmeter /thermopile), skin and airway temperatures, vital signs, ambient temperature and relative humidity were measured during the study periods. IWL in infants receiving warm humidified air was reduced by 38% (room air 2.89 ± .51 ml/kg/hr, warm humidified air 1.78 ± .41 ml/kg/hr, $p < .05$). Servo-controlled radiant warmer power delivery was unchanged (14.6 ± 1.6 vs. 14.5 ± 1.7 mw/cm^2). Heart rate, respiratory rate, skin and ambient air temperature and relative humidity were not significantly different pre-and post- extubation. The reduction in IWL in infants intubated for RDS and receiving humidified air is consistent with values for respiratory water loss previously reported in well babies. Failure to observe a significant reduction in radiant warmer power delivery following extubation, suggests that respiratory water loss may not exert a major effect on heat balance.

1382 HYPERVENTILATION THERAPY FOR PERSISTENT PULMONARY HYPERTENSION OF THE NEONATE AND OCCURRENCE OF A TRANSITION PHASE. Richard Sosulski and William W. Fox. Univ. of Pa. Sch. of Med., and Div. of Neonatology, The Children's Hospital of Philadelphia, Phila., PA.

Hyperventilation has been shown to improve oxygenation in neonates with persistent pulmonary hypertension of the neonate (PPHN). The use of high inflating pressures and rates to lower PCO_2 levels may result in acute parenchymal damage, air leaks, and chronic lung disease. A transition phase (TRANS) was recognized in PPHN treated with hypervent. when hypoxemia was no longer due to R to L shunt but to vent./perfusion abnormalities in the lung. 14 neonates with PPHN who survived after hypervent. were studied. Diagnosis was confirmed by cardiac cath. in 7, contrast echo. in 4, and hypervent.-hyperoxia challenge in 3. Sex: 10 male, 4 female, birth-wt. 2.98 ± .19 SEM kg, gest. age 37.8 ± .8 wks. All patients were hypervent. to a mean low PCO_2 of 22 ± 1.2 mmHg. The time to TRANS varied from 27 to 188 hrs. The best clinical indicator of TRANS was decreased PaO_2 lability during hypervent. $\Delta PaO_2/\Delta PCO_2$ at equivalent FiO_2 levels was compared 12 hours pre TRANS and 12 hours post TRANS. Pre TRANS mean PaO_2=127 mmHg (range 79-257 mmHg) and mean PaO_2 post TRANS =79.5 (range 42-121 mmHg). Pre TRANS mean PCO_2 =28.8 mmHg and mean PCO_2 post TRANS 34.9 mmHg ($p < .002$). The mean $\Delta PaO_2/\Delta PCO_2$ values were 22.2 mmHg/mmHg ΔPCO_2 pre TRANS and 4.2 mmHg/mmHg ΔPCO_2 post TRANS ($p < .001$). Lung hyperinflation was often seen on chest radiographs at TRANS but this finding was less sensitive than PO_2 lability. Contrast echo. also showed lack of R to L shunt at the time of TRANS. The recognition of TRANS during hyperventilation for PPHN allows for management of the patient at higher PCO_2 levels and less aggressive ventilator therapy.

1383 ASSOCIATION OF ACQUIRED CYTOMEGALOVIRUS INFECTIONS AND BRONCHOPULMONARY DYSPLASIA IN PREMATURE INFANTS: Stephen A. Spector, David K. Edwards, and Ronald W. Coen (Spon. by James D. Connor) University of California, Departments of Pediatrics and Radiology, San Diego.

From 15-30% of infants in ICNs for >3 wks acquire CMV infections. This study assessed the association of bronchopulmonary dysplasia (BPD) and acquired CMV infections in 38 babies <32 wks gestation. All infants had weekly urine cultures for CMV. The 19 CMV(+) infants were matched with 19 CMV (-) babies for mean gestational age (28.4 wks vs 29.2 wks), mean birth wt (1062g vs 1094g), apgar scores, incidence of PDA (13/19 vs 14/19), and initial evidence of RDS (13/19 vs 13/19). The 19 CMV(+) babies were a mean age of 44.5 days (range 21-128 days) when they began to excrete CMV in their urine. CMV(+) infants received a mean of 17.6 blood transfusions vs 9.4 for CMV(-) babies. Xray evidence of BPD, defined as persistent interstitial pulmonary infiltrates, was identified in 16/19 CMV(+) babies vs 9/19 CMV(-) infants ($p<.05$). CMV(+) infants required increased inspiratory O_2 for a mean of 70.3 days vs 25.1 days for controls ($p<.05$). 6 infants who acquired CMV from 21-28 days old required increased O_2 for a mean of 70.3 days vs 38.7 days for infants who acquired CMV at >28 days. These findings suggest that babies who acquire CMV infections while hospitalized in ICNs are more likely to develop xray evidence of BPD associated with prolonged O_2 requirements, and indicate that effective methods to minimize the transmission of CMV to premature infants are necessary.

●1384 AWAKE APNEA-RELATIONSHIP TO GASTROESOPHAGEAL REFLUX. Alan R. Spitzer, John T. Boyle, David N. Tuchman, William W. Fox. Univ. of Pa. Sch. of Med., and Dept. of Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA.

Few reports to date have stressed the differences between the infant who presents with apnea while awake compared to those who have apnea during sleep. Recently, we studied a group of 8 patients from 7 weeks to 22 weeks of age who had significant episodes of apnea while awake requiring vigorous stimulation or resuscitation. All infants had their apnea ½-1 hour after feeding. Each child was considered to be alert at the time of the event and was either being held, sitting in an infant seat, or lying supine while attended by a parent. All infants had negative EEG and EKG studies, and none had evidence of pulmonary disease. To determine if gastroesophageal reflux (GER) was related to apnea in these children, each had 24 hour continuous pH probe monitoring with simultaneous nasal airflow-pneumogram recording using nasal thermistor and chest-wall impedance. All 8 children had GER as demonstrated by pH probe monitoring during the study. Four children (50%) had either concurrent obstructive apnea (2/8) or partial airway obstruction (2/8) at the time of GER as evidenced by bradycardia or tachycardia, increased chest wall movement and complete or partial reduction of nasal airflow. The number of episodes per recording ranged from 2-9. Conclusion: Awake apnea during infancy with normal EEG and EKG may be a manifestation of GER and/or laryngotracheal chemosensitivity. Children presenting in this manner should be evaluated with continuous pH and nasal airflow-pneumogram recording.

1385 EFFECT OF INTENSIVE CARE UNIT EXPOSURE ON TEMPERAMENT IN HIGH-RISK PRETERM INFANTS. Linda Spungen, Anne Farran, Frances Borian, Judy Bernbaum. (Spon. by D. Cornfeld). Univ. of Pa. Sch. of Med., and Dept. of Peds., Children's Hospital of Philadelphia, Phila., PA.

The stress of intensive care unit (ICU) treatment on high-risk preterm infants may predispose them to a more irritable, difficult temperament. We compared temperament at 6 mos adjusted age (AA) in 3 types of infants: 1) high-risk term (HRP) transferred to our level 3 nursery (n=26); 2) healthy preterm (HP) managed at level 2 nurseries (n=14); 3) normal full-term (FT) (n=26). Social class, sex, and birth order showed no sig. diff. The Infant Temperament Questionnaire (ITQ) (Carey & McDevitt, Peds., 1978), completed by all mothers, yields scores based on 1) objective ratings of infants' behavior 2) maternal perceptions of her infant. Objective ratings showed that, by 6 mos, temperament of HRP's was no different from that of HP's or FT's. However, maternal perceptions differed ($p < .005$) : 31% of HRP mothers rated their infants as "difficult" compared to 0% of HP and 4% of FT mothers. To examine ICU exposure within the HRP group, objective ratings for a sub-group (n=13) of infants with bronchopulmonary dysplasia (BPD) were compared to those without BPD (n=13). Mean ± SD days of hospitalization for BPD infants was 133.3 ± 57.2 vs. 49.7 ± 27.2 ($p < .01$) for the non-BPD group. At 6 mos AA, sig. more BPD infants were rated "difficult" than non-BPD infants ($p < .05$). Longer ICU exposure or the disease itself may have contributed to these findings. Conclusions: ITQ ratings suggest that any effect of ICU treatment on infants' temperament was resolved by 6 mos AA. Parents of HRP infants, however, continued to view their infants as more difficult and vulnerable at 6 mos. In BPD infants with long hospitalization, adverse effects on temperament persisted.

1386 RAPID CHANGES IN OXYGEN REQUIREMENTS OF ASPHYXIATED NEONATES DURING THE FIRST 24 HOURS OF LIFE - Gary E. Stahl, William W. Fox. Univ. of Pa. Sch. of Med. and Dept. of Peds., Children's Hosp. of Phila., Philadelphia, PA.

Asphyxiated neonates are often diagnosed as having a specific respiratory syndrome (RDS, TTN, etc.) on admission to the NICU. Asphyxia, however, is often the most important factor determining O_2 requirements during the 1st 24 hours. Due to changes in pulmonary vascular resistance, asphyxiated newborns can frequently be weaned rapidly from high O_2 levels during the 1st day of life and do not display the characteristics of their primary pulmonary disease until the 2nd day of life.

The ABG data of all neonates admitted to the NICU from 8/1 - 10/1/81 requiring resp. support for 24 hours was reviewed. Infants with cong. defects which might affect the cardio-respiratory system were excluded. Infants with asphyxia (1 min. Apgar $\leq$ 5) were compared to those without asphyxia (1 min. Apgar > 5). The groups were comparable in birth wt. (1.69 kg $\pm$ 1.3 vs. 2.0 kg $\pm$ 0.6) and EGA (32.3 wks $\pm$ 5.4 vs. 33.7 wks $\pm$ 2.4). Max. FiO_2 required during the 1st 24 hours by asphyxiated neonates (ASPHX) was sig. ($p<.05$) higher than that required by non-asphyxiated infants (NASPX). Min. FiO_2 required was not sig. different. Decrease in $D_{A-a}O_2$ during the 1st 24 hours was sig. ($p<.02$) greater in asphyxiated babies.

Group	N	Maximum FiO_2	Minimum FiO_2	Δ $D_{A-a}O_2$
ASPHX	14	92.5% $\pm$ 15.0	55.3% $\pm$ 17.0	169.4 $\pm$ 70.2
NASPX	12	80.0% $\pm$ 21.0	47.3% $\pm$ 14.3	103.3 $\pm$ 79.8
		$p < .05$	NS	$p < .02$

The presence of asphyxia, as reflected by an Apgar score $\leq$5 at 1 minute, is a major factor contributing to the severity of respiratory distress in the first 24 hours of life. Asphyxia should be considered the primary diagnosis during that period of time.

1387 POSTERIOR TIBIAL ARTERY CATHETERS (PTAC) IN NEWBORNS: MAINTENANCE TECHNIQUES AND FACTORS AFFECTING DURATION. Virginia F. Stanford, Joseph A. Garcia-Prats, James M. Adams. (Spon. by Arnold J. Rudolph.) Baylor College of Medicine, Department of Pediatrics, Houston, Texas.

A prospective randomized study compared 3 maintenance techniques for PTAC. Group A (Todres, J. Pediatrics 87:273,1975)PTAC cleared by residual pump pressure; Group B (Adams, Pediatrics 55:261,1975) 2-3 cc of blood required for infusate clearing with return of blood through PTAC plus flush to clear PTAC; Group C modification of Group B returning clearing blood through peripheral vein but clearing PTAC by flushing solution. Statistical analysis was done by analysis of variance,student t test,survival curves, and chi square.

	Group A(N=12)	Group B(N=12)	Group C(N=11)	
mean weight (g)	2038	1952	1749	NS
weight range (g)	810-3960	790-4190	630-3625	
mean gestation (wks)	31.9	32.7	29.8	NS
mean post conceptional age (wks)	37.2	34.2	34.2	NS
Pavulon,sedation,shock	8	9	2	P<0.05

Groups A and B were significantly better maintenance techniques as demonstrated by survival curves. Group C had significantly fewer patients with conditions which reduce patient activity and increase catheter survival. When PTAC were compared to radial artery catheters (RAC),RAC survival was significantly longer irrespective of maintenance technique. At 5 days 57% of RAC were functional vs 32% of PTAC($P< 0.05$). At 9 days, 44% of RAC were functional vs 16% of PTAC($P<0.05$). The difference may be due to inability to immobilize the foot as adequately as the wrist after catheter placement.

1388 RADIAL ARTERY CATHETERS (RAC) IN NEWBORNS: MAINTENANCE TECHNIQUES AND FACTORS AFFECTING DURATION. Virginia F. Stanford, Joseph A. Garcia-Prats, James M. Adams. (Sponsored by Arnold J. Rudolph.) Baylor College of Medicine, Department of Pediatrics, Houston, Texas.

A prospective, randomized study compared 3 maintenance techniques for RAC. Group A (Todres, J. Pediatr. 87:273,1975) RAC cleared by residual pump pressure; Group B (Adams, Pediatrics 55: 261, 1975)2-3 cc of blood required for infusate clearing with return of blood through RAC plus flush to clear RAC;Group C modification of Group B returning clearing blood via peripheral vein but clearing RAC by flushing solution. Statistical analysis was done by analysis of variance, student t test, survival curves,chi square.

	Group A(N=24)	Group B(N=23)	Group C(N=26)	
mean weight (g)	1814	2195	1940	NS
weight range (g)	750-3780	620-3850	660-4060	
mean gestation (wks)	32.1	34.0	32.9	NS
mean post conceptional age (wks)	33.2	36.4	34.9	NS
Pavulon,sedation,shock	12	11	15	NS

No significant difference in maintenance techniques was demonstrated by survival curves. Group A remained functional longer than Groups B and C after 3rd day. By day 7, 63% of Group A were still in use vs 45% of Groups B and C. Catheter life varied directly with conditions reducing patient movement, namely: immaturity, lower birth weight, shock, sedation, use of neuromuscular blockade. Major complications(persistent blanching of forearm,fingers, distal extremity) were more often found in Group B(3/23) than in Group A (1/24) or Group C (0/26).

1389 TRANSCUTANEOUS OXYGEN MONITORING IN NEONATAL AIR TRANSPORT. Dennis C. Stevens, Guy A. Carter, Lawrence J. Fenton. Univ. of S. Dakota, School of Med., Sioux Valley Hospital, Dept. of Pediatrics, Sioux Falls, S. Dakota.

A portable, battery-operated device (Novametrix, Inc.) was used to monitor transcutaneous oxygen tension ($TcPO_2$) in 42 neonates transported to a regional intensive care nursery. Twenty-eight were transported by non-pressurized, fixed wing aircraft and 14 by ambulance. Simultaneous arterial (PaO_2) and $TcPO_2$ measurements demonstrated a high degree of correlation before ($r=0.87$, $n=23$), and a lesser degree at the end of transport ($r=0.75$, $n=28$). Prior to transport the $TcPO_2$ and PaO_2 indicated hypoxia ($PaO_2 \leq$ 50 mmHg) or hyperoxia ($PaO_2 \geq$ 100 mmHg) in 65% of cases. During transport the FiO_2 was adjusted on the basis of the $TcPO_2$ and clinical condition. At the end of transport, $TcPO_2$ indicated hyperoxia or hypoxia in only 21%, whereas, 46% of neonates fell into these categories by PaO_2 measurement. A group of 10 spontaneously breathing and 4 ventilated neonates were selected for a high degree of $TcPO_2$ to PaO_2 correlation. Those spontaneously breathing had a significant decline in $TcPO_2$ from 112 $\pm$ 16 mmHg at take-off to 86 $\pm$ 9 mmHg ($\pm$SEM) during flight. ($p< .05$ by single tailed t-test.) Ventilated neonates showed a non-significant decline. The mean change in oxygenation for spontaneously breathing neonates was predictable using the alveolar air equation, whereas, the change in ventilated neonates was less, suggesting an improvement in oxygenation in flight. It is concluded that $TcPO_2$ monitoring in neonatal transport is useful, however, the accuracy of measurement may decline with time.

1390 MULTIVARIATE ANALYSIS OF RISK OF NEONATAL SEPSIS FOLLOWING PROLONGED RUPTURE OF AMNIOTIC MEMBRANES (PROM). J.St.Geme,C.Hobel,J.Carter,D.Murray,R.Leake, B.Anthony,D.Thibeault,I.Ross, and J.Drage, Harbor-UCLA Medical Center(HUMC),Torrance,California and NINCDS,Bethesda, Maryland.

Chi square and logistic stepwise multiple regression analysis (LMRA) of perinatal determinants of infant sepsis following PROM greater than 24 hours was applied to 33 infected infants and 66 matched control infants from the NINCDS Collaborative Project. In order of statistical significance, the important variables were: placental inflammation(P.002),gestational age <34 wks(P.008), gestational age 34-37 wks(P.013), male sex(P.015), Apgar <6 at 5 mins(P.023), and clinical amnionitis(maternal fever,fetal tachycardia, or amniotic fluid bacteria)(P.044).

Using these predictive variables, capture of infected infants for either microbial surveillance (superficial and systemic cultures) or microbial surveillance and anticipatory antibiotic therapy was highly significant(P.0001).Incorporating these variables and derived coefficients from the LMRA,a mathematical model was used for evaluation and prediction of neonatal sepsis with a sensitivity of 82% and specificity of 58%.

Analysis of 46 PROM infants before and 216 PROM infants following implementation of this process at HUMC indicated significant improvement in infant risk management(from 59% to 81%,P<.05). Indiscriminate antibiotic therapy decreased from 35% to 15%(P<.05). In the absence of a shift in the median days of hospitalization of non-PROM infants,determination of the grand median days of PROM infant hospital stay showed a decrease(P<.01)following the initiation of this evaluation and management scheme.

1391 BEHAVIORAL EFFECTS OF ELECTIVE VS EMERGENCY CAESAREAN DELIVERY. Joseph W. Sullivan, Joseph Byrne, & Frances D. Horowitz (Spon. by William K. Frankenburg). University of Colorado Medical School, Psychiatry Dept., Denver.

Given the rise in the number of Caesarean births, data are needed which document the behavioral effects associated with Caesarean versus vaginal delivery. Few studies, however, have made a distinction between Elective and Emergency C-sections thereby potentially confounding the effects of Caesarean delivery with the effects of the perinatal complications which may have necessitated the C-section. The objective of this study was to directly compare the effects on neonatal behavior of three types of delivery: 1) Elective C-section (i.e., repeat or scheduled); 2) Emergency C-section; and 3) uncomplicated vaginal. One hundred and eighty newborns (60 per group) were assessed shortly after birth with Brazelton's (1973) Neonatal Behavioral Assessment Scale with Kansas supplements (NBAS-K). The 38 item scores were summarized for analysis using the 6 clusters developed by Lester et al. (1978) and two clusters for the Kansas supplements. Oneway Analysis of Variance was employed to compare the three types of delivery. Significant differences ($p<.05$) were found between the groups on the Orientation Modal, Interactive, and Autonomic Regulation cluster scores. A performance trend of Elective>Vaginal>Emergency was evident for 6 of the 8 clusters. This trend suggests that, overall, the Elective group performed better than the Vaginal group. The Emergency group had the lowest performance of the three. These results suggest that Elective Caesarean delivery may enhance neonatal performance. Longitudinal studies are needed to assess the longterm effects of these early behavioral differences.

1392 TRANSCUTANEOUS PCO_2 ($TCPCO_2$) MONITORING IN NEONATES. Shyan Sun, Zanaida Aranda, Nora Ruiz, Anita Baldomero Minerva Castillo. (Spon. F. Behrle) New Jersey Med. School. Dept. Neonatology, Newark, New Jersey

Thirteen mechanically ventilated newborn infants (GA 26 to 44 wks. BW 700 to 4000 gm) were monitored from day 1 to day 11, using a heated transcutaneous $TcPCO_2$ monitor (Biochem) at 2 different electrode temperature settings (42° C and 44° C). 105 Simultaneous $TcPCO_2$ and $PaCO_2$ readings (umbilical arterial or radial arterial) were compared:

	42° C	44° C
Linear Regression	$PaCO_2=0.5xTcPCO_2+15$	$PaCO_2=0.6xTcPCO_2+11$
Regression via Origin	$PaCO_2=0.779xTcPCO_2$	$PaCO_2=0.8xTcPO_2$
Correlation (r)	0.621	0.796
P	0.0001	0.0001
Response Time	1.28 min	1.92 min
Stabilization Time	12.87 min	9.8 min
Skin Hyperemia at 3 hrs	minimum	severe

At 44oC, $TcPCO_2$ correlated better with $PaCO_2$ (r of 0.796 vs 0.621), stabilization time was shorter (9.8 min vs 12.87 min) compared to $TcPCO_2$ at 42° C setting, but these advantages are traded off by considerably higher incidence of skin burn especially in very low birthweight infants. Continuous non-invasive monitoring of PCO_2 may soon become equally important as that of PO_2 in the sick preterm infants, since it has become increasingly evident that prolonged high PCO_2 may contribute to the pathogenesis of retinopathy of prematurity (RLF) & intraventricular hemorrhage in preterm infants.

1393 THEOPHYLLIN RESISTANT APNEAS. Shyan Sun, Anita Baldomero, Kamtorn Vangvanichyakorn. (Spon. F. Behrle) New Jersey Med. School, Dept. Neonatology, Newark, NJ

During a 4 month period (Aug. to Nov. '81) nurses were instructed to observe and record frequency of apnea in all preterm infants <2000 gms in NICU. Infants on respirators were excluded. Apnea was defined as cessation of spontaneous respiration of more than 20 sec. associated with bradycardia and cyanosis. All other causes of apnea were excluded except prematurity and IVH. At the first episodes of apneas, Theophyllin was given to maintain blood level of 8 to 12 ug/ml. All infants were scanned for IVH with ultrasound (ATL Mark III).

	Apnea	GA(wks)	B.W.(gm)	Theo.(ug/ml)	Apnea Stop
IVH	6	$\bar{m}$ 27.5	$\bar{m}$ 973	13.06	1
Control	9	$\bar{m}$ 30	$\bar{m}$ 1263	9.36	9
P					<0.002

6 apnea infants had IVH grades I to III. Inspite of adequate blood level, none responded to Theophyllin treatment except one who had minimal subependymal hemorrhage. All 9 infants with uncomplicated apnea of prematurity responded to Theophyllin as soon as therapeutic blood level was established. 5 unresponsive IVH infants required on and off mechanical ventilatory support and took an average of 37 days (33, 66, 23, 49 & 16 days respectively) before they regained regular spontaneous respiration. We concluded that apneas associated with or resulting from IVH (grade II-III) were on the whole resistant to Theophyllin treatment. This refractory period coincided with duration of ventricular dilatation. They seemed to start to breathe regularly as ventricles began to reduce in size.

1394 NEONATAL SICK CELL SYNDROME. Shyan Sun, Minerva Castillo, Kamtorn Vangvanichyakorn, Anita Baldomero (Spon. R. Levine) New Jersey Med. School. Dept. Neonatology, Newark, New Jersey

During a one month period (Nov.'81) all serum electrolyte studies were accompanied by simultaneous blood oSmolality (oSm) determinations using 5100 C Vapor Pressure Osmometer (Wescor). 107 paired studies were done in 25 neonates. Observation was made on the difference (Δ mOsm) between measured and "expected" oSm (2 Na+urea+glucose in mmol)

Δ mOsm/L	<15	16-20	21-30	>30
Sample	64(59%)	9 (9%)	18(17%)	17(16%)
Patient	20	6	9	6

17 samples of 6 neonates with Δ mOsm > 30 mOsm/L had mean blood oSm 287 mOsm/L (281-330) and mean Na 134 mEq/L (124-147). Only 3 specimens had Na < 130 mEq/L. All 6 patients suffered severe tissue anoxia (2 coma after anoxia, 3 IVH, 2 tension pneumothoraces). This phenomenon of oSm discrepancy uniformly occurred 1 to 2 days after the anoxic insult and last 2 to 20 days (av 7 days) depending on the severity and duration of initial insults. Our experience revealed that not all sick cell syndromes are associated with hyponatremia as originally described by Flear & Singh (1973). It is our impression that a large Δ mOsm is a better indicator of the syndrome than hyponatremia alone. Sick cell is associated with serious illness (3 of our 6 infants died) and widespread bodily insults which impair the permiability of the cell membranes. Knowledge of oSm as well as electrolyte will prevent not uncommon mismanagement of fluid & electrolyte disorder associated with this syndrome.

1395 SEVERE PERINATAL ACIDOSIS ($pH \leq 7.00$) AND LUNG FUNCTION IN NEWBORN INFANTS. Donald W. Thibeault and Frederick K. Hall, University of Missouri School of Medicine, The Children's Mercy Hospital, Kansas City, Missouri.

Perinatal asphyxia and acidosis have adverse effects on neonatal lung function but their importance in the clinical care of infants is not well defined. The pulmonary effects of severe acidosis i.e. $pH_a \leq 7.00$ in the first 2 hrs of life were studied on 29 term and 26 preterm infants consecutively admitted to a NICU and an additional 16 preterm infants were observed who developed a $pH \leq 7.00$ after 24 hrs of life. The major cause of death was CNS damage. The 37 surviving infants required assisted ventilation for 84 ± 5 hrs. The term and preterm infants with $pH \leq 7.00$ in the first 2 hrs of life ran similar pulmonary courses. Their mean FiO_2 was 0.7 to 0.8 for the first 4 hrs of life which decreased to 0.5 at 36 hrs and approached room air at 6 days of age. The mean peak inspiratory ventilator pressure reached a maximum of 19 ± 2 cm H_2O at 6 hrs, and then decreased to less than 6 cm H_2O at 6 days. The lung changes were severe but life-threatening only in those infants with RDS or meconium aspiration. In the preterm infants older than 1 day that acutely developed a $pH \leq 7.00$, the peak ventilator pressure and FiO_2 one hr prior to the acidosis was 13 ± 1 cm H_2O and 0.5 and 4 hrs following the return of blood gases to normal the peak pressure and FiO_2 were still elevated to 19 ± 2 cm H_2O and 0.6 respectively. We conclude that severe acidosis and asphyxia results in right to left shunting and a decreased dynamic compliance. However, in the absence of RDS and meconium aspiration the pulmonary changes are severe but short-lived and full clinical recovery should occur if barotrauma during resuscitation is avoided.

1396 DYNAMIC SKINFOLD THICKNESS MEASUREMENTS: NON-INVASIVE ESTIMATES OF NEONATAL EXTRACELLULAR WATER. C.Thornton D. Shannon, M. Hunter and Y. Brans. Univ. of Texas Health Science Center, Perinatal Res. Lab., San Antonio.

Application of a Harpenden caliper to a neonate's skinfold results in an exponential decline of the skinfold thickness, stabilizing within 50 to 60 seconds. In order to elucidate the meaning of this decline, simultaneous measurements of expressible skinfold thickness (ΔSFT), extracellular water (ECW, by bromide dilution), plasma volume (PV, by T-1824 dilution) and interstitial water (IW=ECW-PV) were obtained. Skinfold thickness was measured at the midtricipital (MT) and subscapular (SS) sites with a Harpenden caliper modified to permit recording of the thickness reading on a chart recorder. Expressible SFT was estimated (1) as the difference between 0" and 60" readings, expressed as % of the 0" reading (%ΔSFT); (2) by the slope of the decline curve, on semilog plot, from 4" to 20" after caliper application (sΔSFT).

Eighteen term and 18 preterm neonates were studied within 12 hours of birth. Birthweights ranged from 640 to 3700g and gestational ages, from 27 to 41 weeks. There were good linear correlations (r=0.70-0.71) between %ΔSFT and ECW, and %ΔSFT and IW at both MT and SS sites. Correlations between SΔSFT and ECW or IW (r=0.42-0.51) at both sites were more moderate but statistically significant ($p<0.02$). These data suggest (1) that material expressible from skinfolds is probably water, (2) that the amount of expressible material and its rate of expression are proportional to ECW and IW, and (3) that dynamic skinfold measurements might produce adequate estimates of ECW and IW.

1397 EFFECT OF POLYCYTHEMIA AND ITS TREATMENT ON NEONATAL BODY WATER ESTIMATES. C. Thornton, D. Shannon, M. Hunter, R. Ramamurthy and Y. Brans, Univ. of Texas Health Science Center at San Antonio, Perinatal Res. Laboratory.

In order to determine whether neonatal polycythemia (umbilical venous hematocrit, UV Hct, ≥63%) and its treatment by partial exchange transfusion (PET) affect body water estimates, 10 normo- and 8 polycythemic term neonates were studied. Total body water (TBW, antipyrine dilution), extracellular water (ECW, bromide dilution), intracellular water (ICW=TWB-ECW), plasma volume (PV, T-1824 dilution) and interstitial water (IW=ECW-PV) were determined within 12 hours of birth immediately prior to and following PET. There were no significant differences between normo- and pre-PET polycythemic neonates in mean (±SD) TBW (722±77.6 vs 742±60.6 ml/kg), ECW (510±67.8 vs 520±95.8 ml/kg), ICW (212±92.8 vs 223±90.7 ml/kg) and IW (460±67.7 vs 477±96.2 ml/kg). In the polycythemic group, PET with an average of 12±0.8 ml/kg of Plasmanate did not affect mean TBW (727±78.2 post vs 742±60.6 ml/kg pre-PET) but decreased mean ECW (405±60.9 vs 520±95.8 ml/kg, p=0.002) and mean IW (348±62.4 vs 477±96.2 ml/kg, p=0.001) and increased mean ICW (321±88.5 vs 223±90.7 ml/kg, p=0.019). Mean transcapillary escape rate of T-1824 was not affected by PET (30±13.0 vs 35±7.8 %/hour). The data suggest that polycythemia does not affect body water compartments but that PET produces a shift of water from ECW to ICW. This might be due to a state of cellular hypoxia, possibly transient, following rapid removal of a portion of the blood's O_2 carrying capacity. Correction of asymptomatic polycythemia might be more harmful than the polycythemic state.

1398 TRANSCUTANEOUS BILIRUBINOMETRY: CORRELATION IN PREMATURE INFANTS. Theodore Tolentino, Ian Gertner, I. Mark Hiatt, Thomas Hegyi,(sponsored by L. Stanley James)Department of Pediatrics, Monmouth Medical Center, Long Branch, NJ and Department of Pediatrics, CMDNJ-Rutgers Medical School, St. Peter's Medical Center, New Brunswick, NJ.

The predictive accuracy of the transcutaneous bilirubinometer (TcB) was evaluated in 50 premature white (W) and 16 preterm black (B) infants. None of the infants were exposed to phototherapy. Groups were divided in subgroups based on birth weight, (A-< 1500g, B>1500g). The results of the analysis are shown in the table.

	GROUP A		GROUP B	
	W	B	W	B
N (infant)	8	5	42	11
n (samples)	13	18	80	26
BW (gms)	1236±302	1256±139	1800±525	1997±333
GA (weeks)	31±3	30±1	34±1	34±2
Postnatal age (hrs)	81.0±81.0	51.7± 43.4	75.5±77.6	45.8±43.6
r	0.445	0.894	0.610	0.695
p	N.S	0.01	0.01	0.01

In both black and white preterm infants>1500 grams, there was a significant correlation between serum bilirubin and TCB($p<0.01$) In infants less than 1500 grams the correlation was valid only for the group of black infants. Although statistically significant relationships were obtained, the TcB cannot yet be recommended as an effective method of screening for hyperbilirubinemia in premature infants weighing less than 1500 g.

1399 TRANSCUTANEOUS BILIRUBINOMETRY: CORRELATIONS DURING PHOTOTHERAPY. Ted Tolentino, Robert Zanni, Ian Gertner, I. Mark Hiatt, and Thomas Hegyi(sponsored by L. Stanley James). Department of Pediatrics, CMDNJ-Rutgers Medical School, New Brunswick, NJ and Department of Pediatrics, Monmouth Medical Center, Long Branch, NJ.

The transcutaneous bilirubinometer was evaluated in 14 white infants treated with phototherapy in whom an opaque patch 2.5 cm in diameter was used to cover a small skin area for four hours. Five infants (BW 2250±850 g, GA 35±3 wks) were eposed to blue light (intensity 12.0±1.6 uW sq. cm2/nm at an age of 29.2±21 hrs and nine infants (BW 1810±640 g, GA 32±3 wks were subjected to white light intensity 5.7±1.8 uW sq.cm2/nm) at a mean age of 31.2 ±17.4 hrs. Twenty seven simultaneous measurements obtained from exposed skin (TcB-E) patched skin (TcB-P) and serum biiirubin (SBC), yielded the following results:

		Correlation Coefficients:		
Light	N	TCB-E and SBC	TCB-P & SBC	TCB-E & TCB-P
Blue	8	.719	.917	.739
White	19	.474	.624	.843

All correlation coefficients were significant at a $p<0.01$ level except for the TCB-E and SBC under white light which was at $p<0.05$ level. Fifteen measurements obtained during the first hour of phototherapy resulted in different correlation coefficients from twelve measurements obtained from the second through the fourth hour (0.802 vs. 0.613).

Although statistically significant relationships are retained the clinical use of TcB measurements under phototherapy may not be acceptable since the linear relationship between TCB and SBC may be markedly affected by duration of exposure to light.

1400 DERMAL BILIRUBIN KINETICS DURING PHOTOTHERAPY Theodore Tolentino, Robert Zanni, I. Mark Hiatt, Thomas Hegyi(sponsored by L.Stanley James)Department of Pediatrics, Monmouth Medical Center, Long Branch, NJ, and Department of Pediatrics, CMDNJ-Rutgers Medical School, St. Peter's Medical Center, New Brunswick, NJ.

The effect of phototherapy on cutaneous bilirubin was evaluated by the transcutaneous bilirinometer (TcB) in 14 white infants mean BW 1900 g (range 600-3200) and mean GA 33 weeks (range 28-40) at a mean postnatal age of 30 hrs. (range 4-60). An opaque patch 2.5 cm in diameter was utilized to cover the skin that served as a source for TcB control values. Simultaneous TcB measurements were obtained from exposed and patched areas every 15 minutes during four hours of phototherapy (mean light intensity 8.0± 3.8 uW sq.cm2/nm).

The calculated rise in dermal icterus from birth was 0.6 TcB units per hour (TCB u/hr). After the onset of phototherapy the rate of TcB change per hour under the skin patch was approximately 0.0 TcB u/hr. Data from exposed skin showed that the initial rate of TcB fall during the first hour was significantly faster than the successive values during the next three hours.

Hr of Photo	TcB u/Hr
0-1	-3.0±1.6
1-2	-0.7±1.7
2-3	-0.1±1.3
3-4	-0.0±1.5

There were no significant correlations demonstrated between the rate of TcB decrease and birth weight, gestational age, postnatal age, and light intensity. The results of the study indicate that:1) The rate of decrease of dermal bilirubin is non linear with respect to duration of phototherapy which may be due to kinetics of bilirubin migration following exposure to light. 2) There is an apparent steady state of dermal bilirubin under the patch which can be explained by the establishment of an equilibrium between the movement into and out of this area.

1401 NEURODEVELOPMENTAL FOLLOW-UP OF <1500 GRAMS NEONATES WITH INTRAVENTRICULAR HEMORRHAGE (IVH). Jose Urrutia, Kathy Tuta, Malini Satish, Sidney Kripke, Gerald Katzman, Venkatesan Krishnan, Warren Kleinberg, P.L.S. Amma, Irwin Weinfeld. (Spon. by M. G. Robinson) Medical College of Ohio, The Toledo Hospital, Dept. of Ped., Toledo, Ohio.

Computerized tomography of the brain (CT) was done in 106 neonates admitted to the NICU from January, 1978 to August, 1980. Bleeding was documented in the first 3 weeks of life and CT was graded according to "Papile". Eighty-four infants were alive at 12 or 18 mo. post-term. Twenty of the 36 surviving with IVH and 22 of the 42 with no IVH (Control) were evaluated at 12 or 18 mo. Results are shown below. Chi Square statistical analysis was done for Groups III and IV vs. Control (C) for death and neurologic exam. Fisher Exact Test for Bayley Scores (BS).

<1500	I	II	III	IV	CONTROL
Total CT	1	3	36	13	53
Death #	1	1	9	6	5
Follow-Up #	0	1	15	4	22
Neurologic					
Normal		1	6	0	20
Abnormal			9	4	2
DDST Pass			6	1	12
DDST Suspect			2	0	0
DDST Fail			1	1	0
BS N≥84		1	1	1	7
BS Abn. ≤83			5	1	3

A significant relationship of Grades III and IV is found with mortality $p<0.007$ and abnormal neurologic examination $p<0.0003$, when compared with controls.

1402 FETAL SOMATIC GROWTH IN DIABETIC RAT, Maruthi Vadapalli Cathy Hammerman, Benjamin Thysen, Michael Gatz, Jim Kambosis and Emile M. Scarpelli.Albert Einstein College of Medicine,Bronx & Univ. of Chicago,Depts. of Pediatrics (sponsored by Kwang-sun Lee)

The relationship of insulin,glucose (gluc.) and hemoglobin A_1c levels to fetal growth has been examined in newborn pups of streptozotocin-induced diabetic rats.Pregnant control,mild diabetic (urine gluc.≤1gm/per day) and severe diabetic (urine gluc.>1gm/per day) rats were compared.

	Control(C)		Mild(M)		Severe (S)	
	Mat. (N=19)	Fet. (N=95)	Mat. (N=28)	Fet. (N=140)	Mat. (N=19)	Fet. (N=95)
Gluc.(mg%)	82±11*	61±1*	141±8†	40±7	302±7§	30±5§
$HgBA_1c$(%)	1.3±0.3*	1.2±0.4*	4.1±0.9†	2.4±0.9†	7.8±0.4§	2.7±0.8
Insulin	197.4±4.8*	13.7±2.9*	48.9±3.8†	13.7±1.3	28.9±3.6§	8.4±0.7§
Body(gm)	3.76±0.93*		5.18±0.30†		3.06±0.38§	
Lung(gm)	0.15±0.02		0.20±0.04†		0.14±0.01§	
Heart(gm)	0.03±0.01		0.03±0.01		0.03±0.04	
Liver(gm)	0.20±0.05*		1.31±0.47†		0.80±0.08§	

±SD; †:C vs M, $p<0.05$;§:M vs S, $p<0.05$; *C vs S, $p<0.05$

This rat model closely parallels the spectrum of effects of human diabetes in pregnancy on fetal growth.The macrosomia seen in the pups of mild diabetic rats (PMDM) is mainly reflected in lung and liver growth.Pups of severe diabetics were generally growth retarded,but no individual organ had decreased growth.Urine and blood gluc. levels,maternal insulin and Hgb A_1c values correspond to the severity of the diabetic state.However,no correlation with fetal insulin levels was observed,suggesting that factor(s)other than insulin account for the macrosomia of the PMDM.

1403 LUNG DEVELOPMENT IN FETUSES OF DIABETIC RATS. Maruthi Vadapalli,Cathy Hammerman,Benjamin Thysen,Michael Gatz and Emile M. Scarpelli.Albert Einstein College of Medicine,Bronx,N.Y. and Univ. of Chicago,Chicago, IL,Departments of Pediatrics (sponsored by Kwang-sun Lee).

Biochemical and morphologic aspects of pulmonary maturation have been studied in the fetuses of 19 healthy rats (Gp I),28 pregnant rats with mild streptozotocin-induced diabetes (Gp II: Urine glucose ≤1 gm/day) and 19 with severe diabetes (Gp III: Urine glucose >1 gm/day).

	I	II	III
Fetal Weight (gm)	3.76 ± 0.93*	5.18 ± 0.30§	3.06 ± 0.38Δ†
Lung Weight (gm)	0.15 ± 0.02*	0.20 ± 0.04§	0.14 ± 0.01
Lung Phospholipids	30.38 ± 1.54*	19.02 ± 0.05§	17.90 ± 1.90Δ
mg DNA/gm Lung	0.83 ± 0.05*	0.93 ± 0.03§	0.98 ± 0.10Δ
mg Protein/gm Lung	8.97 ± 0.54*	9.90 ± 0.40§	11.03 ± 2.60Δ
Fetal Insulin	13.70 ± 2.90	13.90 ± 1.30§	8.40 ± 0.70Δ

†Mean ± SD; *I vs II: $p<0.05$; ΔI vs III:$p<0.05$;§II vs III:$p<0.05$

Lung DNA and protein are increased even in the severe diabetics without organomegaly,implying cellular proliferation in the face of total organ weight reduction.

Lung phospholipids are significantly decreased in both diabetic groups.Earlier studies have attributed this to hyperinsulinemia, via its antagonism of the cortisol inductive effect on lecithin biosynthesis.Data above show no evidence of fetal hyperinsulinemia,despite suppression of phospholipid synthesis.This suggests that hyperinsulinemia is not critical in the delayed biochemical development of the lung in the fetus of the diabetic rat.

1404 IONIZED CALCIUM (ICA) IN FIRST 10 DAYS OF LIFE. Kamtorn Vangvanichyakorn, Shyan Sun, Anita Baldomero. (Spon. F. Behrle) New Jersey Med. School, Dept. Neonatology, Newark, New Jersey

Ionized Ca is known to be the important physiologic fraction of calcium in the blood and plays more significant role in physiological homeostasis than total Calcium. The new ICAI Ionized Ca Analyser (Radiometer/Copenhagen) measured iCa and pH simultaneously and calculates iCa at pH 7.4 (CiCa). 56 Simultaneous determinations of total Ca and iCa were done on 29 neonates (BW 700-4000 gms, age 12 hrs to 11 days). The relationship of Ca, iCa & CiCa are formulated as follows:

$iCa(mmol/L) = 0.066\ Ca(mg/dl)+0.55$ (r=49, P< .001)

$CiCa(mmol/L) = 0.08\ Ca(mg/dl)+0.4$ (r=0.59, P < .001)

The iCa levels were also followed in 9 preterm infants with av BW of 1673 gms (1200-2540) and av GA of 32.8 wks (29-36) from day 1 to day 10. All had RDS and 4 received feedings (Premie SMA, Wyeth) from day 3 to day 10 along with IV fluids. 5 Received total parenteral nutrition which contained neglegible amount of Ca (0.25 mmol/100 ml) from day 4.

Age	1	2	3	4	5	6	7	8	9	10 (day)
iCa	1.09	1.14	1.16	1.23	1.24	1.32	1.28	1.36	1.30	1.31
ΔiCa		+.05	+.07	+.15	+.15	+.23	+.19	+.27	+.21	+.22
CiCa	1.08	1.10	1.12	1.19	1.19	1.27	1.23	1.31	1.27	1.28
ΔCiCa		+.02	+.04	+.11	+.11	+.19	+.15	+.23	+.19	+.20

Contrary to previous reports, our results revealed that iCa concentration showed upward trend until 6th day of life and leveled off thereafter until the end (10th day) of this study.

1405 EFFICACY & PHARMACOKINETICS OF CEFOPERAZONE (CPZ) IN STAPHYLOCOCCAL SKIN DISEASE (SSD) OF NEONATES. M. Varghese, A.J. Khan, K. Kumar and H.E. Evans. Dept of Ped. Jewish Hosp Med Ctr/SUNY Downstate Med Ctr Brooklyn, NY

CPZ, a 3rd generation broad spectrum cephalosporin with a long half life ($t_{\frac{1}{2}}$) has not been evaluated in infants and children. 24 infants (mean age 18 days) were treated for SSD with CPZ in doses of 25 mg/kg given every 12 hours for an average of 7 days. S. aureus, the etiological agent in each case was sensitive to CPZ (zone size ≥18mm). The MICs ranged from 0.78 to 2.0 mcg/mL (mean 1.56). The skin lesions were healed by 5th day of therapy in all and no clinical side effects were observed. 7 infants developed mild and transient elevations of SGOT. CBC, platelet counts, serum creatinine & BUN levels remained normal. In 16 infants blood levels of CPZ were determined at different time intervals following the last dose which was either 25 mg/kg or 12.5 mg/kg body wt. Mean (± 1SD) serum concentrations and $t_{\frac{1}{2}}$ are presented (table). Blood levels were higher and $t_{\frac{1}{2}}$ longer than

mg/kg	N	½hr	½hr	1hr	2hr	4hr	8hr	24hr	$t_{\frac{1}{2}}$hr
12.5 IM	8	59.2	63	56.8	48.3	35.1	18.2	1.5	4.65
		(28.1)	(24.0)	(22.9)	(23.6)	(17.1)	(8.8)	(2.7)	(1.19)
25.0 IM	8	81.1	82.7	87.2	83.5	56.8	29.2	3.7	4.77
		(33.0)	(19.5)	(21.0)	(25.6)	(15.5)	(12.3)	(4.3)	(1.87)

reported in adults. Following 25 mg/Kg dose the mean peak level at 1 hr was 55 fold and level at 8 hour was 18 fold higher than the mean MICs of the organisms. CPZ was found to be an effective and safe agent in this study. Further studies are needed to evaluate the efficacy in neonatal sepsis/meningitis.

1406 CALCITONIN (CT)GLUCAGON AND GASTRIN IN BIRTH ASPHYXIA AND EARLY NEONATAL HYPOCALCEMIA. P.S. Venkataraman, R.C. Tsang, M.A. Sperling, I-W. Chen, K. Ellis, Dept. Pediatr., Univ. Cinti. Med. Center, Cincinnati, Ohio 45267

Serum calcitonin levels are elevated in newborns as compared with adults; it has been suggested that increased CT in birth asphyxia contributes to neonatal hypocalcemia. To evaluate this thesis we prospectively studied 31 maternal-infant pairs (28-42 wks, birth wt 2260±968 gms mean±s.d.) and sequentially measured serum Ca, P and CT as well as glucagon and gastrin, potential CT secretagogues. Cord P was higher with low 1' Apgar score, p<0.001 and low 5' Apgar p <0.002. Maternal and cord CT, glucagon and gastrin levels were not significantly related to gestation or birth wt of infants. Cord CT of 88±130 pg/ml was higher than maternal level of 27±18 pg/ml, non parametric p<0.004. Cord glucagon of 144±49 pg/ml was higher than maternal 91±55 pg/ml, p < 0.001. Cord gastrin of 118±78 pg/ml was not different from maternal 127±167 pg/ml. Cord CT and glucagon were higher in infants with lower 5' Apgar p<0.05. By 24 hrs serum CT showed a significant rise to 226±187 pg/ml p<0.002, glucagon rose to 255±95 pg/ml, p<0.001 and gastrin rose to 270±131 pg/ml, p<0.001. Cord or 24 hr CT or glucagon were not related to serum Ca at 24 hrs. In conclusion 1) maternal and cord CT, glucagon and gastrin are not significantly influenced by gestation 2) infant CT, glucagon and gastrin levels rise by 24 hrs, 3) cord CT and glucagon are elevated in birth asphyxia 4) although cord CT and glucagon levels are higher in infants with birth asphyxia these hormones do not correlate with serum Ca. We speculate that cord calcitonin and glucagon concentrations may reflect perinatal stress.

1407 EFFECT OF SUNFLOWER OIL (SO) ON INSENSIBLE WEIGHT LOSS IN PREMATURE NEWBORNS (PNB) < 1 KG IN THE FIRST THREE DAYS OF LIFE. S. Voora, L.D. Lilien, G. Srinivasan, R.S. Pildes. Cook County Hospital, Dept. of Pediat. Chicago, Ill.

Effect of BID dermal application of SO (except face) on transepidermal water losses was studied in 32 PNB who were randomly assigned to SO or non-SO group. Six in SO group and 8 in non-SO group survived >72 hrs. PNB were nursed in single walled isolettes with heat shield and skin temp. servo controlled at 36.5°C. Both groups were similar in BWt (0.89±.09kg* vs 0.85±0.12) and GA (29±2.4wks vs 28.2±2.0), incidence and severity of resp. distress. PNB received 100cc/kg of D5W on day 1, 120cc/kg and 140cc/kg of D5W electrolyte soln. on day 2 and day 3 respectively. Additional fluid was given when PNB had phototherapy, Wt loss >5% of BWt or S.Na >150meq/L. S.Na, S.Osm, Wt of PNB were measured and fluid adjustments made BID.

	S. Na >150mEq/L		S. Na		S. Osm.		% Wt Loss		Fluid Req.**	
	SO	non-SO	SO	non-SO	SO	non-SO	SO	non-SO	SO	non-SO
Day 1	0	0	138 ±4	138 ±5	277 ±13	282 ±7	5.3 ±3.0	3.2 ±1.5	99 ±2	99 ±10
Day 2	0	3	141 ±6	145 ±8	297 ±15	305 ±10	8.6 ±5.0	10.8 ±3.7	135 ±26	134 ±18
Day 3	0	2	142 ±4	145 ±8	301 ±17	301 ±11	11.3 ±4.4	11.9 ±4.5	186 ±51	214 ±47
Total	0	5								
P	<0.05		NS		NS		NS		NS	

Though there were no differences between groups in the means of parameters measured, there were more hypernatremic PNB in the non-SO group than the SO group (P<0.05). This suggests that SO may be useful in reducing the effects of high transepidermal water loss in PNB. *S.D. **without phototherapy

1408 VASODILATORY EFFECT OF INTRACAROTID INFUSION OF ADENOSINE ON THE NEONATAL CEREBROVASCULATURE. L. Craig Wagerle, Thomas M. Hefferman, Jacques Belik and Maria Delivoria-Papadopoulos. Univ. of PA., Dept. of Physiology and Pediatrics, Philadelphia, PA.

Previous studies suggest that adenosine participates in the metabolic regulation of cerebral vascular resistance in adult animals To play a role in matching cerebral blood flow (CBF) to cerebral metabolism in the brain, adenosine must show cerebral vasoactivity. The present study examines CBF and cerebral metabolic requirements for O_2 ($CMRO_2$) during intracarotid infusion of adenosine in newborn lambs. Seven lambs anesthetized with alpha chloralose (30 mg/kg) and mechanically ventilated at $PaCO_2$=37 mmHg and PaO_2 >120mmHg were infused at a rate of 0.5 ml/min with saline followed by adenosine (0.12 and 0.25 mg/kg/min) into both common carotid arteries. Measurements of arterial and saggital sinus O_2 sat, [Hb], blood gases, pH and blood pressure were made prior to and after 4 min of each infusion. Total CBF was measured by microsphere injection after 5 min of infusion. Baseline CBF was 37±3 ml/min·100g^{-1} and increased to 84±10 and 88±14 ml/min·100g^{-1} during 0.12 and 0.25 mg/kg/min, respectively. Cerebral vascular resistance decreased from 2.37 to 0.88 and 0.95 mmHg/(ml/min·100g^{-1}), implying maximal dilation at 0.12 mg/kg/min adenosine. $CMRO_2$ was 2.8±0.3 ml/min·100g^{-1} and was unchanged during adenosine infusion (2.9±0.3 and 2.9±0.3 ml/min·100g^{-1} at 0.12 and 0.25 mg/kg/min adenosine, respectively. The increase in CBF therefore was not secondary to increased metabolism for O_2. These data suggest that adenosine has profound vasodilatory action in the newborn brain, thus adding support to increasing evidence identifying adenosine as a regulator of CBF.

1409 POTENTIALLY LETHAL ACCUMULATION OF TOLAZOLINE IN NEONATES WITH OLIGURIA. RM Ward, JW Kendig, and CH Daniel (Spon by MJ Maisels). Penn State Univ Coll of Med, M. S. Hershey Med Ctr, Dept of Peds, Hershey, PA.

Since the first descriptions of persistent pulmonary hypertension of the newborn, therapy has frequently involved tolazoline (TZ). Dosages of TZ have evolved from a recommendation of an IV bolus of 1 mg/kg in 1961 by Grover et al to include larger bolus dosages as well as continuous infusions up to 10 mg/kg/hr. Because of the plasma volume required for analysis, TZ pharmacokinetics have not been studied in newborns.

We have developed a chemically specific assay for TZ by gas chromatography-mass spectrometry capable of analyzing 0.1 ml plasma samples. This assay has been used to study TZ effects in lambs and pharmacokinetics in 5 neonates. The rate of urine output (UO) appeared to affect significantly the rate of TZ plasma elimination. When UO decreased to below 0.92 ml/kg/hr, TZ was not eliminated. When UO was greater than 1.00 ml/kg/hr, plasma elimination occurred with a $t_{\frac{1}{2}}$ of 167±99 min.

One patient treated with TZ by continuous infusion up to 3.9 mg/kg/hr reached a plasma concentration of 17.5 mcg/ml. When her urine output ceased for 4 hrs, 7 consecutive plasma samples showed no elimination. In our lamb studies, acute cardiac toxicity unresponsive to resuscitation has occurred at plasma concentrations as low as 21.85 mcg/ml.

Oliguria in neonates prevents clearance of TZ which may accumulate to potentially lethal concentrations if administration of the drug continues.

1410 COMPARATIVE ANALYSIS OF FETAL GESTATIONAL AGE AND CLASS ASSESSMENT METHODS. Leonard E. Weisman, Stanley Chazal, Kenneth Hopper and Steven Shirts (Spon. by Frederick C. Battaglia), Departments of Pediatrics, Obstetrics & Radiology, Fitzsimons Army Medical Center, Aurora, Colorado.

Gestational age (GA) and class (C) are important indicators of perinatal morbidity and mortality. Accurate estimate of GA and C can lead to detection and prevention of intrauterine problems.

To determine what information available to the practicing physician correlates best with GA (as determined by crown-rump length - CRL), 120 pregnant women were prospectively and blindly evaluated for the following predictors of GA: reliable dates, biparietal diameter (BPD) before 26 wks., BPD after 30 wks., serial BPD's, onset quickening (Q), onset fetal heart tones (FHT), fundal height progression (FHP), and Dubowitz examination (D). The same population was evaluated for serial BPD's, serial BPD's and abdominal circumference (AC) and FHP as predictors of C (as determined by CRL and birth weight).

Ability to predict GA revealed correlation coefficients of: serial BPD's r=.93, BPD prior 26 wks. r=.90, reliable dates r=.85 Q r=.74, FHT r=.73, D r=.70, BPD after 30 wks. r=.49. Multiple regression analysis revealed no combination of predictors better than serial BPD's. Ability to predict C revealed correlation coefficients of: serial BPD's and AC r=.63, serial BPD's r=.54 and FHP r=.37.

Conclusion: Data is presented comparing commonly available methods of GA and C assessment with CRL. Serial BPD's are the most reliable predictor of GA. C was not reliably predicted by any method, probably secondary to poor prediction of weight.

1411 A COMPARISON OF CARDIOVASCULAR RESPONSES DURING ENDOTOXIC SHOCK IN NEONATAL AND OLDER ANIMALS. David L. Wessel and S. Evans Downing, Yale University School of Medicine, Departments of Pediatrics and Pathology, New Haven, Ct.

The cardiovascular effects of endotoxin were studied in newborn piglets and compared to older animals of the same species. Thirty-seven animals were divided into newborn and older age groups and anesthetized with pentobarbital. Cardiac output (CO), arterial and central venous pressure, pulmonary artery and pulmonary artery wedge pressure (PAWP), left ventricular end diastolic pressure (LVEDP), arterial blood gas values, blood glucose concentration and hematocrit were measured. Of 15 newborns (mean age 4.5 days) treated with 5 mg/kg of E. coli endotoxin, 11 survived the three hour protocol. Fourteen older pigs (mean age 37 days) were given an equivalent dose of endotoxin and none survived beyond two hours. Older pigs had persistent pulmonary hypertension and significantly elevated PAWP without elevation in LVEDP. Gross pulmonary edema accompanied their poorer CO and progressive hypotension. Eight age-matched control animals showed no significant circulatory changes. It is concluded that the newborn is less susceptible to the effects of endotoxin than is the older animal, and that maturational changes in the pulmonary circuit provide a major determinant in this difference.

1412 ENERGY STORAGE, NITROGEN RETENTION AND WEIGHT GAIN IN LOW BIRTHWEIGHT INFANTS FED HUMAN MILK OR FORMULA. Robin K. Whyte, Dugal Campbell, Henry S. Bayley, John C. Sinclair. McMaster University, Department of Pediatrics, Hamilton, and University of Guelph, Ontario, Canada.

Energy and nitrogen balance studies were carried out in 28 healthy growing infants of birthweights ranging from 0.78 - 1.70 kg. 9 were fed their own mothers' expressed breast milk and 19 were fed formula. Gross energy and nitrogen intakes were measured over a 14 day period: energy and nitrogen excretions were measured for 3 days each at the beginning and end of this period, and energy expenditures were measured for 3 four-hour periods using a Kipp diaferometer calibrated with human expired air and corrected for the effect of expired hydrogen. There were no significant differences in the birthweights, gestational or postnatal ages between the human milk and formula fed groups. Weight gains were 15.0 (SE 0.9) g/kg.day for human milk fed infants and 16.9 (SE 0.5) g/kg.day for formula fed infants. Energy and nitrogen intake, metabolizable energy intake and nitrogen retention were similar for the two groups. Overall, metabolizable energy intake was 462 (SE 8) kJ/kg.day (87% of gross intake) and nitrogen retention was 268 (SE 6) mg/kg.day (64% of intake). Mean energy expenditure was 238 (SE 6) kJ/kg.day and mean energy storage was 224 (SE 9) kJ/kg.day. Each gram increase in weight was associated with an increase in metabolizable energy intake of 9.5 (SE 2.8) kJ and an increase in energy storage of 8.4 (SE 3.5) kJ. The latter value is close to that predicted for the growing fetus from compositional studies.

●1413 FUROSEMIDE (F) REVERSES THE RENAL SIDE EFFECTS FOLLOWING INDOMETHACIN (I) THERAPY IN PREMATURE INFANTS WITH PATENT DUCTUS ARTERIOSUS (PDA). A. Wilks, T.F. Yeh, M. Betkerur, J. Singh, P. S. Pildes. Cook County Hosp. Dept. of Ped. Univ. of Ill., Chicago, Ill.

Indomethacin, a PG inhibitor, decreases urine output, FENa, and GFR in premature infants. Furosemide on the other hand increases renal PG release. To evaluate if F would reverse the side effects of I therapy, 19 premature infants with PDA were randomized into two groups: 9 received I alone (0.3mg/kg,IV) and 10 received I+F (1mg/kg,IV). The BW (mean±SD, 1.12±0.40 vs 1.19 ±0.33kg), GA (30.4±2.9 vs 30.7±2.5wks), postn. age (13.7±10.2 vs 9.5±5.1 days) and cardiopulmonary status were comparable between the groups.

Gr I (hrs)	Urine Output (ml/kg/hr)	GFR (ml/min/1.73m²)	FENa (%)	CH_2O (ml/min/100 GFR)
Pre 0-24	3.1±1.0	9.2±3.7	3.0±2.1	4.0±2.4
Post 0-12	1.2±0.7*	6.5±2.9*	1.3±0.8**	1.3±1.0*
12-24	1.0±0.6*	6.6±3.8	0.8±0.8	2.4±3.4
Gr (I+F)				
Pre 0-24	2.6±1.2	8.0±2.2	2.5±0.9	3.9±2.8
Post 0-12	2.6±1.5	7.0±2.2	4.0±2.7	2.7±1.4
12-24	2.1±1.0	6.6±2.2	2.0±1.2	5.2±3.7

Gr I infants had sign. (*p<.05, **p<.01) lower urine output, GFR, FENa and CH_2O than Gr I+F at 0-12 hrs post-study. Seven infants in each group responded with PDA closure. The results of this study suggest: 1) F may reverse the renal side effects of I therapy, and 2) F does not affect the PDA closure of I therapy.

1414 RELATIONSHIP OF INTRAVENOUS FAT INFUSIONS IN PREMATURE INFANTS TO OXYGENATION, PLASMA TRIGLYCERIDE AND FREE FATTY ACIDS. Paul R. Williams, Richard A. Sidebottom, John S. Curran, Keith S. Kanarek and Milan Novak (Spon. by John I. Malone), Departments of Pediatrics, College of Medicine, University of South Florida, Tampa; University of Miami School of Medicine, Miami, Florida.

The safety of infusing fat emulsions in premature infants <1 week of age has been questioned based on infusion rates of 0.25 gm/kg/h. We infused fat emulsions (0.1gm/kg/h) in six premature infants (mean gestational age: 29.3 weeks) less than 7 days of age. All had respiratory distress, but were stable at time of study. Three were receiving mechanical ventilation and three oxygen by hood. The transcutaneous PO_2 was continuously monitored. Blood samples were obtained prior to infusing the fat, at the end of infusion (4h) and four hours after discontinuing the infusion (8h). (Results: Mean±SEM)

	0	4h	8h
FiO_2	.37±0.07	.38±0.07	.39±0.08
$TcPO_2$	60±7.7	64.3±4.0	72±3.9
PaO_2 mmHg	63.3±4.0	68.7±5.2	75±4.8
pH	7.32±0.01	7.33±0.02	7.32±0.03
FFA μ mole/ml	0.755±0.120	0.702±0.103	0.672±0.161
Triglycerides mg/dl	58.4±15.0	89.0±28.8	69.4±13.2

No significant changes were observed in any of the parameters measured during the 4h lipid infusion. We conclude that in premature infants <1 week of age with moderate respiratory distress slow infusion of fat emulsions does not have a deleterious effect on oxygenation.

1415 URINE ARGININE VASOPRESSIN (AVP) LEVELS IN HIGH-RISK NEONATES. Suvipa Wiriyathian, Charles R. Rosenfeld, Billy S. Arant, Jr. and John C. Porter, Southwestern Med.Sch., Depts. Ped. & Ob-Gyn, Dallas, Texas.

AVP, a potent antidiuretic and vasoconstrictor, is elevated in umbilical cord plasma of high-risk pregnancies. We have shown in an animal model that this may be reflective of fetal distress. AVP levels in high-risk neonates are poorly described. Urine AVP levels reflect plasma AVP; thus, we sought to determine the relationship between urine AVP levels and various neonatal stresses. Urine was collected in 3h aliquots for 2-7 days in infants who were normal(n=25), or had meconium stained amniotic fluid(n=15), intracranial hemorrhage(ICH,n=8), or hyaline membrane disease (HMD,n=17). AVP was measured by RIA. Urine AVP(μU/ml) fell from 12±2 and 25±6(X±SE) in normal preterm(n=13) and term(n=12) infants, respectively, to <10 by 22±7h of age. In term infants with asphyxia and meconium aspiration(n=6), AVP fell from 78 to <10μU/ml by 54±1h; whereas in infants with HMD AVP did not fall to <10 μU/ml until 90±5h, and remained elevated in infants with ICH until death at 2-7 days. There was no relationship between urine osmolality and AVP (μU/mg creatinine or μU/ml) in normal term or preterm infants or sick infants; rarely did osmolality exceed 400 mOsm/L despite AVP levels >80μU/mgCr. From these data we conclude that the neonatal kidney is refractory to antidiuretic effects of AVP during the first days of life and in most sick neonates urine AVP is <10μU/ml by 24-30h; however, in infants with severe ICH or pulmonary disease urine AVP remains elevated. One might speculate that elevated urine AVP may be reflective of cardiovascular adaptation in the sick neonate, as well as the fetus.

1416 AN EVALUATION OF THE TREATMENT OF METABOLIC ACIDOSIS (MA) IN PREMATURE INFANTS WITH RESPIRATORY DISTRESS. Frederick H. Wirth, Phillip Squires, Spon. by F. Stanley Porter. Eastern Virginia Medical School, Children's Hospital of the King's Daughters, Department of Pediatrics, Norfolk, Virginia.

$NaHCO_3$ and albumin were alternately used by a random decision to treat MA in a group of clinically stable premature infants who were being mechanically ventilated for respiratory distress. Both drugs were used in 12 infants who met the study criteria on two separate occasions separated by at least a 12 hour interval. The drug used first was determined randomly and then the alternate drug was used when the study criteria occurred a second time. The dose of $NaHCO_3$ given was calculated using the Astrup formula with a corrected base deficit for the MA[1]. The dose for albumin was 1gm/kg.

The efficacy of the two drugs was compared by obtaining arterial blood gases and vital signs at intervals for two hours after the infusion. The comparative safety of the two drugs was not evaluated. The $NaHCO_3$ infusion caused a higher rise than albumin in blood pH, base excess and $PaCO_2$. The $NaHCO_3$ infusion switched the infant's MA to a less severe respiratory acidosis. The albumin infusion did correct the MA but to a lesser degree than $NaHCO_3$. These data suggest that $NaHCO_3$ is more efficacious for treating MA. Albumin should be used for treating the metabolic component of a mixed acidosis, or when the expected rise in $PaCO_2$ from $NaHCO_3$ cannot be controlled.

1. Winters, R.W., Perinatal Medicine, 1969, p. 171.

● **1417** TRANSCUTANEOUS BILIRUBINOMETRY AND FACTORS AFFECTING THE TRANSCUTANEOUS BILIRUBIN INDEX. Paul Y.K. Wu, Nancy B. Edwards, Linda Chan, Gehoon Lee, Clementina Wareham. Univ. of So Calif. Sch. of Med., LAC-USC Med. Ctr., Depts. Pediatrics, Family and Preventive Medicine, Los Angeles.

The bilirubinometer (Minolta) was used to measure the relationship of transcutaneous bilirubin index (T_cB) with serum total (TB), direct (DB) and indirect (IB) bilirubin in 383 newborn infants with BW 690-4820g and GA 24-43 wks. The correlation coefficient of T_cB and TB was .710. The correlation was significantly improved to .782 with the inclusion of BW, Hct, and DB in the multiple regression analysis. The relationship of T_cB and IB was similar to that of T_cB and TB, this is expected since the corr. coeff. of TB and IB was .990. The adjusted means and the slopes of linear relationships of T_cB and TB were statistically significant at the .05 level among groups defined by BW (≤1500, 1501-2000, 2001-2500, ≥2501g), Hct (<50, 50-60, ≥61%). DB (<0.3, 0.3-0.4, 0.5-0.9, ≥1.0 mg/dl). IB (<5, 5-10, 11-15, >15 mg/dl) and site of measurement. Thus, for any given value of TB, T_cB is higher for decreasing BW, GA and Hct. For a given value of TB, T_cB was also higher among SGA than AGA and LGA (in that order), and also among lighter than darker skin color. T_cB was negatively correlated to HBABA binding at the .01 level. Postnatal age did not affect the relationship between T_cB and TB. With phototherapy, the average T_cB value was lower for corresponding TB without phototherapy. Since the adjusted average of T_cB for any given TB was found to be statistically different for the variables tested, with the exception of postnatal age, these variables should be taken into account when T_cB is used to evaluate jaundice.

1418 EFFECTS OF MECONIUM ON PHOSPHATIDYLGLYCEROL DETECTION IN AMNIOTIC FLUID. T.J. Yambao, B. Tawwater, J. Chuachingo, P. Kuhl, A. Carrillo (Sponsored by Dr. Surendra Varma), Texas Tech University School of Medicine, Dept. of Obstetrics and Pediatrics, Amarillo, Texas.

Meconium contamination of amniotic fluid (A.F.) affect L/S results. Using a two-dimensional TLC, we studied the effects of contamination of A.F. by meconium on the subsequent detection of PG. A.F. samples with a mature L/S (≥2) and PG present and an immature L/S (<2) with absent PG were used.

Meconium was diluted in 0.9% NSS making a 1:20 dilution of which 0.5 ml. was added to the A.F. L/S and PG were obtained before and after meconium was added. Densitometric readings of all the phospholipids were done and PG expressed as a percentage. The following table shows the PG determination before and after meconium contamination of the ten A.F. samples.

Mature L/S PG Present			Immature L/S PG Absent		
Sample	W/out mec	W/mec	Sample	W/out mec	W/mec
1	8%	8%	1	negative	negative
2	5%	6%	2	negative	negative
3	8%	7%	3	negative	negative
4	7%	6%	4	negative	negative
5	5%	6%	5	negative	negative

In A.F. samples without PG, the addition of meconium did not demonstrate a PG spot on the chromatographic plate. This was further confirmed when meconium alone was utilized in performing the two-dimensional TLC. Contamination with meconium has not been shown to prevent the detection of PG. In conclusion, meconium does not seem to affect the presence or absence of PG.

1419 CHANGES OF O_2 CONSUMPTION (VO_2) IN RESPONSE TO NICU CARE PROCEDURES IN PREMATURE INFANTS. T.F. Yeh, S.T. Leu, S. Pyati, R.S. Pildes. Cook County Hosp. Dept. of Ped., Univ. of Ill., Chicago, Ill.

The effect of NICU care procedures on VO_2 was evaluated in 10 premature infants (mean±SD, BW 1242±111gms, GA 31.5±1.2 wks, postn. age 12.9±5.5 days). VO_2 was measured continuously using indirect calorimetry. The total VO_2 over a given period of time was determined from the area under the O_2 concentration-time curve (AUC) of the expired mixed gases. The VO_2 following each procedure was compared with the baseline data which was obtained with the infant in resting state. The total VO_2 response to each procedure was determined from AUC calculated from time zero to the time when the O_2 concentration of expired mixed gases returned to the baseline.

	Duration of Procedure (min)	VO_2 (ml/kg/min) Baseline	VO_2 (ml/kg/min) Response	VO_2 Changes (%)	p
Abd. palp.	3	6.94±2.3	6.74±2.4	↓ 2.0	ns
Chest percussion	3	6.48±2.3	7.11±2.5	↑ 9.9	<.01
Rectal thermometer	2	6.87±2.1	7.01±2.5	↑ 0.02	ns
Heel stick	3	6.46±1.5	7.35±2.1	↑13.4	<.02
IV insertion	2	6.72±1.7	7.62±1.4	↑13.8	<.01

The total duration of VO_2 changes varied with procedure: heel stick (5.5±1.5 min), IV insertion (5.2±1.4 min), chest percussion (5.2±0.6 min), abd. palp. (4.4±0.6 min), and rectal thermometer (2.4±0.7 min). This study suggests that NICU care procedures may contribute significant energy loss in premature infants and excessive handling and painful stress should be avoided.

1420 EFFECTS OF LEUKOTRIENE D_4 (LTD_4) ON THE PULMONARY AND THE SYSTEMIC CIRCULATIONS IN CONSCIOUS NEWBORN LAMBS. Kazuoki Yokochi, Eleftherios Sideris, Frank Hamilton, Dayle Huhtanen, Flavio Coceani and Peter M.Olley (Sponsored by: Henry Levison) Hospital for Sick Children, Department of Cardiology, Toronto, CANADA.

We studied the effects of LTD_4 on the pulmonary and systemic circulation of newborn lambs chronically instrumented with electromagnetic flow probes around both pulmonary arteries (PA). Bolus injections of 0.1 to 5.0 μg/kg LTD_4 were made in nontreated and indomethacin pretreated lambs under normoxia (72.9 PO_2±11.5 mm HG) and hypoxia (PO_2 33.4±7.3 mm Hg) and caused dose-dependent pulmonary and systemic vasoconstriction under both conditions. The systemic vascular effects of PA injected LTD_4 were biphasic, an initial fall in aortic pressure being followed by an increase. This initial drop did not occur when LTD_4 was injected in the aorta and was also blocked by indomethacin pretreatment. We speculate that this initial drop may be due to PGI_2 release from the lung. LTD_4 effects were reduced by indomethacin pretreatment, suggesting that exogenous LTD_4 may stimulate formation of vasoactive prostaglandins from arachidonic acid. In conclusion, LTD_4 is a systemic and pulmonary vasoconstrictor which releases a systemic vasodilator from the lung, this action is mediated through the cyclooxygenase pathway. LTD_4 is not inactivated by the lung.

(Supported by the Canadian Heart Foundation)

1421 DECREASED INCIDENCE OF RESPIRATORY DISTRESS SYNDROME IN PREMATURE TWINS WITH PROLONGED RUPTURE OF MEMBRANES. J.J. Yoon, J.A. Villalona and S. Ezhuthachan. (Sponsored by M. Cohen). Albert Einstein Coll. of Med., Bronx-Lebanon Hospital Center, Dept. of Peds., Bronx, NY.

The effect of prolonged rupture of membranes >24 hours (PROM) on the incidence of respiratory distress syndrome (RDS) in premature twins was studied. Twins, <33 weeks, who did not receive tocolytic agents or steroids and did not have any malformations were included. Sixteen sets of twins met these criteria. There were six sets of twins in which all had intact membranes and 10 sets of twins in which only one of each set had intact membranes. The incidences of RDS (20%) and mortality (20%) in the PROM group were significantly lower than those (90%, 80%) in the intact group. The major cause of mortality was RDS in both groups. Maternal conditions, sex distribution, mean birth weight, gestational age and Apgar score, were similar in the PROM and intact groups. There was no significant difference in the incidence of severe perinatal asphyxia, amnionitis, hypothermia, hypotension, and acidosis between the two groups. None developed proven infections. However, infants with PROM were more likely, to be born as the first twin ($p < .005$), to be delivered by vertex ($p = .5$-1.0), not to develop RDS ($p < .01$), and to survive ($p < .025$). Since the low incidence of RDS in the PROM group could possibly be due to a preponderance of first born twins and vertex deliveries, an analysis of the relationship of these two factors to RDS in all infants with only intact membranes was undertaken and this showed that the order of birth or the mode of delivery did not significantly alter the incidence of RDS. Therefore, PROM appears to be a factor which decreases the incidence of RDS and mortality rate in premature twins.

1422 EXPERIENCE WITH AUDITORY BRAINSTEM RESPONSE (ABR) IN NEONATES WITH INTRAVENTRICULAR HEMORRHAGE (IVH). Ilana W. Zarafu, Janet Purn, Joyce Chuachingco. (Spon. Franklin C. Behrle) College of Med. and Dent. of N.J.-N.J. Med. School, Newark Beth Israel Medical Center, Dept. of Ped., Newark, N.J. 07112

Between 6/79 and 10/81, 18 preterm infants (mean birth weight 1254gms, gestation age 26-35 wks.) with IVH, documented by computerized axial tomography or ultrasound were evaluated with ABR. ABRs were performed as soon as feasible following IVH. IVHs were classified as follows: severe 11, moderate 1, mild 6. Sixteen infants survived and had follow-up ABR.

The ABR waveforms were analyzed to determine the presence, latency and amplitude of the 5 major components. Interpeak intervals (wave I-V) were calculated at 50 db sensation level. Threshold for response was also determined.

The following abnormalities were noted: peripheral auditory sensory deficit in 14/18(78%) (2 of these with profound loss), prolonged I-V interval in 6/18(33%) (all of whom had severe IVH), and gross distortion of waveform with absence of one or more components in 3/18(16%). With clinical improvement, follow-up ABR improved in 7 patients.

Of all infants with severe IVH 2 had no ABR, indicating end organ dysfunction, 7/9(77%) demonstrated major ABR abnormalities: the absence of one or more components, or significant I-V prolonggation, only 2/9 showed mildly abnormal ABRs.

Of the 6 infants with mild IVH 3 showed threshold deficits only, 2 were normal and 1 showed grossly abnormal waveform which later returned to normal. ABR is a useful adjunct in the management and follow-up of babies with IVH.

1423 INCIDENCE, ETIOLOGY AND MANAGEMENT OF PNEUMOTHORAX (PN): A RETROSPECTIVE REVIEW. Nishat Zedie, Bhakthan Chelliah, Ilana W. Zarafu. (Spon. Franklin C. Behrle) College of Med. and Dent. of N.J.-N.J. Med. School, Newark Beth Israel Medical Center, Dept. of Ped. Newark, N.J. 07112

The incidence of PN in the Newborn Special Care Unit (NBSCU) was reviewed for the years 1977-1980. During this period, we converted from volume to pressure cycled ventilation. Two types of chest tubes (CT), side or end-hole, were used according to personal preference. Sizes varied from French #10-#14.

One hundred thirty seven PNs were reviewed among 113 newborns (NB): 25(22%) NB had spontaneous PN, 10(9%) had post surgical PN, and 78(69%) NB developed PN during assisted ventilation.

During this period 496/1524(32.5%) infants admitted to NBSCU were ventilated. The incidence of PN among the NB on assisted ventilation was 78/496(15.7%). There was no significant change in the annual incidence over the four years. The mean birth weight of the ventilated group was 1737gms. 96 PNs were identified among the 78 NB. 18 NB had bilateral PN; their mean birth weight was 1254gms. The right side was affected twice as often as the left. One hundred eighteen CT were inserted to treat 96 PNs, 1.23 CT insertions/PN. More than 1 insertion was needed in 15 infants.

We feel that the low incidence of PN and the infrequent necessity for CT changes in the population of ventilated NB relates to our use of low peak inspiratory pressures. Our suctioning technique has also been modified: suction catheters are measured and are not inserted beyond 3mm from the distal tip of the endotracheal tube; we have also decreased the frequency of suctioning. In addition most of our chest tubes are placed by pediatric surgeons.

1424 CHANGE IN OUTCOME OF VERY LOW BIRTH WEIGHT (VLBW) INFANTS (B.W. <1250 gms.). R.A. Zenteno, H.B.P. Meyer W.J.R. Daily. Good Samaritan Hospital, Department of Pediatrics, Phoenix, Arizona.

From January through May 1981, 31 VLBW infants were admitted to this institution (Group A). During the period from June through September 1981, 30 such infants were cared for (Group B). The general management of infants in Group A was according to practices in this institution during previous years. Group B infants were managed according to a new protocol designed specifically for this population of high risk infants.

This table shows the comparison between groups.

	GROUP A	GROUP B	P
No. Patients	31	30	
B. Weight gms ($\bar{x}$)	954	997	N.S.
Gestation ($\bar{x}$)	29	28	N.S.
1' Apgar ($\bar{x}$)	4.1	4.0	N.S.
5' Apgar ($\bar{x}$)	6.0	6.6	N.S.
HMD Incidence	14 (.45)	15 (.50)	N.S.
IVH Incidence	15 (.48)	8 (.27)	<0.10
Survival	7 (.23)	22 (.73)	<0.001

Changes in care associated with improved outcome included: stricter temperature control; decreased handling; continuous and more intensive $TcPO_2$ monitoring; restricted use of hyperosmolar solutions in resuscitation; early institution of feedings; and ventilatory parameters delivering the lowest mean airway pressure providing adequate oxygenation.

A rational and well organized postnatal care regimen can improve outcome for VLBW infants.

1425 VASOACTIVE SUBSTANCES IN MOTHER AND FETUS DURING INDUCED HYPOTENSION. Alan B. Zubrow, Salha S. Daniel, Raymond I. Stark, M. Kazim Husain & L. Stanley James. Columbia Univ., Coll. of P & S, Div. Perin. Med., Depts. Ped., Anes., Med., NY.

Maternal hypotension either spontaneous or associated with regional anesthesia is a potentially serious complication during labor. We have investigated the response of both mother and fetus to this insult by studying vasoactive substances during experimental hypotension in the pregnant sheep. The maternal hypotension was induced by nitroprusside infusion. Fetal and maternal vasoactive substances were measured in 5 chronically instrumented fetal lambs. During hypotension, mean maternal BP fell 20% ($p<.01$), while mean fetal BP, heart rate, and arterial blood gas values remain unchanged. Secretion of maternal vasopressin (VP) increased by a factor of 30 ($p<.01$) and renin activity (R) by a factor of 5 ($p<.05$). Fetal VP increased 5-fold ($p<.01$) while R increased only slightly. Similarly, maternal and fetal catecholamines increased but also without statistical significance. Significant correlation was observed between fetal and maternal levels of VP ($r = .69$), R ($r = .52$), epinephrine ($r = .55$), norepinephrine ($r = .81$), and total cate cholamine ($r = .79$). In summary, mild nitroprusside - induced maternal hypotension greatly stimulated release of VP and R in the pregnant ewe while the fetus is able to maintain its BP and blood gases mainly by a moderate elevation of VP.

NEPHROLOGY

● **1426** "NATURAL" Na LOADING, A CRITICAL VARIABLE IN EXPERIMENTAL NEPHROTOXICITY STUDIES IN THE RAT. Raymond D. Adelman and Jan Wright, Department of Pediatrics, Univ. of California, Davis.

Rats given gentamicin (GN) in the morning develop less nephrotoxicity than those injected in the evening (Ped.Res.15:680,1980). Being nocturnal feeders, rats injected in the AM may be in a Na+ loaded, "protected" state. To examine this hypothesis, male Fisher 344 rats were given H_2O, Purina rat chow (containing .4% Na) and injected with GN, 120 mg/kg S.C., at 8 AM (Gr.I) or 6 PM (Gr.II). Groups III and IV, also injected at 6 PM with GN 120/mg/kg S.C., were offered during the 10 hours before injection ad lib D_5W/1% saline or D_5W respectively. By day 9, S_{Cr} in all groups exceeded S_{Cr} in saline injected control (Ctl) rats. Gr.I had lower S_{Cr} ($p<.001$) associated with higher UNa ($p<.005$) compared to Gr.II. This difference in S_{Cr} was eliminated in rats drinking 1% saline/D_5W (Gr.III) but not rats given D_5W only (Gr.IV).

"Natural" Na+ loading confers protection against nephrotoxicity in rats given GN in the AM. The time of drug administration is a critical variable in experimental nephrotoxicity studies.

Group(n)	Injection Time	Baseline Na+ Excretion*	S_{Cr}(mg/dl) Day 9
I(6)	8 AM	.086(.009)	.93(.12)+
Ctl(4)	8 AM	.095(.010)	.52(.01)
II(6)	6 PM	.062(.011)	1.70(.07)++
Ctl(4)	6 PM	.049(.009)	.52(.04)
III(6) NS/D_5W	6 PM	.250(.043)	.94(.06)++
Ctl(7)	6 PM	.135(.031)	.40(.05)
IV(6) D_5W	6 PM	.054(.008)	2.15(.15)

*Total mEq for 10 hours before injection. +$p<.05$, ++$p<.001$ vs Ctls.

1427 TUBULAR PHOSPHATE (P) HANDLING IN X-LINKED DOMINANT RENAL HYPOPHOSPHATEMIC RICKETS (RHR). Uri Alon and James C. M. Chan. Medical College of Virginia, Dept. of Pediatrics, Richmond, VA

Improvement in P balances has been recently demonstrated in children with RHR treated by 1,25-$(OH)_2$-D_3 (1,25-D) and P supplementation. In order to evaluate the effects of 1,25-D on renal handling of P, we studied six children (age 13±4 years) and one adult relative with RHR after four days of control (C) and again after six days of treatment (T) with 1,25-D (84 ± 57 ng/kg/24h). Constant metabolic diet and fluid intakes were maintained throughout the study. Serum P (S_P), calcium (S_{Ca}), PTH; urine P (U_P), tubular reabsorption of P (TRP), tubular maximum of P (TmP), glomerular filtration rate (GFP) as determined by creatinine clearance (C_{Cr}) were performed in each study period.

	S_P mg/dl	U_P mg/kg/24h	TRP %	TmP/GFR mg/dl	C_{Cr} ml/min/1.73 m^2
C	2.6±0.7	45±31	53±26	1.32±0.54	114±15
T	3.5±1.2	50±31	59±21	1.86±0.44	113±21
	P<0.02	N.S.	N.S.	P<0.01	N.S.

With treatment, serum PTH decreased from 63 ± 18 to 50 ± 17 µlEq/ml ($P<0.05$) while S_{Ca} increased slightly from 9.9 ± 0.4 to 10.2 ± 0.6 mg/dl (N.S.). In a 7th RHR child with secondary hyperparathyroidism, these effects could not be demonstrated. We conclude that the significant elevation in tubular threshhold with concomitant increase in Sp, following 1,25-D administration, can be related to the reciprocal decline in serum PTH, and that this is the reason for the lack of tubular response to 1,25-D in the secondary hyperparathyroid patient.

1428 TYPE 4 RENAL TUBULAR ACIDOSIS (RTA-4) FOLLOWING RENAL VEIN THROMBOSIS (RVT). Uri Alon, Michael B. Kodroff, James C. M. Chan. Med Coll Virginia, Richmond, VA

A 21-day-old female infant presented with acute gastroenteritis, dehydration of 15%, hypernatremia (Na 159 mEq/l) and acidosis (HCO_3^- 4 mEq/l). Serum creatinine (S_{Cr}) was 3.4 and BUN 52 mg/dl. Subsequent hematuria, thrombocytopenia and left flank mass, together with radiologic studies, confirmed the diagnosis of RVT. With therapy, the diarrhea resolved and the S_{Cr} and BUN returned to normal. However, persistent hyperkalemic metabolic acidosis (K 5.8-7.1, HCO_3^- 14-18, Na 132-134, Cl 109-118 mEq/l and P_{CO2} 24-32 mm Hg) associated with high urinary pH(6.4-7.5), renal sodium wasting with fractional excretion (FE) of 2.7% and low potassium excretion (FE_K 2.2%) was documented. Plasma renin activity was twice and aldosterone 3 times above normal. Urine 17-OHCS and 17-KS were normal, no glucosuria, phosphaturia or aminoaciduria were observed. With spontaneous acidosis (HCO_3^- 8-10 mEq/l) the minimal urine pH was 5.3-5.8 and net acid excretion 34 μEq/min/1.73 m^2. Taken together, these data established the diagnosis of RTA-4 with tubular unresponsiveness to aldosterone. Treatment with Shohl's solution (5 mEq/kg/day) corrected the acidosis. At 6 months of follow-up, the infant exhibited catch-up growth. In addition, after 5 days without alkali treatment, S_{Cr} was 0.3 mg/dl, HCO_3^- 19, Na 133, K 5.7, Cl 106 mEq/l and aldosterone in the low normal range, while urine pH was 6.4, FE_K 3.7% and FE_{Na} 0.3%. We conclude that this infant represented a case of RTA-4 not heretofore described in association with RVT. The improvement in tubular functions with time indicate recovery and improved responsiveness to aldosterone.

1429 CHLOROTHIAZIDE (CTZ) PREVENTS VITAMIN-D-INDUCED HYPERCALCIURIA IN RATS. Uri Alon, Martha D. Wellons, James C. M. Chan. Medical College of Virginia, Department of Pediatrics, Richmond, Virginia

Vitamin-D metabolites promote marked elevation in urinary calcium excretion (U_{Ca}). To test the effects of CTZ on this vitamin-D-induced hypercalciuria, we carried out 17 studies of 12 days each in adult Sprague-Dawley male rats (465±30 gm), kept in metabolic cages and fed chow-powder 16±2 gm/day.

Three groups were studied: (A) control rats receiving only the vehicle at 0.2 ml/day, subcutaneously (S.C.); (B) vitamin-D_2-treated rats receiving 50 I.U./day, S.C. and (C) rats treated the same as in B, plus CTZ 20 mg/day intraperitoneally for the last 6 days of the study. Twenty-four-hour urine collections during the last 3 days of each study were analyzed for U_{Ca}, creatinine (U_{Cr}) and creatinine clearance (C_{Cr}), with corresponding serum samples for Ca (S_{Ca}) and creatinine.

Groups		(A) n = 5	(B) n = 6	(C) n = 6
S_{Ca}	mg/dl	6.1 ±0.1	6.1 ±0.2	6.0 ±0.2
C_{Cr}	ml/min/kg	4.8 ±0.7	5.2 ±1.2	4.9 ±0.5
U_{Ca}	mg/kg/day	6.7 ±1.0	19.5 ±9.7*	6.8 ±2.5†
U_{Ca}/U_{Cr}		0.19±0.03	0.53±0.25*	0.20±0.07†

* (B) vs (A) p <0.02 † (C) vs (B) p <0.02

We conclude that conventional doses of vitamin-D_2 cause marked hypercalciuria consistently and even without hypercalcemia, and that this hypercalciuria can be reversed by CTZ.

●1430 URINARY PROSTAGLANDIN(PG) EXCRETION RATES(XR) AND RENAL FUNCTION IN HUMAN NEONATES AT BIRTH. Billy S. Arant, Jr., Fielding B. Stapleton, William D. Engle, and William H. Stephenson. Southwestern Med Sch and U TN Ctr Health Sci, Dept Ped. Dallas, TX and Memphis, TN.

PG are considered important in adaptational responses of the fetus to postnatal life. The role of PG on neonatal renal function has been implied from urinary(U) PG factored for creatinine (Cr) or body weight and from indomethacin studies. To study these relationships, timed-urine collections were obtained on the first day of life in 63 unstressed infants of 26-40 weeks gestational age(GA). Plasma and U sodium(Na), Cr and osmolarity(osm) were measured; clearances(C) were calculated. PG in U were determined by RIA. Results are presented in the Table as mean±SEM for each age group.

GA, weeks(n)	26-28(5)	29-30(5)	31-33(11)	34-37(18)	38-40(24)
PGE_2, pg/min	69±29	69±27	52±8	28±6	96±29
$PGF_{2\alpha}$, pg/min	40±19	44±20	60±10	49±9	110±29
$6kPGF_{1\alpha}$, pg/min	17±4	24±11	34±11	25±5	121±27
C_{Cr}, ml/min	0.4±0.1	0.6±0.1	1.0±0.2	1.3±0.2	6.8±1.5
C_{Na}, ul/min	10±4	28±17	11±3	12±2	27±9
U_{osm}, mosm/L	217±27	146±32	168±27	148±21	209±20

PGE_2 XR varied with C_{Na} (r=0.79, p<0.001) but did not vary with C_{Cr}, U_{osm} or GA. UPG/mgCr did not correlate with XR for PGE_2 (r=0.07) or $PGF_{2\alpha}$ (r=0.03) suggesting renal origins. UXR of $6kPGF_{1\alpha}$, a metabolite of the vasodilator PGI_2, varied directly with C_{Cr} (r=0.83, p<0.001) and blood pressure (r=0.47, p<0.001), suggesting a role of renal function in the elimination of circulating prostacyclin and its metabolites.

1431 DAYTIME WETTING AND ENURESIS AS A MAJOR CAUSE OF RECURRENT URINARY TRACT INFECTION (UTI) IN GIRLS. Gerald S. Arbus. (Spon. by Melvin H. Freedman). University of Toronto, The Hospital for Sick Children, Department of Paediatrics, Division of Nephrology, Toronto, Canada.

A prospective study of girls with a history of recurrent UTI and no major urologic structural problems was undertaken. Of 35 such girls (aged 3-12 years, mean 7.7 years) referred for consultation 23% had either improperly collected urine samples taken for culture or no culture to confirm a diagnosis of UTI. Twenty-four (68%) had enuresis and/or daytime wetting causing rather than resulting from UTI. To date, all patients who have stopped wetting have had no episodes of UTI since cessation of wetting. In only 3 children (9%) could no other direct concomitant cause (including bubble bath, improper wiping, constipation, pinworms, sexual intercourse, etc.) for the recurrent nature of the UTI be determined.

More stringent documentation of UTI by primary physicians and correcting "wetting" problems in girls with recurrent UTI could reduce the unnecessary use of antimicrobial therapy and time in seeing consultants.

1432 POSTURAL PROTEINURIA IN PEDIATRIC RENAL ALLOGRAFT RECIPIENTS. Gerald S. Arbus, Stephen Belyea, Joseph Poreipa, C. Phillips Rance. (Spon. by Melvin H. Freedman). University of Toronto, The Hospital for Sick Children, Department of Paediatrics, Division of Nephrology, Toronto, Canada.

To determine whether kidney transplants are capable of manifesting postural proteinuria, 62 pairs of 12 hour urine collections were performed in 40 renal transplant recipients (aged 4.8-20.5 years): one set was taken with the patient upright, the other with the patient reclining. Eighteen patients, including 12 who did not have native kidneys in place, excreted >150 mg protein/24 hours. The 12 without native kidneys excreted significantly more ($p<0.05$) protein in the upright than in the reclining position. Having native kidneys in place did not significantly affect 24 hour urine protein values in the 40 patients. However, there was a significant difference ($p<0.05$) in serum creatinine values between those excreting >150 mg and those excreting <150 mg protein/24 hours.

It appears that postural proteinuria is not a function of direct neural sympathetic activity or lymphatic obstruction to the kidney since these have been interfered with in renal transplant recipients. Renal hilar stretching causing venous congestion is also unlikely since allografts are placed securely in the region and bound tightly by fibrous tissue.

Because renal allograft recipients with no native kidneys in place are capable of manifesting postural proteinuria, some traditional explanations of this phenomenon must be reconsidered.

1433 SHOULD LONG TERM ANTIMICROBIALS BE PRESCRIBED FOR CHILDREN WITH RECURRENT URINARY TRACT INFECTION (UTI) AND MAJOR UROLOGIC PROBLEMS? Gerald S. Arbus, Theresa M. McCann, Mukesh Gajaria, Robert M. Bannatyne, Bernard M. Churchill, Brian E. Hardy. (Spon. by Melvin H. Freedman). University of Toronto, The Hospital for Sick Children, Department of Paediatrics, Division of Nephrology, Department of Bacteriology, and Department of Surgery, Division of Urology, Toronto, Canada.

In a previous study, long term antimicrobial therapy had no significant effect on the incidence of UTI in patients with major urologic problems (in press). In view of this, 50 such patients were randomly selected and studied prospectively. All claimed to be taking antimicrobials. Urine samples, obtained by catheterization as part of urodynamic testing, were cultured. Sarcina plate testing showed no antimicrobial activity in the specimens from 17 patients (34%). The incidence of positive cultures in these patients was more than twice that in patients whose urine specimens showed the presence of antimicrobial activity. Five of the six patients who had positive cultures and evidence of antimicrobial activity in their urine were resistant to the antimicrobials they were taking. Thus, considering the likelihood of antimicrobial resistance developing and the probability of poor compliance, long term antimicrobial therapy does not appear beneficial for these patients. Rather, it is recommended that short term antimicrobial therapy be prescribed to treat acute episodes of UTI.

1434 ERYTHROCYTE (RBC) INSULIN RECEPTOR BINDING IN ADULTS AND CHILDREN WITH END STAGE RENAL DISEASE (ESRD). Watson C. Arnold, Mark Boughter, Tom Sziszak and Donald E. Hill, Dept. of Pedi., Univ. of Ark. for Med. Sci.,LR,AR.

Peripheral tissue resistance to insulin is a common feature of uremia. The RBC offers an easily obtainable means of assessing insulin-receptor interactions. Using a purified RBC suspension ($3.6x10^9$ cells/ml/tube) obtained from fasting nondiabetic ESRD patients, specific ^{125}I-insulin binding was determined over insulin concentrations of 0.2-100 ng/ml. Computerized Scatchard plots were performed, assuming a 2-site model for insulin binding. All values are ± S.D. *p < 0.001.

	N	B/T%	$K_1(nM^{-1})$	R_1(pM)	$K_2(nM^{-1})$	R_2(pM)
Normal adults	24	8.3±1.4	6.4±1.3	12.2±3.2	0.2±0.1	7.1±3
Uremic adults	10	7.9±1.2	12.8±3.7*	8.5±2.1	0.1±0.1	8.0±3
Normal children	20	8.0±1.3	-----	-----	-----	-----
Uremic children	4	7.2±1.2	8.8±4.9	8.0±4.2	0.2±0.2	8.3±5

The maximum insulin bound (B/T%) is not statistically different for any of the uremic groups compared to normal values. However, when receptor site parameters were computerized, in adult uremics, the affinity was increased for site 1(K_1) and decreased at site 2(K_2). For uremic children, receptor affinities and capacities (R_1R_2) were not significantly different from normals. All patients were ingesting <70% of recommended dietary allowance for calories. Anemia, younger erythrocytes, and nutritional status at the time of RBC production all affect RBC insulin binding. Therefore, the Erythrocyte may be less than optimal for quantitation of insulin resistance and receptor changes in ESRD patients and previously reported abnormalities may reflect nutritional in uremic patients.

●1435 SODIUM AND ALDOSTERONE HOMEOSTASIS AFTER TRANSITION FROM CHRONIC SODIUM DEFICIT DURING EARLY DEVELOPMENT TO SODIUM EXCESS IN ADULT LIFE. Abraham Aviv, Tatsuharu Kobayashi, Hirohiko Higashino and John W. Bauman, Jr. Sponsored by O. Robert Levine, N.J. Medical School, Dept. of Pediatrics, Newark, New Jersey.

The impact of chronic low Na intake during immaturity on body Na homeostasis in later life is not sufficiently known. In order to explore this effect, we have investigated the influence of varying degrees of chronic dietary Na deficit during early development (first phase; age 3-7 weeks) and the short term effect of dietary Na repletion (second phase; age 8-9 weeks) on parameters such as: growth rate, urinary aldosterone excretion, ^{22}Na space, and various renal functions. During the first phase, animals with severe Na deficit showed marked growth retardation. All Na deficient rats had extremely high levels of urinary aldosterone excretions. During the second phase, rats originally on Na deficient diets demonstrated expansion of the ^{22}Na space and inability to adequately suppress their aldosterone excretion. Rats originally subjected to severe Na deficit failed to catch up with the body weight gain of their control counterparts despite two weeks of Na repletion. The GFR and RPF were not different among the groups. However, in the second phase, despite expansion of the ^{22}Na space, rats subjected to Na deficit in the first phase showed retarded capacity to excrete an acute IV saline load. These changes were not seen in adult rats subjected to the same experimental regimen. It is concluded that Na deficit during early life profoundly influences Na and aldosterone homeostasis once a transition is made to a higher Na intake in later life.

●1436 RENAL BASEMENT MEMBRANE (BM) DEVELOPMENT IN METANEPHRIC ORGAN CULTURE. E.D. Avner, R. Jaffe, T. Temple, and D. Ellis. (Spon. by T.K. Oliver). Departments of Pediatrics and Pathology, University of Pittsburgh School of Medicine, Pittsburgh, PA.

The non-collagenous glycoproteins of renal BM are important determinants of normal tubular and glomerular morphogenesis, structure, and function. Therefore, the sequential development of fibronectin (F), laminin (L), and entactin (E) was studied in a newly developed, serum-free mouse metanephric organ culture system. In this system, intact embryonic metanephros undergoes tubular differentiation and unique glomerular development without perfusion or urine formation. As in natural nephrogenesis, a highly differentiated proximal tubule with well-defined brush border forms. In addition, a unique glomerulus with differentiated podocytes surrounding areas of BM forms entirely from epithelial elements.

Using specific affinity purified antibodies and immunohistological techniques, the ontogeny of F, L, and E was characterized in vitro. F alone was identified in the undifferentiated embryonic mesenchyme supporting tubule and glomeruli. F, L, and E were present in the BM from the earliest recognizable tubular and glomerular forms.

These studies demonstrate that renal tubular and glomerular development and BM production proceed normally following induction and do not require vascularization, perfusion, or urine formation. Further, glomerular epithelial cells produce normal glomerular BM in the absence of endothelial or mesangial elements.

1437 PROGNOSTIC SIGNIFICANCE OF AMPHOTERICIN ASSOCIATED RENAL TOXICITY IN PRETERM INFANTS. J.E.Baley, R.M. Kliegman, A.A.Fanaroff. CWRU, RB&C Hosp, D.Peds, CLE,O

Despite the immaturity which characterizes renal function in the newborn, complete renal shutdown is relatively infrequent. We report the profound nephrotoxic effects and prognostic significance of amphotericin therapy in low birth weight infants. Data was analyzed from 10 preterm infants, mean BW 0.8 kg (range 0.6-1.1 kg), GA 28 wks (range 26-34 wks), who were treated for systemic fungal infection (Candida 9, Malassezia 1) at a mean age of 6 wks (range 2-16). Oliguria or anuria developed in 7 infants, 6 of whom subsequently died. No deaths occurred in infants with preservation of urine flow. After an initial response to diuretics, including Lasix(≤10mg/kg/day) and dopamine, refractoriness developed. Urine flow, however, was promptly re-established by withholding amphotericin. The onset of oliguria followed a mean total dose of 6.5 mg/kg(range 0.25-15.4mg/kg), commencing 1-20 days after initiating amphotericin therapy (mean 7 days). All the infants had pyuria, hematuria and proteinuria. Urine microscopy revealed renal epithelia or casts in 7 infants. Budding yeasts in the urine or positive urine cultures were found in 9. An abrupt rise in creatinine ≥1.3 occurred in 5. 4 infants exhibited hypokalemia ($K^+ \leq 2.9$) with excessive K^+ in the urine, followed by hyperkalemia when renal failure supervened. Histologically there was relative preservation of all the structural components of the kidney. We conclude that independent of dose, amphotericin may produce renal shutdown in preterm infants. Preservation of renal function in the face of systemic fungal infection during therapy augurs well for outcome.

1438 COMPARISON OF CHRONIC INTERMITTENT(IPD)AND CONTINUOUS AMBULATORY(CAPD)PERITONEAL DIALYSIS IN CHILDREN. Jorge Baluarte, Alan Gruskin, Martin Polinsky, James Prebis, Sharon Perlman,Bruce Morgenstern,JoAnn Maloney. St.Christopher's Hospital for Children, Philadelphia, PA.

An advantage of CAPD over IPD has not yet been established in the treatment of ESRD in children. We have used IPD and/or CAPD to treat 33 children with ESRD. Twenty-one children, ages 2-17.3 yr.received IPD for 2-54 months(254 patient-months)and 12 children,ages 0.8-17.8 yr.CAPD for 1-12 months(63 patient-months).Values for potassium,calcium,phosphate,total protein and albumin were not significantly different between IPD and CAPD. Those receiving CAPD had lower levels of BUN and creatinine. The linear growth rate of 8 patients on IPD for more than 12 months, ranged from 0.09-0.98 cm/month($\bar{x}$ 0.32)and in 5 patients on CAPD for more than 6 months,ranged from 0.06-0.47 cm/month ($\bar{x}$ 0.32). Hypertension in 17/21(IPD)&5/12(CAPD)patients was controlled or improved in 80% in both groups;20% required nephrectomy. The incidence of peritonitis in IPD and CAPD patients was 1 episode for 10.9 patient-month and 1 episode for 4.6 patient-month, respectively. As regards IPD,6/21 remain on IPD,3 changed to CAPD,10 were transplanted; 2 died of nondialysis causes. Regarding CAPD,7/12 remain on CAPD,3 had to return to hemodialysis because of inadequate peritoneal membrane and 2 were transplanted. Conclusions:(1)both modalities are adequate for long-term dialytic therapy in uremic children,(2)peritonitis occurred more frequently in CAPD,(3)both enable hypertension to be adequately controlled,(4)linear growth was similar in both groups,(5)a clear cut advantage of one form of peritoneal dialysis over another remains to be established.

1439 HYPOVOLEMIC SHOCK (HVS) AND RENAL FUNCTIONS IN DEVELOPING BABOONS. Rama Bhat, Eunice John, Bert Braverman, Tonse Raju, Linda Fornell, Morton Schulman, Dharmapuri Vidyasagar, ALSM, University of Illinois Hospital, Department of Pediatrics, Chicago.

One of the common causes of acute renal failure in the newborn is HVS. We studied the effect of acute HVS and recovery (R) following reinfusion in 4 newborn and 4 older baboons. HVS was induced by bleeding till the mean blood pressure (MBP) decreased by 50%. Control (C), HVS and R period lasted 45'. Cardiac output (CO) and renal blood flow (RBF) were measured by the thermodilution and microsphere method. GFR, osmolar clearance (COSM), fractional excretion of sodium (FE_{Na}) and urine volume (UV) were measured during C, HVS and R periods. Oncotic pressure (OP) and hematocrit were also monitored. In both groups CO, Hct, OP decreased and heart rate increased (P<.05) during HVS and recovered to 80% of C values following R. Decrement in UV, GFR and RBF (P<.05) during HVS also

		N+SE	UV(ml/min)		GFR(ml/min/kg)		RBF(ml/min/g)		FE_{Na}	
0-2 wks.	C	4.80	1.0	2.20	0.40	5.00	0.84	13	4.5
	HVS	1.40	0.77	0.82	0.2	2.4	0.38	7.6	5.0
	R	5.60	1.0	1.73	0.42	6.3	0.64	23.8	11.0
4-9 wks.	C	8.5	2.2	2.5	0.3	5.45	1.2	16	4.6
	HVS	1.7	0.66	0.98	0.4	1.63	0.82	5.5	2.6
	R	8.2	2.00	2.5	0.6	2.42	0.88	18	4.85

recovered following R. Similar changes were seen in COSM. Changes in cortical RBF distribution were not significant. In developing baboons acute HVS produced severe decrease in GFR, RBF, COSM, UV and FE_{Na}. In conclusion, the change in renal function in early HVS (45') are transient and reversible with immediate reinfusion.

●1440 EFFECT OF BILIRUBIN ON TRANSEPITHELIAL Na TRANSPORT

(J_{Na}), A.S. Brem, J. Tetreault, M.A. Pacholski, and W. Cashore, Brown Univ., Dept of Peds., Prov., RI.

Hyperbilirubinemia increases urinary Na excretion in both preterm and term infants (Acta Paediatr. Scand. 68:75, 1979), with similar renal Na wasting seen in homozygous jaundiced Gunn rats (Am. J. Physiol. 212:931, 1967). Since the toad urinary bladder resembles the mammalian distal nephron in its ability to increase J_{Na} after exposure to certain hormones, the effect of bilirubin (BR) on J_{Na} was studied in bladders isolated from Dominican toads (Bufo marinus). Tissues were exposed to amphibian HCO_3^- Ringers, pH 8.1 containing BR 0.1 mM and 0.05% bovine serum albumin (BSA) or BSA alone. J_{Na} was measured by the short circuit current technique. BR in the serosal bath did not affect the bladders' basal J_{Na}. When a maximal dose of vasopressin (VP) (4 mU/ml) was added to the serosal bath, peak J_{Na} in tissues exposed to BR was inhibited by 20 ± 6% compared to paired controls (n=8; p<0.02). Exposure to BR caused a similar inhibition in peak J_{Na} (32 ± 5%) following stimulation with the cAMP analogue p-Cl-phenylthic cAMP (10^{-5}M) (n=8; p<0.001). There was no effect on either basal or VP stimulated peak J_{Na} when BR and BSA were placed in the mucosal bath. BR and BSA in the serosal bath were no different from BSA alone in influencing the rise in J_{Na} produced in bladders stimulated with aldosterone (10^{-7}M). Amphotericin B in the mucosal bath stimulates J_{Na} by increasing Na pump activity on the serosal membrane. BR in the serosal bath had no effect on the amphotericin induced rise in J_{Na} when compared to paired controls. Excess albumin (0.5%) abolished any inhibitory effect of BR on J_{Na}. These data show that BR, in the serosal or blood side, inhibits VP and cAMP stimulated J_{Na}. Neither mucosal Na entry nor serosal Na exit via the Na pump appear to be the site of inhibition. The decrease in VP stimulated J_{Na} seems to involve a process beyond the generation of cAMP.

1441 EFFECT OF TRANSIENT RENAL ISCHEMIA (ISCH) ON CEPHALOSPORIN (C) NEPHROTOXICITY (NTOX)

Marc C. Browning, Peter L. Wang, Chieh-Yin Hsu and Bruce M. Tune, Stanford University School of Medicine, Department of Pediatrics, Stanford, California.

Because of an augmentation by ISCH of renal cortical organic anion (PAH) concentrations, we studied the combined effects of unilateral renal ISCH and the NTOX of cephaloglycin (C_G), which is secreted across the tubular cell, and cephaloridine (C_L), which is not. Groups of rabbits received vehicle, C_G (60 mg/kg) or C_L (90 mg/kg) (NTOX equal) immediately after release of 25 min of ISCH. Graded histologic scores (48 hr after C, degree of necrosis 0 to 5) were compared within experimental groups for ISCH and contralateral kidneys (i vs. c) and for i minus c in experimental compared to control group animals [ISCH alone or C alone (sham surgery)]. Cortical C i/c concentration ratios (Conc-i/c) were measured in separate studies 30 min after C infusion.

Necrosis was augmented with C_G for i vs. c [3.00 ± SEM 0.48 vs. 1.07 ± 0.50 (P < .02)] and for i minus c [2.33 ± 0.45 against ISCH alone 0.83 ± 0.30 (P < .02) and against C alone 0.17 ± 0.11 (P < .001)]. ISCH and C_L were not additively damaging (i minus c = 0.88 ± 0.30). As with PAH uptake after ISCH, Conc-i/c for C_G was elevated (1.59 ± 0.18 vs. 1.0, P < .05); that for C_L (1.06 ± 0.04, p < .25) was not. Thus, ISCH augments the Conc and NTOX of the secreted C, possibly by reducing cell-to-tubular fluid-to-urine C movement.

1442 EVOLUTION AND DISPOSITION OF RAT RENAL MYELOID BODIES (MB) INDUCED BY SPERMINES (SPM).

Robert A. Campbell, Robert E. Brooks, Tom LaBerge, Mark Campbell-Boswell and Yeshawant Talwalkar. (Spon. by John W. Reynolds), Oregon Health Sciences University, Dept. of Ped. and Anat. Path, Portland, Oregon.

SPM, a natural aliphatic polycation, when parenterally administered induces proximal tubular necrosis. This study of rat tubular cells was to determine the nature of MB formation and disposition during development of the nephrotoxic lesion. Sprague-Dawley rats were injected I.P. with a single daily dose, 40 mg/kg of SPM hydrochloride, from 1 to 5 days. Animals were perfused by a modified Maunsbach technique. MBs were seen at 4-hours and were identified throughout the 5-day period. Dense MB precursor substance was observed in endocytotic vesicles (EV) beneath the brush border (BB). The first demonstrable event appeared as a separation of the plasma membrane of the EV into two components. The inner (outer) dehiscent membranes formed ring-like structures within the EVs and frequently marginated. Whorl-like condensations were observed. MBs were noted in EVs, lysosomes, cytoplasm and between microvillae. Showers of MBs were seen in the BB suggesting egress into the lumen. Sequestration of MBs in lysosomes and extrusion into the tubular lumen suggest two modes of MB disposition during toxic overload. Polyamines appear to be transported in BB cystine-dibasic AA pathway. SP MBs may result from interactions between cation excess and intravesicular accumulation of outer plasma membrane. Failure to degrade these membranes could be due to enzyme inhibition and/or simple biophysical events.

1443 SERUM IMMUNOREACTIVE ERYTHROPOIETIN (Ep) LEVELS IN PATIENTS WITH CHRONIC RENAL FAILURE (CRF).

Manju Chandra, Marilyn Miller, Joseph F. Garcia, Robert T. Mossey and Melinda McVicar. North Shore Univ. Hospital-Cornell Univ. Medical College, Depts. of Peds. and Medicine, Manhasset, N.Y.; Brookhaven Natl. Lab , Medical Dept., Upton, N.Y. and Lawrence Berkeley Lab., Univ. of California. (Sponsored by Joseph Kochen).

The anemia of CRF is attributed to decreased erythropoiesis. To study the role of Ep in CRF, we measured Ep by a specific radioimmunoassay in patients with CRF of diverse etiologies. Data are expressed as means ± SEM

Group, Ccr †	n	Hct %	Ep mU/ml	Age, years
I Ccr 40-100 (63.2 ± 8.2)	9	39.6 ± 1.5	14.1 ± 2.3	15.4 ± 1.6
II Ccr 10-39 (19.9 ± 2.8)	10	27.8 ± 2.3*	11.5 ± 1.2*	14.7 ± 1.3
III Ccr < 10 (on dialysis)	24	21.2 ± 9.8*	12.4 + 0.7*	31.5 ± 3.4

† Ccr=creatinine clearance ml/min/1.73 M^2, *p= <0.01, CRF vs controls

Hematocrits (Hct) and Ep were lower in Groups II and III as compared to 48 controls (Hct 42.8 ± 0.8%; Ep 18.5 ± 0.7 mU/ml). The decrease in Hct correlated with Ccr in Group II (r=0.83; p < 0.01). Ep levels were inappropriately low for the degree of anemia in patients with Ccr < 40 when compared to Ep levels reported from the same lab in non-uremic patients with hypoplastic anemias (Ep > 500 mU/ml with Hct < 30%). No correlation was found between Hct and Ep levels in any group. This may be due to altered hemoglobin-O_2 affinity which was not measured. We conclude that in CRF: (1) Ep levels are inappropriately low for the degree of anemia (2) Ep levels do not correlate with Hct (3) decrease in Hct occurs only after Ccr falls < 40.

1444 THE EFFECTS OF REDUCED RENAL MASS ON GLOMERULAR DYNAMICS IN EARLY POSTNATAL DEVELOPMENT.

Robert L. Chevalier (Spon. by Thaddeus Kelly), University of Virginia Medical Center, Dept Pediatrics, Charlottesville, VA.

In the newborn guinea pig (NBGP), deep nephron function predominates until 10-20 days of age, when superficial single nephron glomerular filtration rate (SNGFR) rises disproportionately. Uninephrectomy at birth (NX) accelerates this transitional increase (Kidney Int. 19:196, 1981). To define responsible glomerular dynamics, NBGP were subjected to NX or sham operation and studied at 10 or 20 days of age. Superficial glomerular capillary (P_{GC}), proximal intratubular (P_T), and effective filtration pressure (EFP) were determined by micropuncture. Outer cortical glomerular perfusion rate (GPR) was determined by microsphere and glomerular counting techniques. Ultrafiltration coefficient (est. K_f) was estimated for each group. Results were as follows:

	Group	P_{GC} mmHg	P_T mmHg	EFP mmHg	GPR nl/min	est. K_f nl/s·mmHg
10d	Sham	34.1±0.5	10.3±0.2	8.6±0.6	42±4	0.006
	NX	35.6±0.5*	9.5±0.3	11.3±0.5*	60±5*	0.008
20d	Sham	34.3±0.9	9.6±0.2	9.2±0.4	71±6*	0.017
	NX	36.4±1.1	9.0±0.2	12.0±0.9†	109±11†	0.018
N per group		9	9	9	5	-

Mean ± SE. * p < 0.05 vs 10d Sham; † p < 0.05 vs 20d Sham.

Conclusions: With normal maturation, the transitional sharp increase in SNGFR from 10 to 20 days follows enhanced glomerular permeability and increased GPR without change in P_{GC} or EFP. The increment in SNGFR due to NX differs from normal development by an adaptive rise in EFP without a further increase in est. K_f.

● 1445 SERUM OSTEOCALCIN: RESPONSE TO CALCITRIOL [1,25(OH)$_2$D$_3$] THERAPY OF X-LINKED HYPOPHOSPHATEMIA (XLH) AND AUTOSOMAL RECESSIVE VITAMIN D DEPENDENCY (ARVDD).

David E. C. Cole, Caren M. Gundberg, Jane B. Lian, Paul M. Gallop (Spon. by John F. S. Crocker). Dalhousie Univ., I. W. Killam Hosp. for Children, Dept. of Pediatrics, Halifax, NS; and Harvard Medical School, Children's Hosp. Medical Center, Depts. of Orthopedic Surgery and Biological Chemistry, Boston, Ma.

Osteocalcin, a bone-specific protein containing γ-carboxyglutamate [*gla*] residues, is detectable in serum. *In vitro* studies have shown that its synthesis in bone is vitamin D responsive. Using a specific radioimmunoassay, we find that serum osteocalcin increases with 1,25(OH)$_2$D$_3$ treatment of XLH and ARVDD. In 6 XLH patients, levels rose from 19.4±5.6 to 42.7±9.4 ng/ml ($\bar{x}$±SE, p<.01) after institution of 0.5-2.0 μg/day 1,25(OH)$_2$D$_3$ therapy for 7 to 12 months. Increases in the preadolescent group ($\bar{\Delta}$=376%, n=4) were greater than in the postadolescent group ($\bar{\Delta}$=181%, n=6), reinforcing the conclusion drawn from histomorphometry and routine chemistry that response to 1,25(OH)$_2$D$_3$ therapy was greater in the growing child. In 6 ARVDD patients, osteocalcin rose from 35±7 ng/ml to 83±32 ng/ml after 1 week (p<.05) and 120±42 ng/ml after 3 weeks (p<.05) of 1 μg/day 1,25(OH)$_2$D$_3$ therapy. Prepubertal and pubertal patients showed a greater response ($\bar{\Delta}$=305% at 3 weeks, n=3) than did the postpubertal ones ($\bar{\Delta}$=67%, n=3). Serum calcium increased modestly, but alkaline phosphatase, which was elevated prior to therapy, remained unchanged. Serum osteocalcin determinations may provide an earlier non-invasive measure of bone mineral response to 1,25(OH)$_2$D$_3$ and improve management of metabolic bone disease.

●1446 UREA ENHANCEMENT OF ANGIOTENSIN (A-II)-INDUCED HYPERTENSION. K. C. Corley, H. P. Mauck, J.C.M. Chan. Med Coll Virginia, Depts of Phys, Med, Peds, Richmond, VA

Studies in cats (Pediatr Res 14:617, 1980) confirmed clinical impressions that urea has synergistic effect on endogenous pressor agents. To further delineate the mechanisms of such synergism, 20 studies were conducted in 3 groups of anesthetized cats: (1) 6.6M urea as the vehicle for A-II in place of 5% dextrose/water, D_5W, (2) 6.6M methylurea or 1.4M mannitol as the vehicle, with Evan's Blue (4 mg/kg i.v.) to measure volume by spectrophotometry and osmolality by freezing-point depression, (3) spinal cord transection or sympathetic nervous system blockade with propranolol (3 mg/kg i.v.) or prostaglandin inhibitors (Ibuprofen 20 mg/kg i.p. or Indomethacin 5 mg/kg i.a.) to test factors inhibiting this synergism. Venous infusions (0.5 ml/min) alternated at 5-min intervals between: (a) D_5W alone (b) the test dose of A-II in D_5W (c) A-II in the other vehicles in place of D_5W. The pressor dose was defined as A-II achieving elevation of mean intra-arterial blood pressure (BP) by 20 mm Hg over that of control BP. Thus, in Group 1 (n=8) the pressor dose in ng/kg/min was 72±31 with D_5W/A-II and 14±17 with urea/A-II. ($p < 0.02$). In group 2 (n=7), although increases in volume and osmolality were achieved, methylurea or mannitol did not elevate the BP by themselves, but potentiated the hypertensive effects of A-II. In group 3 (n=5) spinal cord transection, propranolol or prostaglandin inhibition removed the urea/A-II synergism. Thus, the data suggest that while systemic osmotic changes were not contributing factors, prostaglandins and blood-brain barrier appear to be controlling factors in this synergism.

●1447 GENETICAL ASPECTS OF STEROID INDUCED POLYCYSTIC KIDNEY DISEASE IN THE MOUSE. John F.S. Crocker and Stan R. Blecher, Dalhousie University and the Izaak Walton Killam Hospital for Children, Departments of Pediatrics and Anatomy, Halifax, Nova Scotia.

Polycystic kidney disease (PKD) has several forms in childhood. Although genetic control is often felt to be a factor, virtually nothing is known of the molecular nature of the gene product defect(s) or the sites of action. Newborn mice of specific genetic strains, when injected intramuscularly with hydrocortisone acetate (HCA), will develop PKD from days 5 to 12 post injection, and a number will die of uremia. This glucocorticoid-induced PKD is felt to be a model of infantile PKD.

We previously reported strain differences in susceptibility, including high frequency in C3H and total resistance in CBA mice homozygous for the kd gene. The results demonstrate genetic control of the trait of susceptibility to HCA. They also suggest, as one possibility, that kd is epistatic to genes for HCA susceptibility. We now have preliminary results from 3 litters born of a C3H · CBA (kd) cross. A high degree of positivity for PKD was observed. This indicates that if kd is epistatic, it is not dominantly so. Further analysis of crosses in this system will enable us to discriminate between epistatic and additive genetic control in the case of the kd and other negative strains, and to estimate the heritability of this trait.

●1448 CYCLOPHOSPHAMIDE THERAPY IN FOCAL SEGMENTAL GLOMERULAR SCLEROSIS: A CONTROLLED CLINICAL TRIAL. A Report of the International Study Of Kidney Disease In Children.

Focal segmental glomerular sclerosis (FSGS) frequently follows a progressive clinical course leading to end stage renal disease despite treatment with prednisone (P). In order to determine if therapy with cyclophosphamide (C) and P is superior to P alone, a controlled clinical trial was undertaken. Sixty-three children with FSGS and nephrotic syndrome who failed to respond to daily P therapy (60 mg/m^2/day for at least 28 days) were allocated randomly either to P (40 mg/m^2 given on alternate days for one year) or to C (2.5 mg/kg/day for 90 days) in addition to alternate day P. Outcome variables were defined as: remitted = absence of proteinuria and normal glomerular filtration rate (GFR); improved = proteinuria decreased by 2+ or more on semiquantitative testing and GFR normal or increased by > 30%; and deteriorated = either proteinuria increased to 3+ or more, or GFR decreased by > 30%. The table shows the clinical status observed after 1 to 7 years of follow-up.

	Remitted	Improved	Unchanged	Deteriorated	
P	7 (27%)	2 (8%)	11 (42%)	6 (23%)	
C + P	10 (27%)	2 (5%)	12 (32%)	13 (35%)	$p > .7$

The rate of remission in children treated with C + P was not different from that found in patients given P alone. Although a greater percentage of patients deteriorated on C + P than on P alone, life table analysis failed to confirm a detrimental effect of C. We conclude that children with FSGS should not be treated with cyclophosphamide.

1449 ROLE OF B-ADRENERGIC SYSTEM IN THE FETAL RENAL RESPONSE TO HYPOXIA. Salha S. Daniel, Raymond I. Stark, Alan B. Zubrow, Harold E. Fox and L. Stanley James. Columbia U.,Coll. of P&S, Div.Perin.,Depts.Ped.,Anes.,Obs., NY.

Stimulation of B-adrenergic system in the adult alters renal function indirectly through changes in the circulation and directly through its stimulation of the renin angiotensin system and release of vasopressin. The contribution of this system to the changes in renal function with hypoxia(H) was studied in 7 chronically instrumented fetal lambs (120-134 days gestation) given 1mg/kg propranolol (Exp.) and compared to 7 control(C). A 50% reduction in PaO_2 in both groups was induced by administration of 10% O_2 to the ewe for 30 minutes. The fall in urine output(V) and rise in osmolality and Na concentration during the hypoxic episode were similar in both groups. The changes from pre-hypoxia values after 90 minutes of recovery were:

	ΔV(ml/kg,min)	ΔGFR(ml/kg,min)	ΔOSM(mOsm/kg)	ΔNa(mEq/L)
C	-0.01±0.058	+0.15±0.29	+12.3±25.90	+19.5±5.81
Exp.	-0.06±0.017*	+1.10±0.26*	+131.6±24.46*	+33.6±9.80*

*P<0.05 compared to C

Plasma vasopressin concentration, which rose significantly in both groups during hypoxia, was still elevated during the recovery in the experimental group.

These results show that changes in renal function during an hypoxic episode are not appreciably affected by B-adrenergic blockade. However, recovery from hypoxia is delayed significantly possibly as a result of the persistence of elevated vasopressin levels as well as the absence of tachycardia which occurred in the control but not in the experimental group.

1450 URIC ACID EXCRETION AND RENAL FUNCTION IN CHILDREN UNDERGOING CARDIOVASCULAR SURGERY. EN Ellis, BH Brouhard, V Conti. Univ. of Texas Medical Branch, Depts. of Pediatrics and Surgery, Galveston, Texas.

Renal function abnormalities and increased uric acid crystals in urine have been noted as a complication of cardiovascular surgery; etiology is unknown. To evaluate renal function and uric acid excretion, 11 children were studied preoperatively with sera and urine collections one day before surgery. One day after surgery, similar collections, inulin and PAHA clearances were done. 8 patients were acyanotic while 3 were cyanotic. Mean age in both groups was 6.1 years. There were no significant differences in preoperative values of C_{Cr}, FE_{Na}, FE_K, FE_{ua}, Na_s, K_s, uric $acid_s$, $osmolality_s$ and $creatinine_s$ between the cyanotic and acyanotic groups.

Mean postoperative values for all patients showed C_{IN} 60±15 ml/min/m^2, CPAHA 426±222ml/min/m^2, FE_{Na} 1.6±1.0%, FE_K 22.4±16.2%, C_{osm} 4.4±3.7 ml/min/100 ml GFR, $creatinine_s$ 0.5±0.1mg/dl, $PO4_s$ 3.6±0.6mg/dl. The FE_{Na} FE_K and C_{osm} were significantly elevated over the mean preoperative values($p<0.05$). $PO4_s$ were significantly decreased over the mean preoperative value of 5.3±1.6mg/dl($p<0.01$). The cyanotic group had a mean uric $acid_s$ of 11.7±3.8mg/dl and a mean FE_{ua} of 4.9±4.7% postoperatively; these were significantly different from the acyanotic group with a mean uric $acid_s$ of 5±1.4mg/dl($p<0.005$) and a mean FE_{ua} of 12.8±6.4%($p<0.05$) postoperatively. The increased uric acid crystals in urine postoperatively in cyanotic patients may be related to the high uric $acid_s$ levels. The reason for this elevation is unclear; it may be related to the resolution of the cyanotic state.

1451 IMMUNOLOGIC RESPONSE FOLLOWING BLOOD TRANSFUSIONS: IMPLICATIONS FOR RENAL TRANSPLANTATION. Robert B. Ettenger, Stanley C. Jordan, Janice Arnett, Rebecca S. Sakai, Brenda Robinson, Richard N. Fine. UCLA Sch. Med., UCLA Cntr. for Health Science, Div. Ped. Nephrology, Los Angeles, Cal.

Controversy exists over the mechanisms by which blood transfusions (Tfs) improve renal transplant (Tx) outcome. It has been hypothesized that Tfs exclude potential Tx recipients by inducing adverse presensitization with anti HLA lymphocytotoxic antibodies (LCA), thus improving Tx outcome by selecting out the "high responder" who will reject. We have examined multiple humoral immunologic parameters, including anti blood-donor LCA, following 45 Tfs in 12 uremic children. Weekly sera were obtained for 6 weeks following Tf. They were tested for LCA against Tf donor T & B cells at 5C, 20C & 37C incubation temperatures, autolymphocytotoxic antibodies, & circulating immune complexes (CIC) by Raji cell & C1q solid phase assays. Anti-donor LCA were present following 14 of the 45 Tfs (31%). However, only 5 Tfs (11%) resulted in anti HLA LCA against both donor T & B cells at 37C. Nine Tfs (20%) produced LCA against donor B cells only; 6 at all incubation temperatures & 3 at 5C only. Autolymphocytotoxic antibodies were not found after any Tf, but surprisingly, CICs were present in 37% of the sera studied. We conclude that while a donor-specific LCA response occurs after 1/3 of Tfs, generation of LCA against donor T cells is uncommon. This suggests that Tfs do not improve Tx by a selection process, but by as yet undefined active mechanisms, perhaps mediated in part by CICs.

●1452 SENSITIZATION AFTER DONOR-SPECIFIC TRANSFUSIONS FOR RENAL TRANSPLANTATION. Robert B. Ettenger, Ronald Kerman, Stanley C. Jordan, Janice Arnett, Barry L. Warshaw, Richard Harris, Richard N. Fine. UCLA Sch. Med., UCLA Center for Health Sciences, Div. Pediatric Nephrology, L.A., Cal.

We have used donor-specific transfusions (DST) to improve renal transplant (Tx) outcome of one-HLA haploidentical live-related allografts. The mechanism is not understood, but has been assumed to be one of "selecting out" the recipient who will reject, based on his production of complement-dependent antibody (CDA) against donor lymphocytes in response to DST. To examine this hypothesis, we used sensitive radiolabelled chromium 51 (^{51}Cr) assays for CDA & lymphocyte dependent antibody (LDA), as well as the standard dye-exclusion CDA assay, to serially test for antibody against donor T & B lymphocytes following DST. Sixteen pts. received 3 DSTs; 4 (25%) developed dye-exclusion CDA against donor T & B cells. ^{51}Cr testing was performed in 7 of the pts. who did not develop dye-exclusion CDA. Two of these 7 developed CDA by ^{51}Cr testing, one against B & one against T & B cells. Moreover, 5 of these 7 developed LDA against donor B cells by ^{51}Cr testing. Two of the pts. with positive LDA have received Txs from the DST donor & both Txs are functioning 9-12 mos. post-Tx; both have developed post-Tx CDA against donor B cells by dye-exclusion testing. We conclude that when more sensitive assays are used, post-DST sensitization, especially against B cells, is more common than previously suspected. It is, therefore, unlikely that DST works solely by selection of the non-responder, since both pre & post Tx sensitization is present against B cells.

● 1453 DOPAMINE RECEPTORS IN THE PROXIMAL TUBULE OF THE RABBIT. Robin A. Felder, Melvin Blecher and Pedro A. Jose Georgetown University Medical Center, Depts. of Pediatrics and Biochemistry, Washington, D.C.

We have previously reported dopamine I (DA) receptors in plasma membranes from whole kidneys of rats using radioligand binding and adenylate cyclase methods(Clin Res 29:462A,1981). These experiments were designed to identify DA receptors in isolated proximal tubule(S_1 and S_2)of the rabbit nephron using radioligand binding. Tubules were dissected at 5°C after incubation at 37°C with collagenase. Tubules (80-100 mm total length) were incubated for 45' at 23°C in 15 µL of buffer containing 1-25 nM ^{3}H-haloperidol. Specific binding was defined as the difference between binding of the radioligand in the presence or absence of 10 µM cis-flupenthixol,a dopamine antagonist. The radioligand bound to the tubules were separated from free radioligand by rapid filtration under reduced pressure. Specific binding was consistently demonstrated for ^{3}H-haloperidol(47.7±3.4% of total binding n=30). At 10-14 nM ^{3}H-haloperidol, specific binding was 0.097±0.017 fmol/mm tubule(n=7) and 0.043±0.0047 at 7-9 nM(n=6). The apparent dissociation constant was 16nM. In additional studies specific binding was also demonstrated for pars recta(53.2±5.6% n=27). In contrast, the specific binding of ^{3}H-dihydroalprenolol(in the presence of 10 µM isoproterenol)a radioligand used to identify beta adrenergic receptors was inconsistent with no specific binding in 19 of 24 experiments.

These studies identify for the first time DA receptors in the proximal tubule. In agreement with cyclase studies, beta adrenergic receptors could not be identified in these same nephron segments..

● 1454 RENAL BETA ADRENERGIC RECEPTORS IN THE MATURING CANINE R.A.Felder, L.Schoelkopf, D.P.Sporn, M.Connell, G.M. Eisner, P.L.Calcagno and P.A. Jose. Georgetown Univ. Med. Ctr., Depts. of Peds. and Physiol. Washington, DC

We determined age related changes of beta adrenergic receptors (BAR) in renal plasma membranes(RPM) using the radioligand binding method. Protein(Pro) recovery, enrichment of the basolateral marker Na-K-ATPase were similar in outer cortex(OC), inner cortex(IC) and medulla(M) in all age groups(Gr) studied(Gr I=0-2 wk, Gr II=4-6 wk, Gr III=adult). Specific binding(SB) was defined as the difference between the binding of ^{3}H-dihydroalprenolol(1-10nM) in the presence or absence of 10 uM (-)-isoproterenol. SB was rapid, reversible,saturable, of high affinity and stereoselective. Competition studies were suggestive of B_1 subtype of BAR.The dissociation constant(K_d nM), maximum receptor density(B_{max} pmol/mg pro) and Na K-ATPase activity(umol/mg pro/min) M±SEM are tabulated:

Gr	N	K_d			B_{max}			Na-K-ATPase		
		OC	IC	M	OC	IC	M	OC	IC	M
I	4	5.26* ±1.03	4.59* ±1.51	3.08 ±0.94	.019* ±.004	.041* ±.014	.058 ±.006	.243 ±.032	.235 ±.015	.224 ±.020
II	6	2.63 ±0.48	3.31 ±1.11	2.74 ±0.78	.057 ±.012	.071 ±.009	.072 ±.020	.219 ±.040	.373 ±.147	.398 ±.110
III	6	1.49 ±0.27	1.36 ±0.21	1.91 ±0.53	.049 ±.005	.152 ±.031	.076 ±.025	.294 ±.046	.330 ±.024	.369 ±.020

*p=< 0.05 I vs III.B_{max}/umol Na-K-ATPase increased with age. Thus the increase in BAR density with age is not due to changes in RPM/cell protein ratio. These studies combined with our previous report of decreasing alpha adrenergic receptors(AAR) with age suggest significant AAR control of the kidney in the newborn.

1455 ANTITHROMBIN-III LEVELS AND COAGULATION TIME IN CHILDREN WITH HEMOLYTIC UREMIC SYNDROME. Jack S.C. Fong* and Bernard S. Kaplan, McGill University-Montreal Children's Hospital Research Institute, Department of Pediatrics, Montreal Children's Hospital, Montreal, Que., Canada.

Although antithrombin-III levels in patients with chronic renal failure are essentially normal, marked reduction of this protein in an adult patient with HUS has been documented. However, studies on 19 children with HUS revealed minimally reduced levels of AT-III in only two of them. We studied nine HUS patients whose average age was 3.6 years old (range 11 months-5 years) during their acute illness. Laboratory investigation revealed hemoglobin of 5.7 ± 0.9 g/dl, platelet count of 51000 ± 28000/ul, blood urea nitrogen of 83 ± 14 mg/dl and creatinine of 3.6 ± 1.6 mg/dl. Prothrombin times of all platelets studied were normal. As a group, the partial thromboplastin times (PTT) were not significantly different from that of controls - at 28 ± 5 seconds versus 31 ± 3 seconds. However, two of the nine patients had significantly shortened PTT at 22/30 seconds and 23/31 seconds respectively. Plasma AT-III levels of HUS patients at 25 ± 6 mg/dl during their acute illness were not significantly different from normal values of 30 ± 5 mg/dl. However, four of the nine HUS patients studied had AT-III levels at less than two standard deviations from the normal mean. This finding demonstrates the heterogenous nature of this syndrome and emphasizes the need to assess the patient's AT-III level if heparin therapy is contemplated.

1456 CLINICAL SLE WITH DENSE DEPOSIT DISEASE, Aaron L. Friedman, Russell W. Chesney, Terry D. Oberley, Paul T. McEnery, [§] Univ. of Wisconsin Hospitals, Depts. of Pediatrics, Pathology, Madison, Wisconsin, and [2]Cincinnati Children's Hospital, Dept. of Pediatrics, Cincinnati, Ohio.

A variety of pathologic lesions have been noted in SLE nephritis. Renal pathology in SLE has served as a prognostic indicator and guide to therapy. We report a 13-year-old female who presented with joint swelling and pain, gross hematuria and fever. Lab studies showed homogeneous ANA 1:80, 1+ direct Coombs, elevated ESR, serum albumin 2.4 mg/dl and 24-hr urinary protein of 5.7 gm. Serum creatinine, BUN and creatinine clearance were normal. Double-stranded DNA antibodies were negative. Renal biopsy showed diffuse proliferation with deposition of C_3 and fibrin. Electron microscopy showed the lamina densa changes of membranoproliferative glomerulonephritis. Serum complement profiles pre- and post-treatment are noted below.

	C_3*	C_4*	C_{1q}*	C_2*	C_3Nef**
pre-Rx	78	70	5.95	2.3	2.4%
post-Rx	116	56	5.1	2.4	-
normals	90-200	21-75	5.0-7.6	2.0-3.7	0-15%

(*values are in mg/dl; **value is percent breakdown)

Prednisone relieved all symptoms and returned serum abnormalities to normal. Twenty-four-hour urinary protein was reduced to 800 mg. This patient shows the heretofore unreported association of chemical and serologic SLE with the renal biopsy picture of dense deposit disease.

● 1457 IMPAIRED PRIMARY ANTIBODY RESPONSE IN NEPHROTIC SYNDROME Eduardo H. Garin, Pamela J. Sausville, and George A. Richard, (Spon. by Elia Ayoub), University of Florida College of Medicine, Department of Pediatrics, Gainesville, Florida.

The effect of the nephrotic state on primary antibody response was studied in the aminonucleoside of puromycin (AP) induced nephrosis in the rat. The primary antibody response to sheep red blood cells (SRBC) was determined four days after the intraperitoneal administration of SRBC (1 ml., 20%) by measuring anti SRBC IgM antibody producing spleen cells by Jerne plaque forming cell (PFC) (PFC/1x10^6 spleen cells) assay. In nephrotic rats, SRBC were injected when animals were fully nephrotic.

A significant decrease in the number of PFC was observed in 27 nephrotic (mean 12.8±SD 13.5) compared to 28 normal animals (78.6 ±92.1) (p<0.01). Treatment of seven nephrotic rats with indomethacin for 5 days (5mg/kg/d) normalized the antibody response (65.5±43.8) while the administration of indomethacin to eight control rats did not alter the antibody response (69.1±79). When six rats were immunized one day after AP administration, the antibody response observed (49±50.6) was not statistically different than the one seen in five control animals (84±50.5), suggesting no direct effect of AP upon antibody response.

These data suggest that the observed impaired antibody response is secondary to the nephrotic state. Since indomethacin inhibits prostaglandin synthesis and prostaglandins are known to decrease the primary antibody response, we postulate that the impaired antibody response in nephrotic syndrome may be mediated by prostaglandins.

● 1458 CELLULAR PRESERVATION BY ATP-$MgCl_2$ IN RENAL ISCHEMIA.

Karen M. Gaudio, T. Ardito, M. Kashgarian, N. Siegel. Yale Univ Sch of Med, Dept of Ped, New Haven, CT.

We have previously demonstrated a beneficial effect of ATP-$MgCl_2$ after a ischemic renal injury. To determine the mode of action of ATP-$MgCl_2$, tubular integrity as defined by the % recovery of microinjected inulin (InR) and cellular damage as detected by IV infusion of horseradish peroxidase (HRP) were evaluated at 2, 6 and 24 hrs after 45 minutes of renal ischemia in rats treated with either normal saline (NS) or ATP-$MgCl_2$.

At 2 hrs: both groups of rats demonstrated increased permeability to inulin with only 32±9% InR, (98±2% InR in control rats). Morphologic studies revealed a proponderance of necrotic cells and transcellular staining with HRP. At 6 hrs: ATP-$MgCl_2$ rats had less tubular backleak, 55±5% InR, as compared to 29±9% in NS rats ($P<0.05$). Ultrastructural studies demonstrated that ATP-$MgCl_2$ rats had diminished cytoplasmic staining of HRP, intact brush border and improved cellular morphology. The NS rats continued to have ischemic cellular damage. At 24 hrs: ATP-$MgCl_2$ rats had re-established tubular integrity, 92±3% InR, while NS rats still had significant backleak, 72±7% InR ($P<0.05$). In both groups the ischemic changes were improved with only focal evidence of necrosis and HRP staining in NS rats.

This study demonstrates that: 1) In NS rats, cellular damage continues to occur for at least 6 hrs after ischemia and tubular backleak follows a transcellular pathway. 2) Treatment with ATP-$MgCl_2$ enhances recovery of tubular permeability and cellular morphology. 3) These beneficial effects are related to preservation of sublethally injured cells by ATP-$MgCl_2$.

1459 ISOLATED MICROSCOPIC HEMATURIA (IMH): A CLINICAL AND FAMILY STUDY.

Bernard G. Gauthier (Spon. by Philip Lanzkowsky). SUNY at Stony Brook, Health Sciences Center. Long Island Jewish-Hillside Medical Center, Department of Pediatrics, New Hyde Park, N. Y.

IMH (dipstick positive for blood, no proteinuria, gross hematuria or UTI) was studied in 79 children (40 boys, 39 girls, 0.5-18 years old at detection - mean 8.5 years). All had GFR>80 ml/min/1.73 m^2 (>89 in 96%). All had normal diastolic BP. Syst. BP was >95th percentile at least once in 9%. RBC casts were found in 67%. The following were normal (in brackets the number of patients (pts) tested): IVP(31), Audiogram(32), C_3(21), C_4(10), ANA (10). ASLO was high in 2 of 16 pts tested. Biopsies in 4 pts showed: IgA nephropathy, hereditary nephritis, thin GBM, normal kidney. 36 pts were followed for 2.8±2 years (1-11 years). IMH persisted in all but none had decrease in GRF or developed proteinuria.

Family studies in the majority of pts included inquiries about a family history (FH) of kidney disease (KD) (other than UTI or urological disease) deafness (D), and tests of family members for IMH. A FH of KD was found in 15%, of D in 18% (of KD and D in 10%. IMH was found in 58% of families tested. In those families, 52% of those tested were affected. Their BP, S. Creatinine and audiograms were normal.

Conclusions: In 10-15% of children with IMH, the FH suggests hereditary nephritis. In half the other cases, IMH is familial and inherited as an autosomal dominant. The good health of the pts and of affected parents and grandparents suggests familial IMH has a good prognosis. In non-familial cases the short term prognosis is good but the long term prognosis is not known.

● 1460 ANGIOTENSIN II INFLUENCES THE ACCUMULATION OF AMINO ACIDS BY IMMATURE & ADULT RAT ISOLATED RENAL TUBULES,

Robben Gingery, Theodore Goodfriend, Russell Chesney, Univ. of Wisconsin Hospitals, Dept. of Pediatrics, Madison, WI.

Angiotensin II (Ang II) can directly affect the handling of sodium (Na^+) in the renal tubule. Hollemans et al (Fed Proc 31: 542, 1972) showed that Ang II caused enhanced Na^+ efflux from kidney cortex and Ang II blocks Na^+ reabsorption by the proximal tubule. Since the amino acid taurine (T) is transported by an Na^+-dependent mechanism, we measured the influence of Ang II on T accumulation in collagenase-isolated tubules. Ang II was found to block the uptake of 10 µM T by tubules. This concentration of T is accumulated by the low-Km, high-affinity transport system. The 5-min distribution ratio (DR), or (CPM ^3H·T/ml intracellular fluid (divided by) CPM ^3H·T/ml extracellular fluid) was altered in tubules.

Ang II	0	10^{-4}M	10^{-6}	10^{-8}	10^{-10}	10^{-12}
DR ($\bar{x}$ ± SE) (*p<.05)	15.7 ± .4	12.7* ± .3	14.7* ± .5	15.5 ± .3	15.6 ± .3	14.9 ± .5

Similar results were found using 4-week-old weanlings. This inhibition of uptake was found throughout the time course of uptake. The initial rate of uptake was decreased to 66.7% of control at 15, 30, 60 and 120 sec. The efflux of T from tubules pre-loaded with T was unaffected by Ang II. These results suggest that high concentrations of Ang II can influence the renal handling of organic solutes transported by an Na^+-dependent mechanism.

1461 ROLE OF ANGIOTENSIN II (AII) ON THE ADRENAL AND VASCULAR RESPONSES TO HEMORRHAGE (H) DURING DEVELOPMENT IN FETAL LAMBS.

R. Ariel Gomez, Jean E. Robillard, University of Iowa, Department of Pediatrics, Iowa City, IA.

The adrenal and vascular responses to 3 fetal H levels (H1=7-10%, H2=15-20%, H3=25-35%) were studied in 2 groups of chronically catheterized fetal lambs (7 <120 days, 7 >130 days gestation; term 145 days). Blood pressure (BP), plasma renin activity (PRA), Aldosterone (Aldo) and AII concentrations during H are shown:

	<120				>130			
	Con	H1	H2	H3	Con	H1	H2	H3
PRA ng/ml/hr	2.2 ±0.5	2.7 ±0.8	6.0* ±2.4	11.7* ±3.3	8.3 ±2.8	16.8 ±7.7	23.7* ±7.7	48.4* ±12.7
AII pg/ml	40.6 ±5.3	37.0 ±5.4	42.6 ±5.5	54.4* ±6.6	45.1 ±8.2	57.8 ±11.2	77.1* ±16.3	135.1* ±37.4
Aldo pg/ml	41 ±5	38 ±7	42 ±8	48 ±6	47 ±9	68 ±18	73* ±14	121* ±16
BP mmHg	42 ±1	38 ±1	37* ±1	36* ±2	47 ±2	46 ±3	46 ±4	47 ±1

(*p<0.05 when H values are compared to control.) PRA and AII rose in both groups ($p<0.05$), but during H3 the rise was higher in fetuses >130 days ($p<0.05$). The slope of the regression line between PRA and AII was similar in both groups. Aldo did not change in young fetuses but increased ($p<0.001$) in old ones, correlating with the rise in AII ($r=0.70$, $p<0.001$). BP did not change in fetuses >130 days but decreased in those <120 days ($p<0.05$). We conclude that while the AII response to rise in PRA is similar for both groups, the stimulation of the renin-angiotensin system during H is age-dependent and modulates Aldo and BP responses during the last third of gestation.

1462 ROLE OF ANGIOTENSIN II (AII) PRODUCTION ON THE RENAL AND VASCULAR RESPONSES TO HEMORRHAGE (H) DURING FETAL LIFE.

R. Ariel Gomez, Jean E. Robillard, University of Iowa, Department of Pediatrics, Iowa City, IA.

The renal and vascular responses to 3 levels of H (H1=8-10%, H2=18-20%, H3=30-35%) were studied in 2 groups of chronically catheterized fetal lambs >130 days gestation (term 145 days). A control group (H-C, n=7) was compared to a second group (H-CEI, n=6) which received a constant infusion (5 µg/kg/min) of captopril. During H, AII levels rose from 45±8 to 145±37 pg/ml ($p<0.005$) in H-C and correlated with H levels ($r=0.61$, $p<0.01$), while no changes were observed in H-CEI. Strong correlations were also observed in H-C between H levels and the % changes (%Δ) in renal blood flow (RBF) ($r=-0.75$, $p<0.001$) and renal vascular resistance (RVR) ($r=0.67$, $p<0.001$) while no correlations were found between these parameters in H-CEI. %Δ in glomerular filtration rate (GFR), RBF, RVR, filtration fraction (FF) and blood pressure (BP) in H-C were also compared to %Δ observed in H-CEI for each H level.

	H-C			H-CEI		
	H1	H2	H3	H1	H2	H3
GFR	3±4	-5±8	-23±10	-10±17	-10±14	-23±15
RBF	-11±5.5	-24±6	-52±8	6±12	-21±12	-52±14
RVR	11±8*	34±13	155±56	-19±9*	3.4±10	37±46
FF	8±5*	10±15	173±29	-25±9*	9±22	71±52
BP	-3±4	-3±5	-3±5*	-5±7	-15±9	-28±1*

(*p<0.05 when H-C compared to H-CEI (BP) at that H level) It is suggested that AII is an important modulator of renal and BP responses to H during fetal life. The increase in FF in H-C and the decrease in H-CEI at the first H level suggests that A-II controls GFR at low H levels by constricting the efferent arteriole.

1463 HEMATURIA ASSOCIATED WITH TRANSFUSIONS IN SICK PREMATURES: A POSSIBLE CAUSE FOR "SPONTANEOUS" HEMATURIA.

Ronnie Guillet, Jerene S. Delaney, Susan H. Sniderman, Roberta A. Ballard, Ronald I. Clyman. Mt. Zion Hospital and Medical Center, Department of Pediatrics, San Francisco, California.

Spontaneous hematuria has been shown to be more frequent in the sick premature than in the full-term neonate (Ped. Res. 15:692, 1981). We have observed that hematuria among premature infants frequently follows transfusions. We therefore investigated the frequency of transient heme-positive urine by dipstick (Ames) related to transfusions in sick prematures. Twenty-two infants in our NICU were studied by placing dipsticks in their diapers so that each urine voided could be assessed. All infants had heme-negative urines for several hours prior to a transfusion. Ten of 22 developed heme-positive urine within 6 hours of beginning a transfusion of packed red blood cells. Those who developed heme-positive urine had a lower birth weight (1010 ± 253 gm vs 1590 ± 688 gm, mean ± S.D., $p<0.025$) and were of younger gestational age (28.2 ± 2.1 wks vs 31.6 ± 3.3 wks, $p<0.01$) than those with heme-negative urines following transfusion. There was no difference in postnatal age at transfusion, amount transfused, route employed (umbilical artery vs peripheral vein), changes in blood pressure, nor incidence of hyaline membrane disease between the 2 groups. Transient heme-positive urine following transfusions may be a function of renal maturation and may explain some of the transient "spontaneous" hematuria observed in sick premature infants.

1464 ANATOMICAL AND PHYSIOLOGICAL EFFECTS OF EXPERIMENTALLY INDUCED CONGENITAL HYDRONEPHROSIS DURING FETAL LIFE: A PRELIMINARY REPORT. Charles E. Hawtrey, Jean E. Robillard, Univ of Iowa, Depts Urology and Pediatrics, Iowa City, IA.

Unilateral congenital hydronephrosis was produced in 5 fetal lambs between 80-100 days gestation (term 145 days) by inducing sclerosis in a small segment of the ureter near the pelvis using a solution of 100% ethyl alcohol and 4% formalin. All fetuses were returned to the uterine cavity and studied between 18 and 44 days after birth. In all animals studied the degree of hydronephrosis and of muscular hypertrophy of the pelvis was proportionate to the duration of obstruction. The hydronephrotic kidneys demonstrated a significant decrease in glomerular filtration rate (GFR) and urine osmolality (Uosm) and a rise in fractional excretion of sodium ($FE_{Na}+$) when compared to the control kidney. Renal blood flow (RBF) decreased in 4 of 5 animals studied.

	Control Kidney	Hydronephrotic Kidney
RBF ml/min	187±67	83±21
GFR ml/min	17.1±3.8	5.5±2.8*
$FE_{Na}+$ %	0.54±0.35	1.79±0.65*
Uosm mosm/kg H_2O	800±203	262±14*

(* $p<0.05$) The present study demonstrates the feasibility of inducing congenital hydronephrosis during fetal life. Moreover, the present model may be used in the future to evaluate the effect of relieving in utero urinary tract obstruction on the anatomical development of the kidney and on the maturation of the renal function after birth.

1465 A NETWORK REVIEW OF CHILDREN AND ADOLESCENTS UNDERGOING CHRONIC DIALYSIS. Ronald J. Hogg, Robert E. Lynch, Susan Conley, and John Murphy (Sponsored by Billy S. Arant, Jr.). Univ TX Depts Ped, Dallas, Galveston and Houston, and ESRD Network 11, Texas.

We have assessed the health care delivery to all children and adolescents under 21 years being treated in pediatric and adult dialysis centers in our ESRD Network. At the time of review, 115 patients(pts) under 21 years were being dialyzed in 38 of the Network's 65 facilities. This represented 3% of all pts on dialysis in the Network. 20% of pts were on home peritoneal dialysis. Age ranged from 7 months to 20 years with a mean age of 15 years in the 50 boys and 16.5 years in the 65 girls. 33 pts had previously rejected renal transplants(TP), 4 had rejected 2 TP. 57(50%) were considered active candidates for living related or cadaveric TP. Of the 58 pts who were not, 33 were medically unfit and 25 refused. 30 of the medical reasons were temporary (less than 6 months on dialysis--10; recent TP rejection--6; awaiting pre-TP surgical procedure--10). 23 of the 25 pts refusing TP were aged 16-20 years; 6 had previous unsuccessful TP. 94 pts (82%) were evaluated in a TP center within 3 months of starting dialysis. Nutrition status was checked monthly in 84% and quarterly in 16%. Social work services were available to all pts with assessment monthly in 98%. Continuing education was maintained in all 32 children aged 6-15 years (29 school, 1 home, 2 in-unit). 68% received vitamin D supplement, 99% were on phosphate(phos) binders, 70% had pre-dialysis serum phos less than 6 mg/dl, 95% had bone x-rays at least biannually and 70% had serum calcium, phos and alkaline phosphatase measured monthly.

1466 CAPTOPRIL: LONG-TERM MANAGEMENT IN A PRETERM INFANT AND OLDER CHILDREN WITH HIGH RENIN HYPERTENSION: LEONARD C. HYMES, BARRY L. WARSHAW (Spon. by G. Brumley): Emory University School of Medicine, Dept. of Ped., Atlanta.

Six children with high renin hypertension were effectively treated with angiotensin converting enzyme inhibitor-Captopril (C) for a mean period of 9.5 mo. All pts. had failed to respond to conventional therapy. Age groups included a 3 wk. preterm (33 wk. gestation)with renovascular compromise related to umbilical artery catheterization and older children 6-13 yrs. Peripheral renin activity ranged from 12.9 to 168.4 ng/ml/hr. All pts. exhibited a triphasic BP response during the first week of treatment. Pretreatment MAP ranged from 122.0 to 155.3 mm Hg (mean: 135.3 mm) and 78.3 to 111.5 mm Hg (mean: 95.4 mm) after sustained C therapy. C dose ranged from 1.4 to 5.4 mg/kg/day. In addition, 4 pts. required diuretics for adequate BP control. Significant adverse reactions occurred in 2 pts. The preterm infant exhibited a transient rise in creatinine (0.7 to 1.7 mg/dl) which returned to normal within 2 mo. without altering C. treatment. A second pt. with chronic renal failure exhibited a marked increase in BUN (80 to 276 mg/dl) requiring chronic dialysis but without a corresponding rise in creatinine. Renal function in a third pt. with chronic progressive renal failure continued to deteriorate but could not be directly attributed to C. In all, C was effective therapy, especially in the preterm pt. who exhibited normal growth velocity while treated with C (18.7 lbs. at 11 mo.). However, C may adversely effect renal function when MAP is markedly reduced especially in pts. with compromised renal blood flow and chronic renal failure.

1467 ABNORMAL CIRCADIAN BLOOD PRESSURE VARIATION IN RENAL TRANSPLANT RECIPIENTS.

Julie R. Ingelfinger, Michele Topor, Warren E. Grupe, and Raphael H. Levey. Children's Hospital Medical Center, Boston Mass. 02115

A disproportionate number of night-time episodes of hypertensive crisis in renal transplant patients (Tx) led us to examine the phenomenon of circadian variation in blood pressure (BP) in that population. A variety of studies in normal individuals confirm that both systolic and diastolic BP is usually lowest in the morning and rises during the day, becoming maximal in the late afternoon and early evening. Seventy-nine hospitalized Tx patients with sufficiently frequent BP measurements beyond the first post-operative week were included in the present study. 52/79 (66%) showed delayed circadian rhythm; 27/79 (34%) had usual variation. All 52 Tx with delayed circadian rhythm had some degree of hypertension; but the delay continued, even when all blood pressures in the 24 hour cycle were within a normal range. In contrast, only 12 of the 29 Tx with normal circadian rhythm were hypertensive. To control marked nocturnal increases in BP, we have administered increased doses of night-time antihypertensives in those Tx with severe evening or night-time hypertension. We have been able to control hypertension in over 80% of Tx with elevated BPs. The mechanism of reversed circadian rhythm of BP is unknown at this time. However, the fact that Tx patients take exogenous steroids which interfere with endogenous glucocorticoid production may be related. Elucidative studies are ongoing.

● **1468** THE EFFECT OF CHRONIC METABOLIC ACIDOSIS ON CALCIUM AND PHOSPHOROUS BALANCE. B.A. Kaiser, H. Leitz, E.S. Moore, M.J. Favus, F.L. Coe. Michael Reese Med. Ctr., Univ. Chicago, Pritzker Sch. Med, Depts Ped and Med, Chicago, IL.

Chronic metabolic acidosis (CMA) is usually accompanied by hypercalciuria and a negative calcium (Ca) balance in adults. However, the effect of CMA on Ca and phosphorous (P) balance during a period of rapid growth has not been studied. Therefore, we placed weanling rats on drinking water containing increasing amounts of NH_4Cl (1.5 to 2.0%) to produce CMA, acid group A (n=8), and pair-fed a vitamin D replete diet containing 0.4% Ca and P, to a control group C (n=8), who received distilled water. Group A developed CMA (pH 7.23±.04 vs 7.46±.01 units, $p<.001$; HCO_3^- 12.5±1.3 vs 21.3±0.6 mM, $p<.001$). Serum Ca (10.1±.1 vs 9.2±.3 mg%, p=ns) and serum P (9.2±.5 vs 9.2±.3 mg%, p=ns) did not differ between A and C. The Ca intake of A and C were the same (142.3±16.8 vs 143.4±17.5 mgs/3 days(d), p=ns). However, A had a higher urinary Ca excretion (6.0±1.4 vs 1.8±0.9 mgs/3d, $p<.001$), but a lower fecal Ca loss (13.2±4.7 vs 20.8±5.9 mgs/3d, $p<.05$) resulting in a similar Ca balance between A and C (120.0±16.1 vs 119.0±18.0 mgs/3d, p=ns). P intake (132.9±8.7 vs 132.9±8.4 mgs/3 d) was equal for A and C, but A had greater urinary P excretion (13.4±1.6 vs 5.3±2.0 mgs/3d, $p<.01$) and lower fecal P loss (16.1±2.0 vs 24.2±6.1 mgs/3d, $p<.05$)resulting in similar P balance (110.3±5.4 vs 114.1±8.7 mgs/3d, p=ns). Therefore CMA induced by oral NH_4Cl during rapid growth produced the expected hypercalciuria, but this is accompanied by an increase in intestinal Ca absorption that allows the animal to remain in Ca balance.

● **1469** DEVELOPMENTAL CHANGES IN THE FACTORS AFFECTING VOLUME FLOW ACROSS THE INTERCELLULAR CHANNELS OF THE PROXIMAL TUBULE. Frederick Kaskel, Adarsh Kumar, Earle Lockhart, Andrew Evan, and Adrian Spitzer. Albert Einstein Col. of Med. & Indiana Univ. School of Med., Depts. of Pediat. & Anat., Bronx, NY & Indianapolis, Ind.

The osmotic conductance of the proximal tubule is ≈10 fold higher in the newborn than in the adult due mainly to a higher permeability of the intercellular channels (ICC). In order to assess the impact of this difference on fluid flow through the ICC, measurements of the variables involved in this process were performed in guinea pigs of 1 to 68 days of age. A servo-nulling device was used to measure hydrostatic pressure and the micro method of Viets et al was used for protein determinations. The diameter of the zona occludens, estimated from microinjections of tracer amounts of non-electrolytes of graded molecular weights, was found to decrease from 4.5 to 3.5 Å (n=21) while the length of the ICC, measured on photomicrographs of thin sections (15000X), increased from 5 to 8.9 μm (n=16). The morphologic changes can account for a ≈5 fold increase in resistance across the ICC at comparable rates of flow. Concomitantly, intratubular hydrostatic pressure rose from 5.8 to 12.1 (n=11, r=.96), peritubular hydrostatic pressure from 4.2 to 9.1 (r=.95) and oncotic pressure of the peritubular blood from 12.5 to 29.7 mm Hg (r=.90). These changes resulted in an increase in the transtubular pressure gradient from 14.0 to 32.7mm Hg (≈2.5 fold). Thus, the increase in resistance of the ICC exceeds by at least 2 fold the rise in forces promoting the reabsorption of fluid from the proximal tubule. A disproportionate increase in active Na^+ transport needs to be postulated in order to account for the maintenance of the glomerulo-tubular balance observed to obtain throughout development.

1470 DEFECT OF NEUTROPHIL (PMN) CHEMOTAXIS IN URINARY TRACT INFECTION (UTI). Abdul J. Khan, Kusum Kumar, Mathew Varghese, Parvin Khan and Hugh E. Evans. Dept. of Ped. Jewish Hosp Med Ctr/SUNY Downstate Med Ctr Brooklyn, NY

PMN chemotaxis in UTI has not been studied. 17 patients (Mean age 5.5 years) were studied before therapy of an acute UTI and within 3 days post therapy. Studies were repeated 4-12 weeks later and again in a subsequent recurrent UTI in 7 cases. Modified Boyden's technique was utilized. PMNs were placed in the upper and chemotactic factors (CF) in the lower compartment with 3μ micropore filter between. Three types of CF were utilized namely 1) endotoxin activated serum (EAS) 2) CF derived from an standard E Coli (ECF) 3) Patients' own bacterial factors (PBF). PBF was prepared from each organism isolated. 17 subjects matched for age served as controls. Mean (± 1SE) chemotactic Indices (CI) are presented in the table. CIs with

	Control	UTI	After Therapy	4-12 wk	Recurr,UTI
EAS	63(4.1)	33(2.2)	43(2.5)	62(2.7)	30(3.1)
ECF	60(2.6)	33(2.3)	41(2.3)	64(5.4)	31(3.1)
PBF	59(3.5)	30(1.1)	37(2.8)	62(4.4)	28(2.4)

UTI were lower than those of controls ($P < 0.005$ in each instance) and improved just after therapy but remained lower than control values ($P < 0.02$). Values became normal 4-12 weeks later but during the recurrent UTI decreased again ($P < 0.005$). PMN chemotaxis is defective during UTI and returns to normal gradually after therapy. The defect is not specifically associated with any CF and appears to be secondary to UTI episodes.

1473 CLINICOPATHOLOGIC CORRELATES OF ECHOGENIC KIDNEYS. Alan M. Krensky, Joseph Reddish, and Rita L. Teele. (Spon. by John A. Kirkpatrick, Jr.) Harvard Medical School, Children's Hospital Medical Center, Boston, MA.

A retrospective review of all echogenic kidneys discovered by abdominal ultrasonography from 1979-1981 revealed 37 patients. Six had small, highly echogenic kidneys associated with end-stage renal disease. Of the remaining 31, 11 had glomerular disease (4 nephrotic syndrome, 4 hemolytic uremic syndrome), 17 had tubulointerstitial disease, and 2 had no evidence of renal disease. Large kidneys were typically seen in nephrotic syndrome, acute tubular necrosis (2 myoglobinuria, 1 toxic, 1 anoxic), and storage diseases (3), while small kidneys were typical of renal dysplasia (4). Three of 4 kidneys studied in hemolytic uremic syndrome were of normal size. Two general patterns of echogenicity were defined (1) diffusely increased echoes with or without medullary involvement, and (2) blotchy focality of echoes with relative sparing of the medulla. We were unable to correlate specific patterns of echogenicity with either general categories of glomerular or tubulointerstitial disease or specific clinical or pathologic diagnosis. This suggests that echogenicity is the non-specific result of changes in renal perfusion, cellular infiltrate and scarring. Therefore, although increased echogenicity was associated with renal disease 95% (35/37) of the time, the pattern of echogenicity was apparently non-specific and of no further diagnostic significance.

● 1471 PHYSIOLOGICAL BASIS OF GLOMERULOTUBULAR BALANCE GTB) IN MATURING RATS. V. Kon and I. Ichikawa. Harvard Medical School, Children's Hospital Medical Center and Brigham & Women's Hospital, Boston, MA.

The increase of single nephron (SN) GFR in young growing rats (>40 day) is a consequence of rise in glomerular plasma flow (Q_A) and ultrafiltration coefficient (K_f) presumably reflecting growth of the renal microvascular tree. To define the mechanism of increased absolute proximal fluid reabsorption (APR) associated with this rise in SNGFR, the APR and determinants of peritubular capillary uptake of APR were measured in ~40 day old Munich-Wistar rats. Results were compared with those of adult rats (JCI 65:1192 1980). (Mean ± 1 SE; †P<0.05).

	SNGFR	APR	Q_E	Π_E	P_E	$\bar{P}_T$	K_T
	nl/min			mmHg			nl/(s·mmHg)
YOUNG (n=8)	16±1†	6±1†	31±3†	28±2	20±1	10±2	.014±.004†
ADULT (n=7)	58±2	24±2	98±5	31±1	21±1	10±1	.043±.004

Thus, proportional increase in SNGFR vs. APR was demonstrated in the maturing rats. As with interstitial pressures, oncotic (Π_E) and hydraulic pressure (P_E) at the beginning of the peritubular capillary network remain essentially unchanged. Since pressure disequilibrium prevails along the peritubular capillary, a marked rise in plasma flow entering the capillary (Q_E) also fails to affect mean net reabsorptive pressure ($\bar{P}_T$), hence APR. Instead, peritubular capillary reabsorption coefficient (K_T) rose markedly, accounting entirely for the increase in APR. These data indicate that the maintenance of GTB reflects harmonious growth of renal microvasculature, i.e., glomerular (K_f↑)& arteriolar (Q_A↑) maturation balances development of peritubular capillaries (K_T↑).

1472 HEMOLYTIC UREMIC SYNDROME (HUS) AND CRESCENTIC GLOMERULONEPHRITIS COMPLICATING CHILDHOOD NEPHROSIS. Alan M. Krensky, Julie R. Ingelfinger, Warren E. Grupe and Seymour Rosen, Children's Hospital Medical Center and Beth Israel Hospital, Boston, Mass. 02115

We report three cases of nephrotic syndrome complicated by fulminant loss of renal function, microangiopathic hemolytic anemia, and thrombocytopenia. Though primary childhood nephrotic syndrome, due to a well-described spectrum of glomerular alterations such as focal and segmental glomerulosclerosis, and mesangial proliferative glomerulonephritis may progress to renal failure by an indolent course characterized by progressive glomerulosclerosis, interstitial fibrosis and tubular atrophy, these cases seem distinct. At HUS episode platelets fell from elevated levels to 104,000/mm^3 ~ 143,000/mm^3. Hematocrits varied from 11-20%, and reticulocyte counts from .8-12%. All patients required dialytic therapy acutely; two had severe hypertension; one had GI bleeding; one had prolonged PT/PTT. Two patients had several hemolytic episodes.

These three children had mesangial proliferation and/or focal segmental glomerulosclerosis on original renal biopsy but developed crescentic glomerulonephritis related to HUS. None regained renal function; two who had renal transplants have had episodes of nephrosis responding to steroids. The third patient is on chronic hemodialysis. These cases suggest an association between lipoid nephrosis, focal segmental glomerulosclerosis and crescentic glomerulonephritis, and may represent an unusual pathway in the evolution of childhood nephrosis.

1474 SINGLE DOSE GENTAMICIN THERAPY (SDT) OF URINARY TRACT INFECTIONS (UTI). K. Kumar, A.J. Khan, M. Varghese and H.E. Evans, Dept. of Ped. Jewish Hosp. Med Ctr/SUNY Downstate Med. Ctr. Brooklyn, NY

SDT, effective in adults with UTI has not been evaluated in infants and children. 20 consecutive episodes of UTI (mean age 8 years) were treated with 5 mg/kg of Gentamicin given as one single IM dose. Equal number of UTIs in age matched patients given multidose therapy (MDT) for 10 days served as control. DX was based on 2 positive urine cultures (U/C) with $\geq 10^5$ colonies/ml. U/C were repeated at 4 different times during 4-6 weeks of follow up. Cure was defined as absence of recurrence, relapse and reinfection as recurrence due to same and different organism respectively. UTIs were characterized as cystitis (CYS) or pyelonephritis (PN) based on elevated CRP and/or ESR as indicative of PN. Results are presented (table). Cure and recurr rates in SDT and MDT group

RX Group	N	CURE #(%)	RECUR #(%)	RELAPSE #(%)	REINFECT #(%)
SDT(Total)	20	15(75)	5(25)	1(5)	4(20)
SDT(CYS)	14	12(86)	2(14)	0(5)	2(14)
SDT(PN)	6	3(50)	3(50)	1(17)	2(33)
MDT(PN)	6	6(100)	0(0)	0(0)	0(0)
MDT(CYS)	12	10(83)	2(17)	0(10)	2(17)
MDT(Total)	20	18(90)	2(10)	0(0)	2(10)

were similar ($P > 0.5$). In SDT group patients with PN had significantly higher relapse and reinfection rates than CYS ($P < 0.05$). Recurrences in PN patients given SDT were more than those given MDT ($P < 0.01$). Results in CYS patients given single or multiple doses were similar. We conclude that single dose is as effective as 10 day therapy in cystitis but not in PN.

● 1475 DIETARY STIMULATION OF 1,25(OH)$_2$D (1,25D): IN VITRO STUDIES IN D-REPLETE (D+) RATS. C.B. Langman, V. Tembe, E.S. Moore, F.L. Coe, M.J. Favus. Michael Reese Med. Ctr., Univ. Chicago, Pritzker Sch. Med., Depts. Ped. and Med. Chicago, IL.

Measurements of 1,25D were made in renal slices from D+ rats on either normal chow (NC:1.2% calcium (Ca), .99% phosphorus (P), or very low calcium diet (VLCD:.002%, .34%P). Slices were incubated in 1.5 ml Krebs bicarbonate with 11.1 mM glucose, 60 µM 25OHD$_3$, at 37°C in a metabolic shaking water bath. 1,25D was quantitated by competitive protein binding assay. Results (mean ± SEM) expressed in pmol 1,25D/mg protein in slice and pmol/ml in serum were:

	NC	VLCD	
Basal:	0.86±.2(4)	21.8±8(11)*	( )=No. of observations
+60′:	2.8±1.6(4)	15±6(10)*	
Serum:	0.11±.03(8)	0.5±.06(9)*	*p<.05 vs NC

Significant correlations existed between serum 1,25D and basal slice content ($r=.76$, $p<.01$) between basal slice content and net synthesis ($r=-.76$, $p<.01$) and between animal weight (age) and basal slice content for each diet (VLCD: $r=-.72$, $p<.01$; NC: $r=-.81$, $p<.01$). These results suggest (a) basal 1,25D content reflects synthesis rate and serum 1,25D levels (b) in vitro 1,25D synthesis is tightly regulated by slice 1,25D content (c) diet is a major influence to 1,25 synthesis rate (d) previous studies utilizing radiolabelled 25OHD$_3$ conversion may have underestimated enzymes kinetics because of existing basal levels.

● **1476** THE ROLE OF BONE IN ADJUSTING TO A HIGH SALT DIET IN THE GROWING PIGLET. H. Leitz, E. Simpson, E.S. Moore, B.A. Kaiser. Michael Reese Med. Ctr., Univ. Chicago, Pritzker Sch. Med., Dept. Ped., Chicago, IL.

Studies have shown that growing animals exposed to a high sodium intake retain Na in excess of that needed for growth. We have studied the influence of high NaCl intake on kidney function and body composition in growing piglets. Group 1 (G1) received a formula providing 2-3 mEq Na/kg/day (normal Na diet). Group 2 (G2) received the same formula with an additional 20 mEq/kg/day (high Na diet). Some piglets in each group were used for kidney function determinations (G1a, n=5 and G2a, n=5) and others were used for tissue and bone analysis (G1b, n=7 and G2b, n=7). Kidney function, GFR (G1a 0.32±0.13, G2a 0.38±0.12 ml/min/gm kidney, p= ns), FENa (G1a 1.10±0.44, G2a 0.82±0.12, p=ns) and NaKATPase (G1a 1.23±0.39, G2a 1.23±0.36 mmoles Pi/gm kidney/30 min, p=ns) was equal in the two groups. However, serum aldosterone concentration was lower in G2 (G1 33.7±9.0, G2 21.1±9.4 ng/dl, p<.05). Tissue analysis showed that Na content did not change with high Na intake in either the liver (G1b 0.13±0.02, G2b 0.11±0.03 mEq/g FFDW, p= ns) or muscle (G1b .084±0.033, G2b 0.096±0.027 mEq/g FFDW, p=ns). However, there was a significant increase in bone Na in the high Na group (G1b 0.150±0.018, G2b 0.164±0.016 mEq Na/g wet wt., p< 0.01) with a concomitant loss in bone water (G1b 41.8±6.1, G2b 37.6±5.3% H_2O, p<0.025). In addition, in 4 animals from each group the exchangeable ^{24}Na space showed a corresponding decrease (G1b 52.5±0.8, G2b 48.0±1.5%, p<0.02). Bone metabolism seems to be a major factor in a growing animal's ability to adjust to a high Na intake.

1477 CHRONIC PERITONEAL DIALYSIS IN CHILDREN: A COLLABORATIVE EXPERIENCE. Gary M. Lum, Southwest Pediatric Nephrology Study Group.

Intermittent (IPD), Continuous Ambulatory (CAPD), and Continuous Cycling (CCPD) peritoneal dialysis were evaluated in 30 children, ages 1-19 years, who received chronic peritoneal dialysis (PD) for at least 6 months. This report focuses on the access-related and infectious complications of the various PD techniques employed from July 1975 to August 1981. Average time on PD was 17.02 months per patient. 95.5% of patients used the Tenckhoff catheter. 60% of all patients had a catheter complication requiring revision for obstruction, exit site infection, or persistent peritonitis. There was no significant difference in the occurrence of obstruction between surgically-placed catheters and those inserted at the bedside. A significantly greater percentage of exit site infection occurred in those placed surgically (81.8% versus 19%). Average catheter life was 29 months. 60% of all patients developed peritonitis, averaging one episode per 13 patient months. A decrease in occurrence of peritonitis was observed the longer the patient received PD with only 4.8% of all episodes of peritonitis occurring in the group at 19 months or greater. Of all episodes of peritonitis, 44% occurred with CAPD and 17% with CCPD. Although experience with these latter modes is too short to compare with IPD, our results to date suggest that all three forms of PD continue to be acceptable treatment for ESRD in children. Additional therapeutic benefits that may result from the use of CAPD or CCPD are currently being evaluated.

1478 THERAPEUTIC AND COGNITIVE EFFECTS OF ALPHAMETHYLDOPA AND TIMOLOL IN HYPERTENSIVE CHILDREN. S. MacLeod, J. Balfe, J. Correia, W. Logan, D. Stefanaitis and J. Swanson. Research Institute (Spon by S. Spielberg), The Hosp. for Sick Children and Depts. of Paediatrics and Pharmacology, Univ. of Toronto, Canada.

Most antihypertensive drugs cause CNS side effects which may deter treatment of mild or moderate hypertension in children of school age. We studied 16 children (9 F, 7 M) aged 6-18 (mean±S.E.; 13.2±1.1 years) with established hypertension secondary to renal disease. Patients received alphamethyldopa (A) or timolol (T) on an escalating dosage scale until optimal control was achieved in an open, randomized, crossover design. Mean final daily dose was 1000mg A and 28.8mg T. Each 12 week treatment block was preceded by a 4 week washout period. Results of treatment at peak drug effectiveness were:

	CONTROL	A	T
HR (beats/min)	86.6 ± 2.8	86.4 ± 2.1	77.6 ± 2.4
systolic BP (mmHg)	132.8 ± 3.4	127.8 ± 5.4	116.6 ± 2.7
diastolic BP (mmHg)	95.9 ± 2.9	89.0 ± 3.4	82.1 ± 2.6

T was more effective than A in 10 of 16 patients and approximately equal in efficacy in a further 5 patients. Cognitive effects of drug treatment were tested at 2 week intervals in all patients and at the same intervals 10 healthy controls were tested. Hypertensive patients showed cognitive impairment relative to normals but no significant difference was detected by ANOVA among control, A or T treatments in paired associate learning, arithmetic skills and performance on a tracking test. T appears preferable to A in young hypertensive patients although both are free of major cognitive effects.

1479 MESANGIAL IgM DEPOSITS IN MINIMAL CHANGE (MC) NEPHROTIC SYNDROME (NS): LACK OF PROGNOSTIC CORRELATION. Melinda McVicar, Myron Susin, Reid Selden, Manju Chandra. North Shore University Hospital-Cornell Univ. Medical College, Dept. of Pediatrics and Laboratories, Manhasset and New York, N.Y. (Sponsored by Fima Lifshitz).

Immunofluorescent deposits (IF) in the glomeruli of some patients with MCNS have been well documented and some authors have designated IgM mesangial nephropathy a distinctive entity with possible prognostic implications. In order to determine the significance of IF in MCNS, we reviewed the renal biopsy findings of 20 patients who were available for follow up 3-20 years (mean 7 years). IF was pos in 14: IgM 14, C_3 8, IgG 7. Mild mesangial hypercellularity was present in 9/14 patients with pos IF and in 0/6 patients with neg IF. The remainder had normal light microscopy. All patients were treated with prednisone 60 mg/M^2/day for 4 weeks followed by 40 mg/M^2, 3/7 days for 4 weeks. The clinical response of IF pos patients was 2 non-responders (subsequent remission), 7 frequent relapsers (> 2 relapses/6 mos), 1 infrequent relapser and 4 non-relapsers. The clinical response of IF neg patients was 1 non-responder (subsequent remission), 2 frequent relapsers, 1 infrequent relapser and 2 non-relapsers. IF was correlated with clinical response (non-responders + frequent relapsers vs. infrequent relapsers + non-relapsers) on the basis of whether IF was pos or neg. The difference was not significant (Chi square= .357). At final follow up all patients were in remission at least two years. We conclude that pos IF in MCNS does not worsen the usually good prognosis of this disease or alter the clinical response after treatment with prednisone.

● **1480** CELLULAR MALNUTRITION IN CHRONIC UREMIA. J. Metcoff, S. Dutta, G. Burns, P. Costiloe, J. Pederson, W. Matter. Depts of Pediatrics, Biochemistry, Medicine & Biostatistics, Univ. of Oklahoma Health Sci. Ctr., Oklahoma City.

The carbohydrate intolerance & distorted cellular balance of amino acids (AA) found in chronic uremics (CRF) suggest that malnutrition at the cellular level reduces energy metabolism & protein synthesis. This suspected relationship has not previously been demonstrated in CRF. Isolated leukocytes were used as a cell model in 42 adult CRF patients stabilized by hemodialysis 3x/wk & 32 normal control subjects. Plasma AA levels also were quantified in both groups. Plasma iron was reduced & HIS, ARG, SER, GLY, & ORN were increased; TAU & GLU were low in CRF. In the cells, ILE, LEU, VAL, & MET, were reduced while GLU, TAU were increased (all p<.05). Cell ATP, energy-related enzyme activities (pyruvate kinase & adenylate kinase (AK)), & protein synthesis (PS=3H-LEU inc.) also were reduced (p <.05). The low cell energy levels, PS, & AA imbalance were interrelated by matrix correlation, consistent with cellular malnutrition. Multiple regression best subset analysis indicated that cell levels of VAL + ORN best "explained" the variance in PS, while the energy-related activity of AK was best explained by the cell AA combination: ASP+THR-SER-GLU/AS-GLU+VAL+ILE. 18 patients received a standard AA infusion mixture post dialysis, dialyzer detached, 3x/wk for 4-5 weeks in an effort to improve the cell AA imbalance. Significant increases resulted for intracellular protein, ATP, AK, PS (in 12 of 18 patients; for 18, p=.07), GLU & GLY. The data suggests that some non-essential AA &/or increased energy levels may improve PS in CRF without correction of the essential AA imbalance.

1481 GAS EXCHANGE DURING HEMODIALYSIS (HD). Lawrence S. Milner, Alan D. Rothberg, Peter D. Thomson, Margaret Stothart (Spon by M. Jeffrey Maisels). Witwatersrand Univ, Johannesburg Hosp, Dept Peds, Johannesburg, South Africa.

Five children between 7 and 15 years who required chronic HD for renal failure were studied to evaluate the central and pulmonary effects of HD on gas exchange. Acetate dialysate was used, and dialysate pO_2 and pCO_2 (DpO_2, $DpCO_2$), arterial pO_2 and pCO_2 (paO_2, $paCO_2$), end-tidal CO_2 ($ETCO_2$) and minute ventilation (MV) were measured pre-HD and 15, 30, 60, 120 and 240 mins. after commencement of HD. Arterial-alveolar CO_2 gradient ($aADCO_2$) was calculated ($paCO_2$-$ETCO_2$). MV did not change significantly from pre-HD value of 8.9±1.1 l/min. (mean±SD). $aADCO_2$ increased significantly from 3.2 mmHg to 8.4±2.4 mmHg at 15 mins. (p<.01) and was still elevated at 120 mins. (9.1±3.4 mmHg, p<.02), indicating a sustained ventilation:perfusion (V/Q) mismatch. The $paCO_2$ increased from 29.8±3.5 mmHg pre-HD to 34.3±3 mmHg at 15 mins. (p<.05), but thereafter values were not significantly increased. $DpCO_2$ increased from 7.2±0.5 mmHg pre-HD to 13.6±2 mmHg at 15 mins. (p<.01) and remained significantly elevated whereas DpO_2 decreased from 112.7±7.8 mmHg pre-HD to 101.9±6.4 mmHg at 15 mins. (p<.05) and remained significantly depressed. There was an inverse correlation between $aADCO_2$ and paO_2 (r=.55, p<.01). These data show a significant V/Q mismatch, demonstrated particularly by the high $aADCO_2$ and the relationship to paO_2. The impairment in CO_2 excretion appears to be partially compensated by the loss of CO_2 into the dialysate, while uptake of O_2 from the dialysate partially corrects hypoxemia.

1482 AGE-RELATED DIFFERENCES IN CIS-DICHLORODIAMMINE PLATINUM (P)- INDUCED NEPHROTOXICITY. Donald I. Moel, Robert L. Safirstein, Wei Hsueh, Harold Thies, and Richard A. Cohn, (Spon. by George R. Honig). Northwestern Univ. and Children's Mem. Hosp., Chicago and Mt. Sinai Sch. of Med., NY.

Since young animals are often more resistant to nephrotoxins than adults, we compared the nephrotoxicity of P, an effective antineoplastic drug, in young rats (YR) and adults rats (AR). YR (133.3±1.9g) and AR(377.1±5.7g) were given a single ip dose of P at 35mg/m^2. Plasma creatinine (PCr) in YR on day 4 (1.61±.08mg/dl) day 7 (.47+.04mg/dl), and day 10 (.45±.14mg/dl) were significantly lower ($P < .01$) than that in AR on day 4 (2.8±.3mg/dl), day 7 (1.68±56mg/dl), and day 10 (.81±.27mg/dl); baseline values were similar. These differences were not due to differences in weight loss. To determine whether these age-related differences in nephrotoxicity were a function of differences in renal accumulation, excretion, or metabolism of P, analyses were performed by atomic absorption spectroscopy, scintillation counting and high performance liquid chromatography (HPLC). Renal tissue content was the same in YR(19.7±.53mcg/g tissue) compared to AR(19.9±.61mcg/g tissue) 24 hours after exposure to P. Plasma P levels were also similar at 24 hours, YR(1.61mcg/ml) vs AR(1.72mcg/ml). The % of labeled P dose excreted during the first 24 hours was similar in YR(53.7±2.4%) vs AR(50.1±2.1%). Unbound labeled P in renal tissue homogenates had similar HPLC profiles in YR and AR. As yet the basis for these age-related differences is unknown but is not due to differences in renal accumulation, excretion or metabolism of P. Since the efficacy of P is limited by its nephrotoxicity it is speculated that children with malignancies treated with P might tolerate higher doses with less nephrotoxicity.

● **1483** DIVALENT MINERAL METABOLISM IN UTERO. E.S. Moore, C.B. Langman, M. Loghman-Adham, M.J. Favus, F.L. Coe. Pritzker Sch. Med., Univ. Chicago, Michael Reese Med. Ctr., Depts. Ped. and Med., Chicago, IL.

To evaluate the role of fetal lamb (FL) kidneys in Ca and Pi homeostasis in utero, studies were done in 12 chronically prepared ewes and their FL age 100-148 days gestation (term=150). 6 control (C) Fl had sham bilateral nephrectomy (Nx) and 4 experimental FL had Nx. 2 separate FL had Nx and 1,25(OH)$_2$D$_3$ (NxD) (0.25-0.35 µg/24 h) was given IV after surgery (S) and daily for 4 days. FL blood was drawn at S and on Post S days (D) 1,3,5,8 and 10 for pH, ionized Ca^{2+}, total Ca, Pi and PTH. FL pH remained normal from S to D 10 in all groups. Results are mean ± SEM at S and D5:

	Ca		Ca^{2+}		Pi		iPTH	
Group	S	D5	S	D5	S	D5	S	D5
C	12.2 ±.23	11.8 ±.34	5.34 ±.43	4.90 ±.22	7.32 ±.52	7.33 ±.54	0.54 ±.20	0.58 ±.18
Nx	12.6 ±.36	9.1[b] ±.55	5.90 ±.13	4.00[a] ±.24	7.30 ±.28	9.70[a] ±.47	0.22 ±.14	3.28[c] ±.06
NxD	12.5 ±.44	16.7[c] ±.32	4.46 ±.15	6.96[c] ±.24	9.57 ±.37	8.93[b] ±.43	ND ND	ND ND

Ca, Ca^{2+} and Pi are mg/dl; PTH is ng/ml; ND=not done.
a=p<.01; b=p<.005; c=p<.001.
On D 10, Ca, Ca^{2+} and Pi in Nx were 7.65±.05, 3.01±.18 and 12.1±.43 mg/dl respectively and were significantly different from D (a; c;c). In NxD, D3 was not given after D4 and Ca, Ca^{2+} and Pi on D 10 were 9.35±.95, 2.74±.35 and 9.29±1.10 mg/dl respectively and were significantly different from C (b;a;c) but not from Nx. These data indicate that the intrauterine ewe to FL Ca^{2+} gradient is dependent on D3 produced by FL kidneys.

● **1484** INTRA-ARTERIAL ETHANOL FOR THERAPEUTIC RENAL INFARCTION. John K. Orak, Irvin F. Hawkins, George A. Richard. University of Florida College of Medicine, Shands Teaching Hospital, Departments of Pediatrics and Radiology, Gainesville, Florida

Renal infarction was produced by intra-arterial absolute ethanol to control hyper-reninemic hypertension in three patients, two with end-stage renal disease and one with an isolated area of ischemia in the lower pole of the kidney. A balloon occlusion catheter was placed in the renal artery, or into the segmental artery in the case of the selective infarction, through which 1-3 ccs of absolute ethanol were injected. Angiography performed 15 minutes after infarction revealed complete vascular occlusion of the kidney in the two patients injected in the main renal artery and segmental occlusion in the third patient. Blood pressure was controlled within 24 hours and antihypertensive therapy was discontinued within 4 days. None of the patients has required antihypertensive therapy during the 2-7 months of follow-up.

Renal embolization with particulate material has been used as a substitute for nephrectomy. It has, however, significant morbidity from peripheral embolization and a possibility for recannulization. In animal studies, neither recannulization nor development of collateral circulation have followed infarction produced by injection of absolute ethanol. Absolute ethanol appears to fulfill criteria for an ideal intravascular tissue necrosing agent. In the dosage used it has a profound local effect, with no evidence of peripheral infarction or systemic toxicity. This is the first report of renal infarction with intra-arterial absolute ethanol to control hyper-reninemic hypertension.

1485 NIGERIAN NEPHROTIC CHILDREN HAVE PRIMARY HYPOTHYROIDISM O.A.Oyemade,M.D.;F.A.Lukambi,FIMLA;O.A.Dada,PhD.; and B.Osotimehin,M.D., Ibadan, NIGERIA

Routine thyroid function studies were carried out in 24 children w/clinical and biochemical evidence of the nephrotic syndrome. These children ranged in age from 4-14 yrs., were in the active phase of their disease & presented facial edema, ascites, & pedal edema. There was severe hypoalbuminemia, ranging from 1.1-2.7 mg/dl (mean 1.9mg/dl), hypercholesterolemia ranging from 222-933 mg% (mean 409 mg%), & severe albuminuria, estimated qualitatively w/Albustix, ranging from 100-1000 mg/dl. One patient had microscopic hematuria. There was no clinical evidence of thyroid disease.

RESULTS OF THYROID FUNCTION TESTS (Mean + SE)

	T_3RU	T_4	FTI	TSH
NEPHROTIC	33.1%±1.22	3.9mg/dl±0.5	1.3±0.34	10.6units/ml±0.95
CONTROLS	29.8%±0.21	9.2mg/dl±0.16	2.7±0.16	4.4units/ml±0.17

CONCLUSION: The means of all the parameters measured were significantly different from those of normal controls. The abnormally high levels of TSH obtained in this study differ from results previously published. The low levels of T_4 & FTI in association w/high levels of TSH in patients suggests that a state of primary hypothyroidism exists in these nephrotic patients (in spite of clinical eurothyroidism). These findings are probably related to the severe glomerular lesions associated with Quartan malarial nephropathy.

1486 RENAL OSTEODYSTROPHY IN CHILDREN UNDERGOING CONTINUOUS AMBULATORY PERITONEAL DIALYSIS (CAPD). Luc Paunier, Isidro B. Salusky, Teresa L. Hall, Jack W. Coburn, Joel D. Kopple & Richard N. Fine. UCLA Sch. Med., UCLA Cntr.Hlth. Sci.,Dept. Peds & Med.& VA Wadsworth Med. Cntr.,Los Angeles, Cal.

Although many uremic children are now treated with CAPD, the effect of CAPD on growth & the skeleton are not well characterized Therefore, we evaluated these parameters in 12 pts,ages 2.3-15 yrs (mean,8.8 yrs) who underwent CAPD for a mean of 9.8 mos(range 6-15 mos). Patients received 4-5 exchanges/day with dialysate containing Ca(3.5 meq/L) & Mg(1.5 meq/L). Eleven pts were given 0.125-0.5 mcg/day of 1,25(OH)2D3;1 pt received dihydrotachysterol (0.25 mg/day). All pts ingested phosphate binders & had dietary Ca intake of 500-950 mg/day. At the beginning of CAPD, X-ray signs of osteodystrophy were mild in 6 of the 12 pts & severe in 6. All had elevated serum alk.p'tase (m ± sem 376 ± 20 u)& PTH levels. During CAPD, serum Ca & P averaged 9.7 & 5.5 mg% respectively, & were normal most of the time in 9 pts; 3 had elevated serum P & 3 had brief episodes of hypercalcemia. Serum alk.p'tase rose in 10 pts & fell in 2. Serum PTH levels remained elevated, X-ray signs of osteodystrophy improved in 2 pts, worsened in 1 & remained unchanged in 9. Height & weight were decreased in all pts. Growth velocity was low: 0.1 to 0.54 cm/mo(mean,0.29 cm/mo). These data indicate that hyperparathyroidism, osteodystrophy & diminished growth are common in pts undergoing CAPD. Larger doses of vitamin D or its metabolites or more Ca intake in diet or in dialysate, may benefit such pts.

1487 FOCAL SEGMENTAL GLOMERULOSCLEROSIS(FSGS), CRESCENTS AND RAPIDLY PROGRESSIVE RENAL FAILURE. F Ramirez, B Brouhard, RJ Cunningham, LB Travis, S Rajaraman, E Ellis, A Kalia. Univ. of Texas Medical Branch, Depts. of Pediatrics and Pathology, Galveston, Texas.

FSGS is the second most common cause of nephrotic syndrome(NS) in children. Within 10 years, half of these patients develop renal failure requiring dialysis or transplantation. The usual clinical course is marked by progressive decrease in renal function and sclerosis on biopsy over a period of months to years. We report a variant of FSGS exemplified by two children who developed chronic renal failure within 12 weeks of the onset of NS; repeat renal biopsies demonstrated extensive extracapillary glomerular proliferation(ECGP) and crescent formation. Both patients were male, less than 5 years of age presenting with NS resistant to steroid therapy with normal renal function. Renal biopsies done after 8 weeks of steroid therapy demonstrated findings compatible with FSGS. Within 12 weeks of the onset of NS both patients experienced a decrease in renal function with serum creatinine 2.9mg/dl and 5.7mg/dl respectively requiring dialysis. Repeat renal biopsies revealed extensive ECGP with crescent formation, coarse granular deposits IgG(1+), IgM(1+) and C3(3+), no electron dense deposits were seen. ANA, C3 and ASO titer were normal in both patients. Conditions associated with crescent formation and rapid progressive renal failure were excluded.

These patients represent a variant of FSGS characterized by rapid progression to renal failure with extensive ECGP and crescent formation.

1488 PROGNOSTIC FACTORS IN MEMBRANOUS NEPHROPATHY IN CHILDREN. F Ramirez, B Brouhard, LB Travis, E Ellis. Univ. of Texas Medical Branch, Dept. of Pediatrics, Galveston, Texas.

In trying to determine prognosis in children with membranous nephropathy, we reviewed the clinicopathological features and outcome of 22 pediatric patients, 11 males and 11 females, with membranous nephropathy. Age ranged from 11 months to 19.9 years (mean 12.9 years). Followup time was one month to 11.1 year (mean 4.8 years). All patients were biopsied within 16 months of onset of symptoms. Patients were divided in two groups; Group I (Gluck Stages I-II), Group II (Gluck Stages III-IV). Followup time was identical in both groups (mean 4.8 years). The nephrotic syndrome was present in 13 of 16 patients in Group I and in all six patients in Group II.

In Group I (n=16), eight patients had repeat biopsies 1 to 11 years (mean 3 years) after onset. Of these, two progressed to stages III-IV. Progression to renal insufficiency (creatinine two standard deviations above the mean for age) occurred in one of the 16 patients.

In Group II (n=6), two patients had repeat biopsies two years after, remaining in the same stage. Progression to renal insufficiency occurred in five of six patients.

The difference between the two groups is significant (p=0.001). The stage of glomerular lesion at the time of onset seems to be a factor in predicting the prognosis of membranous nephropathy in pediatric patients.

1491 CONTINUOUS AMBULATORY PERITONEAL DIALYSIS (CAPD) IN CHILDREN. Isidro B. Salusky, Teresa L. Hall, Stanley C. Jordan, Robert B. Ettenger, Richard N. Fine. UCLA Sch. Med., UCLA Cntr. for Health Sci.,Div. Ped. Neph. L.A., Cal.

Between Sept., 1980 & Dec., 1981, 26 children, mean age 9.4 yr (r 1.5-16.8) & mean body weight 22.2 Kg (r 7.16-40.8) received CAPD for a mean of 4.84 mos.(r 1-14). CAPD was the initial treatment for End-Stage-Renal disease (ESRD) in 11 children, whereas in 15 pts, CAPD was initiated following technical problems with hemodialysis (HD), intermittent peritoneal dialysis (IPD) or transplant rejection. Of the 26 children, 22 are currently undergoing CAPD from 1 to 14 mos., 3 have received a renal transplant & one has transferred to continuous cycling peritoneal dialysis. Comparison of current CAPD biochemical parameters with pre-dialysis values of those children who underwent at least 3 mos. of HD or IPD shows lower levels of BUN, serum creatinine, K+ & PO_4 & higher levels of CO_2 & Ca^{++}. Only one pt. required antihypertensive therapy on CAPD. Total energy intake (oral + dialysate) in 12 children undergoing CAPD for more than 3 mos. was 82% of the RDA. Growth velocity was low: 0.29 cm/mo in 9 children undergoing CAPD for more than 6 mos. The major technical complications have been peritonitis (incidence rate 1/12.1 pt. mos.) & the development of ventral (8) & inguinal hernia (1). Only 1 Tenckhoff catheter had to be replaced. Rehabilitation has been excellent, with all school aged children attending school. When indicated, exchanges are performed by the pt. and/or school nurse. We conclude that CAPD appears to be an adequate treatment modality for children with ESRD.

● **1489** CELLULAR AND HUMORAL IMMUNE MECHANISMS IN TUBULOINTERSTITIAL NEPHRITIS (TIN). L. Reisman, M. Suthanthiran, W.W. McCrory. Pediatric Nephrology and Rogosin Kidney Center, The New York Hospital, New York, New York.

Brown-Norway(BN) rats immunized(IR) with renal medulla from Sprague-Dawley(SD) rats, complete Freund's Adjuvant and Pertussis vaccine developed a renal lesion characterized by focal interstitial and perivascular mononuclear cell infiltrates without glomerular involvement. Cellular involvement in the pathogenesis of TIN was indicated by the presence of monocytes 64±6% (mean±SD), T-cells 24±11% and B-cells 26±13% among the cell infiltrates. Humoral participation was indicated by the presence of IgG antibodies directed against tubular basement membrane(TBM) as determined by direct immunofluorescent(IF) assay. The presence of circulating antibody against TBM and tubular cell antigens was determined by indirect IF assay. Sera of IR were used in in-vitro studies to determine the presence of antibody dependent cellular cytotoxicity(ADCC) and complement dependent cytotoxicity(CDC) using naive BN spleen as effector cells and BN kidney and SD kidney and spleen as target cells. In the ADCC significant cystolysis of the above target cells was present. In the CDC there was significant lysis of SD kidney and spleen, but not of BN kidney. In conclusion, antibodies against MHC antigens have been raised; we have also raised IgG antibodies active in ADCC against autologous tubular cells. We have found monocytes bearing Fc receptors among the infiltrating cells, as well as antibodies that can function in unison in ADCC. Our model appears useful in exploring a combined immune effector mechanism that might be operative in TIN.

● **1490** ONTOGENY OF THE RENAL KALLIKREIN-KININ SYSTEM DURING FETAL AND NEWBORN LIFE. J.E. Robillard, W.J. Lawton, D.N. Weismann and C. Sessions. Univ of Iowa, Depts Pediatrics and Internal Medicine, Iowa City, IA.

The ontogeny of the renal kallikrein (U_{Kall})-kinin system and its interaction with the renin-angiotensin-aldosterone (Aldo) and prostaglandin (PG) systems were studied in 43 chronically catheterized fetuses (17 <120 days, 14 between 120-130 days, 12 >130 days; term 145 days) and 8 newborn lambs (5-23 days of age). U_{Kall} was measured by the [^{3}H]-TAME esterase assay and bioassay after partial purification on DEAE-Sephadex. Significant rises in plasma renin activity (PRA), angiotensin II (AII), Aldo and U_{Kall} were observed during development.

	<120 d	120-130 d	>130 d	newborn
PRA ng/ml/hr	3.7±0.7	6.3±1.7	10.0±0.9*	16.6±4.7*
AII pg/ml	32±3	33±3	41±6	150±28*$^{+}$
Aldo pg/ml	32±3	37±5	59±8*	117±21*$^{+}$
U_{Kall} mEU/hr/ml GFR	29±5	49±9*	89±19*	157±35*$^{+}$

(* $p<0.05$ when compared to fetuses <120 days; $^{+}p<0.05$ when newborn values compared to fetuses >130 days.) Significant correlations between AII and Aldo ($r=0.63$, $p<0.001$) and Aldo and U_{Kall} ($r=0.62$, $p<0.001$) were found during fetal life. Urinary PGE and $PGF_{2\alpha}$ excretion ($ng \cdot min^{-1} \cdot ml\ GFR^{-1}$) did not change during fetal life but decreased significantly ($p<0.05$) after birth from 0.26±0.10 to 0.61±0.03 and from 0.49±0.09 to 0.06±0.01 respectively. The present study is the first description of the developmental pattern of U_{Kall} excretion during fetal and newborn life and supports the concept that aldosterone is an important modulator of U_{Kall} during fetal life.

● **1492** CEREBRAL CORTICAL ATROPHY IN CHILDREN RECEIVING TREATMENT FOR END-STAGE RENAL DISEASE (ESRD). H. William Schnaper and Alan M. Robson, Dept. of Pediat., Wash. Univ. Med. Sch., and St.Louis Children's Hosp., St. Louis, MO.

Computed tomography (CT) of the head was performed in 12 ESRD patients, aged 2.7 to 22 yrs, who developed neurologic complications including seizures (n=9), bizarre behavior (n=1), headaches (n=1) and obtundation (n=1). A 13th patient was studied prospectively. Marked cerebral cortical atrophy was found in 7 patients and enlarged ventricles in another 2. Patients with atrophy had received ESRD therapy for 44.1 mo vs 28.6 mo for the remaining patients. Sex, race, age, underlying disease or treatment regimens were comparable in the two groups. Six of the 7 "atrophy" patients had received pulse doses of methylprednisolone. One developed atrophy only after receiving such treatment suggesting a causal relationship between the pulses and atrophy. However, 4 of the patients who did not have cerebral atrophy had received similar steroid regimens. In addition, one "atrophy" patient had never received steroids and only 1 of 5 non-ESRD patients who had received comparable steroids for other indications had cortical atrophy.

The unexpectedly high incidence of cortical atrophy in our ESRD patients is disturbing especially since it was found in an asymptomatic patient. Steroid pulses may be one, perhaps reversible, etiology. However, our data indicate other factors may be equally important. Some aspect of ESRD may either cause the lesion or potentiate the susceptibility to develop it after steroid pulses. These observations indicate an urgent need to study this phenomenon further, to delineate its cause and establish its natural history.

● **1493** DEVELOPMENT OF SOLUTE TRANSPORT IN RABBITS. George J. Schwartz and Andrew P. Evan. Albert Einstein Col. of Med., Dept. of Peds., Bronx, NY and Univ. of Indiana, Dept. of Anat., Indianapolis, Ind. Spon. by Adrian Spitzer.

Infants have a lower renal threshold for bicarbonate than adults. In order to determine whether this phenomenon is due to factors intrinsic to the tubular transporting systems, we measured the absorption rates of fluid (Jv) and bicarbonate ($JHCO_3$) in isolated perfused early proximal convoluted tubules (PCT) taken from the juxtamedullary cortex of rabbits ranging in age between 0 and 8 weeks (adult). Artificial solutions simulating an ultrafiltrate of adult plasma were used to perfuse and bathe the tubule. Electron microscopy confirmed that each PCT was S 1. In the first 4 weeks of life Jv and JHCO3 were low and constant (0.4 ± .05 nl/mm.min and 4.5 ± 0.6 pmol/cm.s, n=14), averaging 1/3 of the values obtained in PCT from 4 adults (1.2 ± 0.7 and 14.9 ± 3). During the next 2 weeks a dramatic rise occurred, so that by the 6th week, Jv was 0.9 ± 0.1 and JHCO3 was 13.2 ± 2.7 (n=7). The surge in transport succeeded by ≈1 week the increase in the basal-lateral membrane surface area (site of Na-K-ATPase). If this increase underlies the surge in $JHCO_3$, the transport of another Na^+-coupled solute, glucose (Jglu), would show a similar pattern. Jglu rose from 30.0 ± 2.8 pmol/mm.min during the first four weeks of life (n=14), to 70 ± 10 by the 2nd month. Thus: a) the low threshold for bicarbonate in the infant appears to be due, at least in part, to a limited ability to reabsorb bicarbonate in the PCT; b) the surges in Jv, $JHCO_3$, and Jglu during maturation occur simultaneously and succeed the morphologic ontogeny of the PCT; c) since there is no similar concordance in whole kindey function, solute interactions in the PCT and/or differences in transport at distal sites need to be evaluated.

1494 NEPHROPATHIC CYSTINOSIS PRESENTING AS BARTTER'S SYNDROME. Sudah Shaheb, H. William Schnaper, and Michael P. Whyte (Sponsored by Richard E. Hillman). St. Louis Children's Hospital, Washington University School of Medicine, St. Louis, Missouri.

A 5-year-old black boy presented with rickets and growth retardation. At age 2, hypokalemic metabolic alkalosis with hyponatremia and hypochloremia had been attributed to an intercurrent illness. At age 2½, hypophosphatemic rickets was treated with pharmacologic doses of vitamin D_2 and persistent electrolyte abnormalities failed to correct with KCl supplementation. On first admission to St. Louis Children's Hospital for diagnostic studies, he was normotensive with serum Na+=129, K+=1.7, Cl^-=88, HCO_3^- = 28.3 mEq/L; venous pH=7.44 (normal; 7.35-7.41); and had glycosuria and aminoaciduria. Review of sequential radiographic studies revealed partial healing of his rickets since age 3 years. Random plasma renin activity (150 ng/ml; normal < 5 ng/ml) was compatible with Bartter's syndrome. As the biochemical findings with the exception of metabolic alkalosis were compatible with Fanconi syndrome, slit lamp examination was requested and revealed the corneal and retinal findings of cystinosis. Elevated leukocyte cystine levels confirmed the diagnosis. No other etiology for proximal renal tubular dysfunction was found. With salt, K+, and phosphate supplementation for 2 weeks, the metabolic alkalosis resolved, serum Na+ and Cl^- levels corrected, and renin levels decreased to 50 ng/ml. Our patient's presentation with clinical and biochemical features consistent with Bartter's syndrome and hypophosphatemic rickets documents an unique presentation of nephropathic cystinosis.

●1495 EXCRETION OF CYCLIC 3', 5'-ADENOSINE MONOPHOSPHATE (CYCLIC AMP) IN THE EARLY NEWBORN PERIOD. Sharon R. Siegel, Department of Pediatrics, UCLA Hospital and Clinics, Los Angeles.

Parathyroid hormone activates adenylate cyclase in the renal cortex to produce cyclic 3', 5' -adenosine monophosphate (cAMP) as the intermediary in phosphate transport; vasopressin activates renal adenylate cyclase in the renal medulla as the intermediary in renal tubular permeability for dilution and concentration. The relationship between cAMP and phosphate transport, and cAMP and osmolality was studied in 25 preterm (28-37 wks gestation), and 9 fullterm infants. Timed urine collections were performed and glomerular filtration rate (GFR) measured by creatinine clearance. Urinary cAMP was directly related to GFR, r=.92 ($p<.001$). When corrected for differences in GFR, urinary cAMP was not related to gestational age. Urinary cAMP was related to osmolality, r=.37 ($p<.05$). Urinary cAMP was not related to phosphate transport. In conclusion: 1) urinary cAMP is derived from the GFR, 2) cAMP is not related to gestational age, and 3) the antidiuretic hormone (vasopressin)-dependent cAMP system for urinary dilution and concentration appears to be functioning in the early newborn period.

● 1496 ASSESSMENT OF THE BENEFICIAL EFFECT OF THYROXINE ON ACUTE RENAL FAILURE. Norman J. Siegel, L. Katz, H. Reilly and M. Kashgarian. Yale University School of Medicine, Departments of Pediatrics and Pathology, New Haven, CT.

We have demonstrated that treatment with thyroxine (T_4) at the peak of a toxic renal injury will enhance recovery of glomerular and tubular function. To assess this effect of T_4, renal function was measured during in-vitro perfusion and morphologic features were determined in rats injected with K-dichromate (15mg/kg) and treated with either normal saline (NS) or T_4 (40ug/kg).

To eliminate any systemic effects of T_4, an isolated perfused kidney preparation was utilized. Kidneys from dichromate injected rats treated with T_4 had significant ($P<0.01$) better Cin (32±5 - ul/min), urine flow (10±2 ul/min) and FE_{Na} (20±9%) compared to rats given NS (Cin: 5±2; urine flow: 1±1; and FE_{Na} 80±5).

To evaluate the direct effect of T_4 on cellular morphology, horseradish peroxidase (HRP) was infused, IV, 24 hrs after treatment. Kidneys from dichromate injected rats given NS demonstrated diffuse necrosis of tubular cells with intracellular staining of HRP and areas of denuded basement membrane. In rats treated with T_4, tubular epithelium was preserved, brush border and mitochondria were intact and HRP appeared only in subapical vacuoles in a manner similar to that seen in control rats.

These data indicate that the beneficial effect of T_4 on recovery from a toxic renal injury: A) Is mediated via a direct and specific effect on the kidney and B) Results in preservation of cellular morphology and integrity of the tubular epithelium.

1497 SINGLE DOSE AMOXICILLIN VS CONVENTIONAL THERAPY FOR TREATMENT OF UNCOMPLICATED URINARY TRACT INFECTIONS. Gary Stahl, Paul Topf, Gary Fleisher, Michael Norman, Howard Rosenblum and Alan Gruskin. Depts. of Ped., Children's Hosp. of Phila. and St. Christopher's Hosp. for Children, Philadelphia, PA.

Outpatients with culture-proven, acute, uncomplicated UTIs and with no signs or symptoms of systemic illness were randomized to either single dose (SD) amoxicillin (50 mg/kg po) or conventional therapy (CT) amoxicillin (10 mg/kg/dose TID po x 10 days). All patients were cultured at 48 hours post-treatment to assure efficacy. Cultures were again obtained 2 days after completion of therapy (SD-day 4-5; CT-day 13-14) to check for relapse. Patients were recultured at 1 and 3 months post-treatment. IVP/VCUG was obtained at 3 months post-treatment.

Response to therapy was similar in the two groups (SD - 6/9 cured = 67%; CT - 10/14 cured = 71%). All SD failures represented failure to clear a sensitive organism but were cured by 10 days of amoxicillin. Although no SD patients relapsed with a newly resistant organism, all CT failures resulted from an initially sensitive organism becoming resistant to amoxicillin. Of CT cures, 2/10 became reinfected during follow-up compared to 0/6 SD cures. Significant urinary tract anomalies were found on 1/6 studies of SD patients and on 2/9 studies of CT patients. Anomalies were found in 1 SD failure, 1 CT failure and 1 CT cure. All patients with identified anomalies either failed to respond to initial therapy or became reinfected during follow-up.

Conclusions: The results support previous reports that SD is as effective as CT for uncomplicated UTIs. However, previously unreported is the observation that SD failures are related to failure to clear a sensitive organism and CT failures are due to induction of resistance in the infecting organism.

1498 THE ROLE OF EXTRACELLULAR FLUID VOLUME UPON RENAL CLEARANCE OF URIC ACID (CUA) IN PUPPIES. F.B. Stapleton, D. Nash and B.S. Arant, Jr. Department of Pediatrics, Univ. Tenn. Ctr. Health Sci., Memphis, TN.

During postnatal development in puppies, fractional excretion of urate(FEUA) and extracellular fluid volume(ECFV) decrease when inulin clearance(CIN) increases and FE sodium (FENa) remains constant. To further clarify the role of ECFV upon CUA, we examined the effects of acute dehydration and volume expansion(VE) with isotonic 5% albumin, 10 ml/kg, with and without pretreatment with pyrazinamide(PZA), an inhibitor of urate secretion. Data from VE studies are shown in the table for FEUA(%) as mean±SEM; no statistical differences were observed for FEUA, CIN, BP and FENa during control periods or for response to VE between the two groups of puppies at similar postnatal ages.

	Hydrated Puppies			Pyrazinamide Studies			
Age	n	PV*	FEUA	VE-FEUA**	n	FEUA	PZA+FEUA	PZA+VE FEUA**
1 day	5	90±9	84±9	86±3	4	94±7	78±7	73±4
30 days	6	77±8	73±4	90±8	2	79	77	86
Adult	2	60	44	83	5	64±6	59±5	85±2

* Plasma volume, ml/kg; ** Maximal FEUA post expansion

Seven puppies 30 days of age were dehydrated by fasting to attain a 8±0.21% reduction in body weight. FEUA was 54±9% in dehydrated puppies ($P<0.001$ from hydrated 30 day puppies) and increased to 75±8% with VE. CIN, BP, FENa and response of FEUA to VE were not statistically different from hydrated 30 day puppies. These data suggest that 1) FEUA is increased in the early postnatal period from an expanded ECFV and 2) VE increases FEUA by decreasing tubular UA reabsorption.

●1499 COMPARISON OF GROWTH IN CHILDREN TREATED WITH CONTINUOUS AMBULATORY PERITONEAL DIALYSIS (CAPD), HEMODIALYSIS (HD) AND RENAL TRANSPLANTATION (Tx). Constantinos J. Stefanidis, Annette M. Vigneux, Brian T. Steele, Ian K. Hewitt, John W. Balfe (Spon. by Sang W. Kooh). University of Toronto, The Hospital for Sick Children, Division of Nephrology, Toronto, Canada.

Growth velocity indices (GVI) of children treated with CAPD were compared with age and sex matched patients on HD and after Tx:

	Number of patients	Study period (months)	GVI > 80% (normal)	GVI 50-80% (fair)	GVI < 50% (poor)
CAPD	16	5 - 33	50%	38%	12%
HD	18	5 - 22	12%	27%	61%
Tx	20	12 - 52	65%	20%	15%

CAPD and HD patients had a good correlation (r:0.71 and 0.59 respectively) between GVI and the change in percentage of ideal body weight during treatment. Total plasma serum protein and albumin were significantly ($p<0.01$) lower in HD patients. Urea nitrogen appearance was decreased in 6 of 9 CAPD patients and all 9 had low serum IgA and IgM. The duration of study period, the percentage of patients with native kidneys, the degree of renal osteodystrophy, or the values of hemoglobin, BUN, serum creatinine, Ca, P, alkaline phosphatase and bicarbonate did not differ significantly between CAPD patients with normal and impaired GVI. Children on CAPD grew better ($p<0.01$) than those on HD probably because of improved (though not adequate) nutrition. However the best growth was achieved after transplantation.

1500 CIRCULATING VITAMIN D METABOLITES IN CYSTINOSIS, Reuven Steinhertz, Joseph Schulman, Hector DeLuca, Russell Chesney, NICHD, NIH, Bethesda, MD, and Univ. of Wisconsin, Depts. of Pediatrics, Biochemistry, Madison, WI.

Hypophosphatemia, acidosis and rickets are universal in cystinosis. Several reports indicate improvement after use of 1α-hydroxyvitamin D therapy. Twenty-two serum samples from 16 patients with nephropathic cystinosis were measured by the multiple vitamin D metabolite assay of Shepard et al. Most subjects had a serum creatinine between 1.1 and 3.0 mg/dl and serum HCO_3 was > 18.0 mEq/L post-alkali therapy. Patients were on various treatment regimens: low-dose vitamin D_2, high-dose vitamin D_2 (>25,000 U), DHT and $1,25(OH)_2D$.

Treatment	n	$25(OH)D_2$	$25(OH)D_3$	$24,25(OH)_2D$	$1,25(OH)_2D$	
<1000 U D_2	3	10.6	11.2	0.3*	10*	(*p<.05)
>25000 U D_2	3	223.0*	5.5*	2.6*	21	
DHT	14	19.1	17.9	0.9	360*	
$1,25(OH)_2D$	3	55.5*	10.9	1.0	76*	
Normal**	68	73±5.2	23.1±8.7	1.7±.5	43±12	(**$\bar{x}$±SD)

These results indicate that $1,25(OH)_2D$ is low after vitamin D_2 therapy, high after $1,25(OH)_2D$ therapy and exceedingly high on DHT. This latter finding indicates that DHT therapy results in a "pseudo-1,25-like" activity, as reported by Gray et al (J Lab Clin Med 93:1031, 1979). $24,25(OH)_2D$ values are low, reflecting renal impairment, and 25(OH)D is normal, except in high-dose D_2 treatment. These data suggest that impaired renal 1α-hydroxylation may contribute to rickets of cystinosis and also indicate that 1α-hydroxy-D metabolites elevate circulating levels. $1,25-(OH)_2D$ status cannot be assessed in DHT-treated patients.

● **1501** SIMILAR RELATIONSHIP BETWEEN PLASMA AND URINARY VASOPRESSIN (VP) IN INFANTS AND ADULTS. Paul Stern and Frederick T. LaRochelle, Jr. (Spon. by Robert Klein). Dartmouth Medical School, Depts. of Mat. and Child Health (Pediatrics) and Physiology, Hanover, NH.

Measurement of VP in urine rather than plasma offer advantages, especially in small prematures, if urinary VP reflects plasma VP concentration. Sampling of plasma is invasive, usually requiring volumes >1 ml. Furthermore, with our antiserum for RIA, extraction of VP from urine is not needed. We compared plasma VP concentrations with VP excretion rates (pg VP/mg creatinine excreted in aliquots of concurrent 2-hour urine samples) in 10 neonates and infants and in 18 older children and adults, with plasma VP >1 pg/ml (limit of detectability). Both groups included patients with partial central and nephrogenic diabetes insipidus and with SIADH. An exponential relationship between VP in plasma and urine was present in the babies (ln y=.20x+ln 49,r=.9, p<.001) and in the older group (ln y=.18x+ln 37,r=.8, p<.001). Neither slopes nor y intercepts were different between groups. Urinary VP excretion correlated with urine osmolality in samples from normal adults (r=.8, n=17, p<.01) and from preterm neonates, some with respiratory distress (r=.8, n=42, p<.001). Intercepts at 50 mOsm/kg H_2O (max. dilution) were similar, but the slope of the adult regression line was steeper indicating greater concentrating ability. VP excretion correlates with plasma VP similarly in infants and adults. Urinary VP can be used to assess pituitary release of the hormone in all age groups.

1502 MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS (MPGN) AND α1-ANTITRYPSIN Pi Type Z IN CHILDREN: ASSOCIATION OR COINCIDENCE. C. Frederic Strife, George Hug, Gail Chuck, A. James McAdams, Charles A. Davis, and Jeffrey J. Kline. Univ. of Cincinnati College of Medicine, Children's Hospital Medical Center, Dept. of Pediatrics, Cincinnati.

An association between α1-antitrypsin (α-AT) deficiency and MPGN has been postulated in 5 previously reported patients. We observed 2 white girls with α-AT deficiency, phenotype ZZ and severe liver disease who developed hypocomplementemic glomerulonephritis associated with elevated circulating immune complexes. Renal biopsies were typical of MPGN Type I. IgA (but not α-AT) was demonstrable immunologically as a component of glomerular deposits. Low classical complement components and C3 were present in both patients. Pi Type Z was not found in 53 patients with idiopathic MPGN and no liver disease, suggesting that an association between these two disorders is not likely. Abnormal complement protein levels such as typically seen in MPGN Type I were not found in 23 patients with phenotype ZZ and no kidney disease. Our observations do not support previous suggestions that MPGN in α-AT deficiency may be the consequence of the abnormal protease inhibitor. Rather, the presence of severe liver disease in all reported patients, the finding of IgA in glomeruli (not present in idiopathic MPGN Type I) and the known occurrence of MPGN in patients with other liver diseases supports the concept that MPGN is acquired in patients with α-AT deficiency as a consequence of their liver disease and is not directly related to the presence of the allelic α-AT variant Pi^z.

1503 EFFECTS OF FASTING ON URINARY CONCENTRATION IN DEHYDRATED RATS. S.M. Suh, K.F. Chang and J.R. Claybaugh. Shriners Hospital, Tripler Army Medical Center, and University of Hawaii. (Spon. by Dexter Seto).

Dehydration is commonly used to induce maximum concentration of urine. Whether fasting exerts any effect on urinary concentration in dehydrated rats is investigated in this study. Wistar rats were dehydrated by withholding water for three days under either fasting or ad lib feeding of rat chow only and the volume, osmolality and ADH contents of the 24 hr urine were measured. Urine volume decreased in both groups and there was no significant difference. The rats in the fasted group had lower urine osmolalities in the first two days of dehydration, as compared to the fed group (1499±79 vs. 2545±65 mOsm/kg H_2O for day 1; 2685±119 vs. 3185±116 for day 2). No significant difference was found in the osmolality of the third day urine (3082±52 vs. 3277±84). The fasted group also had lower urinary ADH as compared to the fed group (204±17 vs. 925±81 μU/mg creat. for day 1; 599±68 vs. 1706±125 for day 2). In a further study, by shortening the periods of urine collection, it was found that a decrease in urine osmolality of fasted rats appeared during the second 12 hr of dehydration. When tissues of the renal cortex, medulla, and papilla were examined from rats after 24 hr dehydration, no significant difference was found in the contents of total solute, Na, K, H_2O and urea between the two groups. We conclude that fasting in the dehydrated rats delays the achievement of maximum renal concentrating ability in the first two days of dehydration and this is accompanied by diminished urinary contents of ADH.

1504 FRACTIONAL BICARBONATE EXCRETION (FE HCO_3^-) IN LOW BIRTH WEIGHT (LBW) INFANTS WITH METABOLIC ACIDOSIS (MA). Shahid Sultan, Gaston Zilleruelo, Eduardo Bancalari, Bernard Steele and Jose Strauss. Univ. of Miami School of Med., Depts. of Peds. and Pathol., Miami, Florida.

The adequacy of the LBW infant's renal acidification mechanisms has been questioned. In addition, capacity for tubular HCO_3^- reabsorption (HCO_3^- TR) and the resultant FE HCO_3^- at different gestational ages (GA) have not been clearly established. This study evaluated tubular HCO_3^- handling during the first week of life in 10 male LBW infants with MA (BE ≥ -5 mEq/L) and subsequent NaHCO3 infusion. Mean birth weight was 1095 g (range 750-1770 g); GA $\bar{x}$: 29 wks (range 25-33 wks). Simultaneous arterial blood (B) and anaerobic urine (U) samples obtained before and during intravenous NaHCO3 infusion were analyzed for pH, pCO2, HCO_3^-, Na+, K+, Cl- and creatinine. To avoid volume expansion, diluted NaHCO3 was given at maintenance rate. U HCO_3^- and U pH had significant direct correlations with B HCO_3^- (r= 0.59 and 0.56, respectively). All infants with BE ≥ -5 mEq/L had FE HCO_3^- < 3% ($\bar{x}$: 0.56 ± 0.97%). FE HCO_3^- had an inverse correlation with B H+ concentration (r=-0.28). All patients with B pH ≤ 7.22 or pCO2 ≥ 48 mm Hg had minimal or absent FE HCO_3^- ($\bar{x}$: 0.17 ± 0.17%) as compared with those who had B pH > 7.22 ($\bar{x}$: 6.8 ± 11.7%) or pCO2 < 48 mm Hg ($\bar{x}$: 7.8 ± 12.2%) (p < 0.001). These results suggest: 1) LBW infants have an adequate HCO_3^- TR during MA; 2) B H+ concentration and B pCO2 appear to play a significant role in HCO_3^- TR; and 3) distal tubular secretion of H+, not HCO_3^- TR, appears to be the limiting factor for acid-base balance in LBW infants.

1505 LUPUS NEPHRITIS IN BLACK AND HISPANIC CHILDREN. Amir Tejani, Senih Fikrig, K. Gurumurthy, Anthony Micastri, SUNY, Downstate Medical Center, Departments of Pediatrics and Pathology, Brooklyn, New York.

18 Blacks and 6 Hispanics form the study group. There were 2 sisters with the disease. The mean age at onset was 10.1 yrs. The mean follow-up was 5.4 yrs. with a range of 2-16.5 yrs. Biopsy showed a renal lesion in all except for 1 child with drug induced Lupus. 4 patients had no renal manifestations, but showed class 2 or 3 lesions. One child had class 2a, 7 had class 2b, 6 had class 3, 6 had class 4, and 3 had class 5 lesion. On repeat biopsy 6 more children converted to class 4; 2 from class 2b, 3 from class 3, and 1 from class 5.

Of 12 children with onset < 10 years, 5 died-4 of renal causes and 1 of sepsis. One is on dialysis, 1 had bilateral hip replacement for aseptic necrosis due to steroid therapy, and 2 have creatinine > 2 mg%. The overall renal mortality and morbidity in our 23 patients is higher than that reported in recent series as shown below.

Author	Age at Onset	Renal Pts.	Renal Deaths	Trans-plants	Dialysis	Renal Failure	Comparison
Garin	12	25	2	0	0	1	p <.05
Walverens	14	40	4	-	-	-	p <.05
Abeles		27	3	-	-	-	p <.02
Fish	12.97	46	0	0	0	-	p <.0001
This Study	10.1	23	5	1	2	1	---

The earlier onset and increased severity in our population may be related to altered immune response controlled by antigens on the DR locus.

1506 HISTOPATHOLOGICAL CORRELATIONS OF RECURRENT HEMATURIA WITH AND WITHOUT MILD PROTEINURIA, Amir Tejani, K. Gurumurthy, Anthony Nicastri, (Spons. by Senih Fikrig), SUNY, Downstate Medical Center, Depts. of Pediatrics and Pathology, Brooklyn, N.Y.

35 children with recurrent hematuria (H) underwent a renal biopsy. Twelve of these patients had associated proteinuria (P) in yellow urine specimens, ranging from 1+ on albustix to 500 mgm in 24 hrs. urine. Children with a history of deafness, familial nephritis or clinical findings of systemic lupus, Henoch's purpura and streptococcal glomerulonephritis were excluded.

Mean age of 12 patients with (H) and (P) at onset was 5.4 yrs. compared to mean age of 7.9 yrs. in 23 patients with H alone ($p < .05$). The sex ratio was not different in the two groups. A variety of abnormal pathology was seen in both groups as shown below, with the (H) alone group having a higher incidence of mesangial proliferation ($p < .05$).

	Normal	Mes+	IF+	Berger's	F.G.S.	Membranous	Alports
H&P	5/12	0/12	3/12	1/12	2/12	1/12	0/12
H	8/23	7/23	1/23	4/23	1/23	0/23	2/23

(Mes+=Mesangial proliferation)(I.F.+=Immunoflourescence Positive) (F.G.S. Focal Sclerosis)

Thirteen of the 35 patients had normal glomerular histology. These 13 could not be distinguished by age at onset, sex, associated proteinuria or the presence of gross (H). Our study suggests that the absence of mild to moderate degree of (P) in association with (H) does not necessarily rule out a significant renal lesion and a biopsy may be necessary for tissue diagnosis.

1507 LONG TERM EVALUATION OF CHILDREN WITH NEPHROTIC SYNDROME AND FOCAL SEGMENTAL GLOMERULAR SCLEROSIS, A. Tejani, A. Nicastri, C.K. Chen, K.M.H. Butt, and K. Gurumurthy, (Spons. by S. Fikrig), SUNY, Downstate Medical Center, Depts. of Pediatrics, Pathology and Surgery, Brooklyn, N.Y.

We studied the long-term outcome of 24 children with the nephrotic syndrome who showed the histological lesion of focal segmental glomerular sclerosis, (F.S.G.S.) during the course of their illness. The follow-up period ranges from 3-19 years. Fourteen children were steroid resistant (S.R.) and had F.S.G.S. at onset. Ten children were initially steroid sensitive (S.S.) and had minimal change lesion which evolved into F.S.G.S. S.R. patients were older 7.7 ± 3.7 yrs. at onset, compared to S.S. patients 3.5 ± 2.5 yrs. ($p < .01$). There were 10 females in the S.R. group, but only 3 in the S.S. group ($p < .02$). More S.R. patients had hematuria-9/14 than S.S. patients-2/10 ($p < .05$). Growth retardation was seen in 9/13 S.R. patients and 1/8 S.S. patients ($p < .02$). After initial biopsy S.R. patients reached end stage renal failure earlier-2.3 ± 1.3 yrs. compared to S.S. patients-10 ± 5.8 yrs. ($p < .01$). Ten of the 14 S.R. patients were dead, on dialysis, transplanted or in renal failure at the end of the follow-up, compared to 5/10 S.S. patients (p. N.S.). A total of 11 patients received 17 kidney transplants. F.S.G.S. recurred in 2 of the 13 kidneys transplanted into 9 S.R. patients, and in 1 of the 4 kidneys transplanted into 2 S.S. patients. Overall recurrence rate of F.S.G.S. in allografts was 17%. Our study suggests that the two varieties of F.S.G.S. occurring in nephrotic patients may be two different diseases, rather than a single disease with varied manifestations.

1508 EXERCISE TRAINING IMPROVES HYPERLIPIDEMIA AND AEROBIC CAPACITY IN PEDIATRIC HEMODIALYSIS PATIENTS. Frank C. Walker, Andrew P.Goldberg, James M.Hagberg, Richard W. Florman, and Barbara R. Cole. Depts. of Pediatrics, Preventive Medicine and Medicine, Wash. Univ. Sch. of Med., St.Louis, MO.

Children with end-stage renal disease treated by hemodialysis have elevated plasma triglyceride (TG) and cholesterol (CHOL) levels and reduced high density lipoprotein cholesterol (HDL-C).Their sedentary lifestyle may contribute to these abnormalities. Endurance exercise training improves hyperlipidemia and aerobic capacity in adult hemodialysis patients (Kid.Inter.18:754,1980). To examine the effects of exercise training on lipid metabolism in pediatric hemodialysis patients, 8 were studied (age: 15.8±4.4 yrs, $\bar{x}$ ± SD). All were anemic (Hct 17-22%), had creatinine clearances <1 ml/min/1.73 M^2 and had required hemodialysis 3 times per week for a mean of 50.8 months. The training program was aerobic, 3 times per week for 45 minutes and work rate was increased progressively from 65% to 80% of aerobic capacity ($\dot{V}O_2$max). Pretraining graded exercise test durations (GXT) were low (8.8±1.3 min) and lipids abnormal (TG=375±244, CHOL=218±98, HDL-C=28±6 mg/dl, $p < .01$, n=8) compared to age and sex matched nonuremic controls (Lipid Research Center population data). HDL subfraction 2 (HDL_2), a better predictor of coronary risk than HDL-C, was 11±4 mg% or 65% of normal. After 3 months of training (n=3) GXT duration rose in all (18±14%), TG decreased 25%, CHOL did not change and HDL-C and HDL_2 rose 12%. Thus, short term endurance exercise training improves hyperlipidemia and aerobic capacity in pediatric hemodialysis patients. Sustained training with even greater improvement could have important therapeutic implications.

● 1509 VARIABLE INSULIN RESISTANCE IN RATS WITH RENAL INSUFFICIENCY. Steven J. Wassner and Jeanne B. Li (Spon. by Nicholas M. Nelson). Penn State Univ. Coll of Med, M.S. Hershey Med Ctr, Dept of Pediatrics, Hershey, PA

Insulin resistance has been suggested as responsible for the altered glucose and amino acid metabolism present in renal failure. Muscle is the site of this resistance but the relationship between tissue and serum factors is unclear. We have examined the role of insulin resistance to glucose and α-aminoisobutyric acid (AIB) distribution ratios in perfused rat muscle. 7/8 nephrectomies (NX) were performed in male rats. Two weeks later BUN's were 20 mM vs 5 mM in controls. Hemicorpus perfusions were performed using standard media with 16 mM glucose. AIB was the only amino acid used. Insulin was added after 1.5 h of perfusion at concentrations of 0 to 25 mU/ml. In controls, glucose uptake with 0 μU/ml insulin was 3.6 μmol/h/g. Glucose uptake increased at 25 μU insulin/ml and plateaued above 500 μU/ml (5.5 μmol/h/g). In NX preparations glucose uptake was no different than controls without insulin, but rose to higher levels (8.5 μmol/h/g) at 1 and 25 mU/ml ($p < 0.01$). The distribution ratio of AIB was lower in NX rats both with and without insulin. Distribution of AIB, but not glucose was inversely related to BUN in NX rats. When perfused with normal media, muscle tissue rapidly regains sensitivity to insulin for glucose but not to AIB uptake. This suggests that abnormalities of protein metabolism in NX rats may have a different pathogenesis than abnormalities of glucose metabolism.

1510 EFFECT OF ANGIOTENSIN CONVERTING ENZYME INHIBITOR (CEI) ON RENAL AND ADRENAL RESPONSES TO HYPOXEMIA IN MATURING LAMBS. D. Weismann, J. Herrig, O. McWeeny and J. Robillard, Univ. of Iowa Col. of Med., Dept. Ped., Iowa City.

Renal and adrenal responses to normocapnic hypoxemia were studied in chronically-catheterized lambs, 4-37 days of age (n=17). Values are mean±SD. CEI (captopril) was continuously infused intravenously in a dose (0.01 μgm/kg·min) sufficient to block the vasopressor effect of an IV bolus of Angiotensin-I (1 μgm/kg) and significantly ($p<0.05$) decrease serum Angiotensin-II concentration (AII, from 111±39 to 71±39 pg/ml) and serum aldosterone concentration (Aldo, from 128±98 to 62±28 pg/ml). CEI was also associated with a significant ($p<0.05$) increase in PRA (from 16.50±9.50 to 100.69±63.57 ng/ml·hr). Furthermore, the change in Aldo with CEI correlated significantly with postnatal age ($r=0.50$, $p<0.05$). Hypoxemia (arterial pO_2 41±8 torr) during CEI was associated with a further significant ($p<0.05$) increase in PRA (to 117.60±55.5 ng/ml·hr), with increases also in serum epinephrine (from 108±65 to 1121±1793 pg/ml), serum norepinephrine (from 453±371 to 3016±5194 pg/ml), and urinary prostaglandin E excretion rate (from 0.655±0.703 to 1.309±1.023 ng/min). Furthermore, plasma cortisol concentration decreased (from 4.44±4.70 to 3.49±5.24 μg/ml) in response to hypoxemia during CEI, whereas AII and Aldo did not change. The cortisol response is opposite to what has been observed during hypoxemia in uninhibited lambs. These results suggest that 1) PRA responsiveness to lack of AII feedback inhibition is present in maturing lambs; 2) linkage of Aldo release to AII matures with postnatal age; and 3) CEI inhibits cortisol release in response to hypoxemia.

1511 RELATION OF ARTERIAL CATECHOLAMINES TO RENAL HEMODYNAMIC RESPONSE TO HYPOXEMIA IN MATURING LAMBS. Douglas Weismann, James Herrig, Oliva McWeeny, and Jean Robillard, Univ. of Iowa Col. of Med., Dept. of Ped., Iowa City.

Baseline values and responses of arterial epinephrine (ΔEpi, pg/ml) and norepinephrine (ΔNorepi, pg/ml) concentration (by radioenzymatic assay) and renal blood flow (ΔRBF, ml/min, determined by radiolabelled microspheres), mean arterial pressure (ΔMAP, mmHg) and renal vascular resistance (ΔRVR, mmHg/ml·min), to normocapnic hypoxemia (mean pO_2±SD: 33±6 torr) were measured in chronically catheterized lambs 2 days to 6 months of age (n=28). Values are mean±SD. ΔRBF was strongly correlated with ΔEpi ($r=-0.84$, $p<0.001$) and Norepi ($r=-0.51$, $p<0.02$). Compatible relationships were noted between ΔRVR and ΔEpi ($r=0.97$, $p<0.001$) and ΔNorepi ($r=0.82$, $p<0.001$). ΔMAP did not correlate significantly with ΔEpi ($r=0.22$, $p>0.2$) or Norepi ($r=0.27$, $p>0.1$). ΔEpi also had good correlation with the change in arterial hematocrit in response to hypoxemia (ΔHct $r=0.55$, $p<0.01$). Baseline arterial concentrations of Epi and Norepi, on the other hand, did not correlate significantly with postnatal age (Epi $r=-0.01$, $p>0.5$; Norepi $r=0.11$, $p>0.5$), baseline RVR (Epi $r=-0.07$, $p>0.5$; Norepi $r=-0.13$, $p>0.5$) or baseline MAP (Epi $r=0.18$, $p>0.4$; Norepi $r=-0.21$, $p>0.3$). These results suggest that 1) baseline renal hemodynamics during maturation are not closely associated with circulating catecholamines; 2) renal vasoconstrictive responses to hypoxemia are closely linked to changes in circulating catecholamines; and 3) changes in circulating epinephrine concentrations may be related to ΔHct through decreased splenic erythrocyte sequestration or decreased plasma volume.

● 1512 AN ABNORMALITY OF THE FOURTH COMPONENT OF COMPLEMENT ASSOCIATED WITH BENIGN RECURRENT HEMATURIA. Thomas R. Welch, Roger E. Spitzer and Ann E. Stitzel. SUNY, Upstate Medical Center, Department of Pediatrics, Syracuse

Seven children with recurrent gross or microscopic hematuria were studied. All have normal blood pressure, growth, and renal function; none has proteinuria. All of these children have decreased serum levels of C4 as measured by a functional (hemolytic) assay. When determined immunochemically, however, their C4's are within the normal range. The ratios of their hemolytic to antigenic C4's ("hemolytic efficiency") average .36 ± .15 (range .16 to .56). The values for hemolytic efficiency in 18 normal patients average 1.01 ± .26 (range .7 to 1.6). Fifteen patients with other hypocomplementemic diseases have ratios averaging .83 ± .32 (range .14 to 1.36). All other complement components (C1, C2, C3, C5-9, properdin, factor B, factor H, factor I, C1 inhibitor) are normal in these patients. The patients' C4 molecules are identical to those of normal serum with respect to charge, mobility, and antigenic configuration as determined by double immunodiffusion and immunoelectrophoresis. When incubated with normal serum, the patients' sera do not decrease the expected C4 titer as would be the case in the presence of a nonspecific inactivator of C4 or an excessive concentration of C4 binding protein. Finally, incubation of the patients' sera with a preformed immune complex made at equivalence leads to complete C3 and C4 consumption suggesting that the abnormal C4 is able to help form a stable and efficient classical pathway C3 convertase. These data suggest either a genetic cause for this abnormality or excessive production of pro-C4 as an underlying defect.

1513 INHIBITION OF THE DIURETIC AND NATRIURETIC EFFECTS OF FUROSEMIDE (F) BY INDOMETHACIN (I) IN PREMATURE INFANTS. T.F. Yeh, M.V. Betkerur, A. Wilks, J. Singh, R.S. Pildes, Cook County Hosp. Dept. of Ped., Univ. of Ill., Chicago, Illinois.

Furosemide (F) has been shown to increase urinary excretion of PGs in premature infants. To evaluate if PG inhibitor, I, would affect the diuretic and natriuretic response of F, 20 premature infants with PDA were divided into two groups: 10 received F alone (1mg/kg,IV) and 10 received F and I (0.3mg/kg,IV). The BW (mean±SEM 1.13±0.15 vs 1.19±0.11kg), GA (29.6±0.7 vs 30.7±0.8wks) postn. age (11.9±2.5 vs 9.5±2.1dys) and cardiopulmonary status before the study were comparable between the groups.

	Urine Output (ml/kg/hr)	FE_{Na} (%)	FE_{Cl} (%)	GFR (ml/min/1.73m²)
Before study				
Gr (F)	2.2±0.3	2.8±0.5	4.0±0.9	7.7±0.9
Gr (F+I)	2.6±0.4	2.5±0.3	3.2±0.4	8.0±0.7
After study 0-12 hrs				
Gr (F)	3.4±0.2	4.8±0.8	5.7±1.3	8.4±1.2
Gr (F+I)	2.6±0.5	3.9±0.9	6.3±1.4	7.9±0.8
After study 12-24 hrs				
Gr (F)	3.8±0.5*	5.1±0.9**	7.3±1.3**	8.7±0.8
Gr (F+I)	2.1±0.3	1.9±0.4	2.6±0.5	6.5±0.7

At 12-24 hrs after the study, infants in Gr F had an increase in urine output, FE_{Na} and FE_{Cl} which was significantly greater (*p< .05, **p<.01)than that of infants in Gr I+F. The results of this study suggest that the diuretic and natriuretic effects of F may be mediated by PGs in premature infants.

1514 PARADOXICAL STIMULATORY EFFECT OF SERUM FROM IDIOPATHIC NEPHROTIC SYNDROME (INS) PATIENTS ON HUMAN FIBROBLAST (HF) CULTURE. Gaston Zilleruelo, Virginia H. Carver, Tom McLeod, Paul Benke, Violet Esquenazi, Carmen Gomez, and Jose Strauss. University of Miami School of Medicine, Depts. of Pediatrics and Pathology, Miami, Florida.

Sera from patients with INS have been reported to inhibit lymphocyte blastogenesis. Characteristics and pathogenetic significance of the circulating factor(s) involved have not been established. To assess specificity of this growth inhibition for lymphocytes, we studied the effect of INS sera on HF. Sera were obtained from 5 children ($\bar{x}$ age: 13 yrs; range 10-16 yrs) with INS (MCNS 2, FSS 2, and membranous GN 1) in relapse (proteinuria > 1g/m²/day). All patients had hypoalbuminemia, hyperlipidemia and normal creatinine clearance; when studied, none were receiving prednisone. Sera were incubated with an HF primary cell line derived from foreskin or skin biopsy. Control medium containing F-12 + FCS was compared to F-12 + FCS + human normal or nephrotic sera at 5, 10 or 20% concentration; HF growth was followed for 8 days. Nephrotic sera produced a 2-8 fold increase of HF growth. Cell counts: normal sera $\bar{x}$ 94,800 ± 21,407 SEM; INS sera $\bar{x}$ 500,700 ± 153,000 SEM ($p < 0.001$). Peak effect was observed at 20% sera concentration in media. Heat treated sera at 56°C for 30 min or dialysis reduced minimally sera's activity. Thus, INS sera during relapse inhibit lymphocyte blastogenesis but stimulate fibroblast growth. Further studies are needed to characterize the circulating factor(s) and determine its pathogenetic role in the progression of renal disease.

● 1515 PERSISTENCE OF SERUM LIPID ABNORMALITIES IN CHILDREN WITH MINIMAL CHANGE NEPHROTIC SYNDROME (MCNS). Gaston Zilleruelo, Sung L. Hsia, Michael Freundlich, Helen Gorman, and Jose Strauss. Univ. of Miami School of Medicine, Depts. of Peds. and Biochem., Miami, Florida.

Hyperlipidemia (HL) is common during relapse in MCNS. This study assessed severity and duration of HL in MCNS children during relapse and remission as compared with age matched controls (Morrison, J. et al.: Pediatrics 62:990, 1978). Serum total cholesterol (TC), triglycerides (TG), low density lipoproteins (LDL), and high density lipoproteins (HDL) were measured in 39 MCNS children; 22 were in relapse (proteinuria > 1 g/m²/day) and 17 were in remission (no proteinuria for > 3 mos, $\bar{x}$: 2 yrs). Results are expressed in mg/dl ($\bar{x}$ ± SD; * p: < 0.01) and age in yrs ($\bar{x}$ and range).

GROUP	AGE	TC	TG	LDL	HDL
MCNS, relapse	9 (2-17)	361±131*	258±188*	238±71*	62±18
MCNS, remission	10 (4-20)	223± 77*	100± 52*	160±79*	59±17
Control	10 (6-17)	160± 25	55± 21	95±24	56±11

LDL/HDL ratios > 2 (normal 1.6-2.0 for ages studied) were observed in 88% of children in relapse and 58% in remission. Duration of lipid changes in remission correlated well with duration of disease and frequency of relapse. Lipid changes in MCNS may last for prolonged periods of time and are frequently associated with abnormal LDL/HDL ratios. This study suggests that MCNS children need lipid evaluation at regular intervals, and follow-up even in remission. Further data should clarify the pathogenesis of persistent HL in MCNS children and its role as a risk factor for premature coronary atherosclerosis.

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1516 CEREBRAL BLOOD FLOW CHARACTERISTICS IN THE ILL PREMATURE: RELATIONSHIP TO SEH/IVH. P.A. Ahmann, F.D. Dykes, A. Lazzara, D.P. Giddens,* T.A. Carrigan,* M.M. Patino. (Spon. by: J. F. Schwartz) Emory University School of Medicine, Department of Pediatrics, and *Georgia Institute of Technology, Department of Aerospace Engineering, Atlanta, Georgia.

Factors associated with alteration in systemic vascular pressure (volume expansion, pneumothorax, etc.) have been associated with intracranial hemorrhage in ill preterm infants and seem to implicate deficient regulation of cerebral blood flow in the etiopathogenesis of SEH/IVH. We have been involved in a prospective study using range gated pulsed Doppler ultrasound to determine carotid and anterior cerebral flow characteristics in ill preterm infants. Serial studies are performed on each infant, and response of cerebral flow to changes in mean arterial pressure is assessed. Thus far, 9 infants have been studied. Five infants demonstrated increased (decreased) cerebral flow velocity in response to increased (decreased) mean arterial pressure and had intracranial hemorrhage. SEH/IVH occurred prior to velocity studies in 4 of the 5 infants. Four infants demonstrated no change in cerebral flow velocity with change in mean arterial pressure, and none of these bled.

In conclusion: (1) Cerebral blood flow velocity alterations as a response to changes in mean arterial pressure appear related to intracranial hemorrhage in the ill preterm infant. (2) Some ill preterm infants can effectively regulate cerebral blood flow.

1517 UNEQUAL ANTERIOR CEREBRAL ARTERY (ACA) BLOOD FLOW VELOCITIES FOLLOWING CAROTID LIGATION Alice F. Andrews, Mary S. Samocha, Robert H. Bartlett (Spon. by Gary W. Goldstein), Univ. of Michigan Hospitals, Depts. of Pediatrics and Surgery, Ann Arbor, Michigan

Ligation of the right common carotid (LRCC) for venoarterial extracorporeal membrane oxygenation (VA ECMO) is always of concern, although no neurologic deficit has been shown to occur from this procedure. We did Doppler studies to measure ACA pulsatility indexes (PIs) in 3 infants who had LRCC, to try to detect changes in cerebral blood flow (CBF).

One infant had ACA PIs measured before LRCC, and her left and right PIs were equal then. 2.5 hours following LRCC the PIs were unequal, with the R PI 0.75 and the LPI 0.62. Two months later the difference persisted, with the R PI 0.76 and the L PI 0.58. Another infant had ACA PIs measured 5.5 mos. following LRCC, with the R PI 0.76 and L PI 0.69. Both infants had CBF and brain scans showing normal and equal perfusion of cerebral hemispheres, without cerebral infarct. Both infants are developing normally.

A third infant had an IVH a few hours after going on VA ECMO. ACA PIs done after the IVH were R PI 0.81 and L PI 0.73. This infant did not survive.

Usually factors determining cerebral blood flow velocities (as measured by ACA PIs) have equal effects bilaterally. An example is asphyxia causing cerebral vasodilation and lowering of the PIs. After LRCC, left sided CBF must also supply the right brain. This increase in the vascular bed of the left internal carotid is reflected in the L ACA by lowering of the L PI with respect to the R PI.

1518 EFFECT OF HYPERVENTILATION UPON CEREBRAL BLOOD FLOW VELOCITY IN NEONATES WITH PERSISTENT PULMONARY ARTERY HYPERTENSION

Alice F. Andrews and Mary S. Samocha (Spon. by Gary W. Goldstein), Univ. of Michigan Hospitals, Depts. of Pediatrics and Surgery, Ann Arbor, Michigan

Hyperventilation is accepted therapy for persistent pulmonary artery hypertension (PPAH), but little is known of the effects of the resulting hypocarbia on cerebral blood flow. We did Doppler studies of anterior cerebral arteries (ACAs) to measure pulsatility indexes (PIs) in 4 neonates who were being hyperventilated.

The infants' birth weights ranged from 2.5 to 3.0 kgs, and gestational ages ranged from 34-40 wks. PPAH was documented by Swan-Ganz catheter and/or differential blood gases and/or echocardiography. The 4 infants had a total of 7 ACA PIs done while being hyperventilated. The average pCO_2 at the time of being studied was 21 (range 17.5 - 25.5), and the ave. pH was 7.54 (range 7.47 - 7.61). For each of the 7 studies, the PI was 1.0, the highest possible value, indicating cerebral vasoconstriction. After coming off hyperventilation, each infant had a normal PI (ave. 0.68, range 0.64 - 0.72). All 4 infants survived and, at discharge, appeared neurologically intact.

Each of the infants was screened with cranial ultrasound and did not have intraventricular hemorrhage. The high PIs while being hyperventilated were independent of dopamine, tolazoline, pneumothorax, or blood pressure.

Doppler studies of ACA blood flow velocities in preterm and term infants who are being hyperventilated indicate cerebral vasoconstriction. This is most likely due to hypocarbia.

1519 EFFECTS OF ELEVATED INTRACRANIAL PRESSURE ON CEREBRAL OXYGEN CONSUMPTION IN NEWBORN LAMBS. Joanne E. Backofen, Raymond C. Koehler, Richard J. Traystman, M. Douglas Jones, Jr. and Mark C. Rogers. Department of Anesthesia/Critical Care, Johns Hopkins Hospital, Baltimore, MD 21205

We studied the effects of elevation of intracranial pressure (ICP) on cerebral blood flow (CBF), cerebral cortical oxygen consumption ($\dot{V}O_2$) and cerebral fractional oxygen extraction. Infant lambs (3 - 10 days old) were anesthetized with pentobarbital, paralyzed, and ventilated. ICP was elevated with mock CSF over 2 min and maintained with a reservoir. A sagittal sinus catheter was used for cerebral venous blood samples. CBF was measured using microspheres. $\dot{V}O_2$ was calculated using CBF and the cerebral arteriovenous difference of oxygen content from the sagittal sinus. Fractional extraction was determined as the ratio of cerebral oxygen consumption to cerebral oxygen delivery. Baseline value and values after 5,15 and 40 min of ICP were obtained.

Moderate ICP to a cerebral perfusion pressure (CPP) of 48 ± 2 mmHg (± SE), increased cerebral fractional O_2 extraction from .48 ±.03 to .57 ± .03 at 5 min and .53 ± .04 at 15 and 40 min. CBF and $\dot{V}O_2$ did not change. With severe ICP (CPP of 22 ± 2 mmHg at 5 min and 26 ± 3 mmHg at 15 and 40 min) there was a decrease in CBF from 53 ± 6 to 37 ± 5 ml/min/100g. Cerebral fractional O_2 extraction increased from .51 ± .05 to .72 ± .05, .66 ± .04, .64 ± .06 at 5, 15, and 40 min, respectively. There was no significant change in $\dot{V}O_2$ (from 3.4 ± .3 to 3.4 ± .3, 3.3 ± .3 and 2.9 ± .2 ml O_2/ min/100g). These data indicate that with a CPP of 48 mmHg, autoregulation maintains CBF. Even at CPP of 26 mmHg, CBF falls but the newborn lamb still of maintains cerebral O_2 consumption.

1520 ALTERATIONS IN CEREBRAL HEMODYNAMICS IN RELATION TO ONSET OF NEONATAL INTRAVENTRICULAR HEMORRHAGE. Henrietta S. Bada, Sheldon B. Korones and Hubert L. Magill (Spon. by George A. Burghen), University of Tennessee, Departments of Pediatrics and Radiology, Memphis.

Previous Doppler studies of the anterior cerebral arteries showed an associated rise in right and left pulsatility indices (RPI and LPI) in the presence of intraventricular hemorrhage (IVH) a finding suggestive of arterial vasospasm. To determine the temporal relationship of this phenomenon to the onset of IVH, we prospectively evaluated 70 consecutive preterm infants with birth weight of 1500 gm or less. For a week each patient had daily real time ultrasound head scan and determination of RPI and LPI from the Doppler flow velocity tracings of anterior cerebral arteries. Fifty-five (79%) of the infants developed IVH, detected at a mean age of 1.5 ± 0.5 days (range 1-3 days). A rise in PI was observed at a mean of 2 ± 1.5 days from the onset of IVH. Mean highest RPI and LPI following IVH were both 0.91 ± 0.10, and in 35 (64%), the RPI and LPI values were over 0.91; only three of 15 infants with no IVH had PI over 0.91 during the first week of life. Twenty-two (31%) died; all had IVH. Ten infants died within 48 hours of age. The other 12 deaths occurred after the second day of life and in 9 infants, both RPI and LPI values were 1.0 and persisted for over 48 hours. These preliminary data show that increase in PI, suggestive of vasoconstriction, occurs frequently with IVH but is not a consistent finding. Following IVH, PI values of 1.0 persisting for 48 hours or longer, indicate poor prognosis.

1521 CEREBRAL VASCULAR RESISTANCE (CVR) AND BLOOD VELOCITY IN NEWBORN PUPPIES BY DOPPLER TECHNIQUE. Daniel G. Batton, Jonathan Hellmann, Milton J. Hernandez (Spon by M. Jeffrey Maisels). Penn State Univ Coll of Med, M. S. Hershey Med Ctr, Depts of Peds and Neur, Hershey, PA.

The pulsatility index (PI) has been related to CVR in newborns (Bada) based on the assumption that changes in diastolic and not systolic velocity occur with changes in CVR. We examined this relationship by studying the effect of $PaCO_2$ alterations on the PI. Ten newborn puppies were tracheostomized, paralyzed, and ventilated, and the cerebral arterial blood velocity measured continuously by Doppler technique. 77 PI determinations were made at $PaCO_2$ levels ranging from 15.2-75.6 torr while PaO_2 and blood pressure were not altered significantly. Analysis revealed PI and $PaCO_2$ were directly and not inversely related as anticipated although this relationship was not strong ($r=.35$; $p<.01$). Furthermore, the systolic, diastolic, and mean velocities were all individually directly related to $PaCO_2$ ($p<.01$; $r=.75$, $r=.51$, $r=.66$ respectively). This suggests velocity changes were closely related to changes in blood flow. Therefore, we defined the ratio (mean arterial blood pressure/mean arterial blood velocity) as an index of resistance and found this ratio to be significantly related to $PaCO_2$ ($r=.68$; $p<.01$). We conclude that under controlled experimental conditions the Doppler technique is a valuable means for studying continuous changes in cerebral blood flow and CVR. However, PI per se is not a reliable indicator of CVR because systolic as well as diastolic changes in blood velocity occur as resistance is altered.

1522 LATE ONSET HYDROCEPHALUS AFTER INTRAVENTRICULAR HEMORRHAGE. Raul Bejar, T. Allen Merritt, Hector James, Brian Saunders, Louis Gluck. Univ. of California, San Diego, Depts. of Pediatrics & Neurosurgery; Kaiser Foundation Hospital, Dept. of Pediatrics

Of 29 infants with grade III or IV intraventricular hemorrhage undergoing sequential lumbar punctures to attempt to control post-hemorrhagic hydrocephalus in the first months of life, only 8 (BW .86-3.1 kg) responded. Six of 8 infants have returned after discharge for clinical and neuroanatomical evaluation by computerized tomography or ultrasonography. Four of 6 infants have shown progressive ventricular enlargement between 5.5 to 9 months accompanied by increasing head growth. Cysternography confirmed evidence of hydrocephalus. One of 4 infants died (SIDS), and 2 of 3 infants have required shunt procedures between 5 and 9 months of age. Three additional infants not treated with sequential lumbar punctures because of stable ventricular size for 1.5-5 months after grade II-III IVH developed insidious hydrocephalus requiring shunting at 2.5-12 months. These data suggest that initial stabilization by sequential lumbar punctures or spontaneous reduction of ventricular size within the first months does not afford protection against later hydrocephalus, and suggests that previous therapeutic "success" from sequential lumbar punctures requires redefinition in terms of postnatal follow-up.

1523 VENTRICULOMEGALY AND SUBARACHNOID FLUID COLLECTIONS IN ≤ 1200 GM INFANTS FOLLOWED TO 8 MO. OF AGE. Mary Ellen A. Bozynski, Michael N. Nelson, Diane R. Genaze, Werner A. Meier (Sponsored by Joseph R. Christian), Rush Medical College, Rush Presbyterian St. Luke's Medical Center, Department of Pediatrics, Psychology, and Physical Therapy, Chicago.

Since March, 1980, real-time ultrasonography has been employed to detect intracranial hemorrhage (ICH) and screen for post-hemorrhagic hydrocephalus in ≤ 1200 gm neonates. All infants were scanned prior to discharge using a Toshiba SAL-20A linear array scanner. Twenty-six of thirty-six were re-evaluated at 4 and 8 months (corrected age). A subgroup of 7 infants have presented with ventriculomegaly and subarachnoid fluid collections confirmed by computerized tomography. Three were diagnosed after discharge. Ventriculomegaly and enlarged subarachnoid spaces usually indicate atrophy, but head growth in these 7 infants was inconsistent with this diagnosis. All 7 infants had a history of ICH, but fluid collections also have been reported in malnutrition, anorexia, and after head trauma or chemotherapy. Follow up results usually have been favorable. Our results are less optimistic. One infant is institutionalized, one underwent V-P shunt placement, and all showed abnormal gross motor development documented by the Milani-Comparetti Motor Development Screening Test. The Bayley Scales of Infant Development were less sensitive to gross motor impairment, but did show improving cognitive development for most infants. There is a probable high incidence of this clinical picture in the extreme premature. Improved developmental assessment techniques and guidelines for intervention are needed.

1524 ACCURACY OF INTRACRANIAL PRESSURE MONITORING BY SUBARACHNOID BOLT IN THE PRESENCE OF AN OPEN FONTANEL. John D. Bray, Frank R. Gioia, Janet Graham, Randall C. Wetzel, and Mark C. Rogers, Depts. of Anesthesiology/Critical Care Med. and Ped., Johns Hopkins Med. Inst., Baltimore, MD

Under clinical conditions, the accuracy of intracranial pressure (ICP) measurement by the subarachnoid bolt (SAB) technique in infants with an open fontanel is unknown. We have been able to verify the accuracy of this technique by simultaneously recording as determined by SAB and an intraventricular catheter (IVC) in a 13 month old patient with a widely open fontanel. Following a severe anoxic insult, ICP was initially monitored with a SAB placed in the right frontal region. Because of intracranial hypertension refractory to medical management, an IVC was placed in the left lateral ventricle to allow periodic cerebrospinal fluid drainage for 72 hours. During this period, ICP as determined by SAB and IVC were simultaneously recorded at frequent intervals. Subsequently, absolute values of ICP, as well as the amplitude of hemodynamic and respiratory fluctuations in ICP, were compared for the two techniques of measurement. The range of ICP during the monitoring period was 0 - 60 torr. Respiratory fluctuations in ICP were identical in both techniques (2.5 - 3.5 torr./breath). However, hemodynamic fluctuations in ICP recorded by IVC were generally twice the amplitude of those measured by SAB. Absolute values obtained with the two techniques never varied by greater than 6 torr. as long as patency of the SAB system was maintained. We conclude that, under proper use of the system, the SAB technique is capable of yielding accurate measurement of ICP in infants.

1525 AUDITORY BRAINSTEM RESPONSE ABNORMALITIES ASSOCIATED WITH VENTRICULAR DILATION IN NEONATES. Jane E. Brazy and Bruce A. Weber, (Spon by Samuel Katz), Duke Univ Med Ctr, Depts of Pediatrics and Surgery, Durham, NC.

The relationship between brainstem function and ventricular dilation was studied by auditory brainstem evoked responses (ABRs) in sixteen infants with ventricular dilation (VD) documented by ultrasound or CT scan. Clinical signs of overt hydrocephalus were present in only ten. Abnormal responses to auditory stimuli during the time of VD were found in 13 of the 16 patients including all of those without clinical signs of hydrocephalus. Marked improvement or normalization of the ABR occurred with resolution of the VD in all infants who survived. Wave III and Wave V response latencies (representing brainstem transmission) significantly shortened after resolution of VD while Wave I (cochlear response) remained unchanged.

RESPONSE LATENCIES (msec) mean +/- SD	WITH VD	AFTER RESOLUTION (corrected for maturation)	p
WAVE I	2.68 (.66)	2.58 (.47)	NS
WAVE III	5.47 (1.67)	5.11 (.88)	.05
WAVE V	8.77 (1.14)	8.03 (.77)	.01

These findings demonstrate that ABR abnormalities occur in most infants with VD; that the ABR is a sensitive indicator of functional compromise; and that significant impairment of auditory brainstem transmission can occur in the absence of overt hydrocephalus. Restoration of function occurs rapidly after therapy.

1526 QUANTITATIVE ANALYSIS OF COMPUTED TOMOGRAMS IN CHILDREN WITH ATTENTION DEFICIT DISORDER. Thomas N. Byrne, Sally E. Shaywitz, Bennett A. Shaywitz, Stephen G. Rothman and Donald J. Cohen, Yale University School of Medicine, Depts. Neurology, Pediatrics, Radiology and the Yale Child Study Center, New Haven, Connecticut 06510.

The advent of computed tomography renewed hopes that this new and powerful diagnostic technique would prove more helpful than earlier, less sophisticated procedures in elucidating brain "damage" in the group of children with disorders of attention, activity regulation and learning disabilities presently classified within the rubric of Attention Deficit Disorder (ADD). We report our analysis of CT scans in two groups of children: a cohort satisfying DSM III criteria for ADD and a contrast (CON) group. Both the ADD (29 boys, 6 girls, ages 5-19 years, mean 10.3) and CON (20 boys, 9 girls, ages 4-18 years, mean 10.9) groups were of normal intelligence (WISC-R). In most cases (19/35 ADD, 20/29 CON) the maximum width of the anterior horns (AH) of the lateral ventricles were symmetric, and when asymmetries were found the left was more often wider than the right (10 L>R, 6 R>L in ADD; 6 L>R, 3 R>L in CON). Evan's Index, (RAH + LAH)/ maximum internal width of the skull, were comparable in ADD and CON, averaging 0.24 $\pm$ .02 and 0.26 $\pm$ .02 respectively, ratios indistinguishable from the 0.26 value reported for normal children. Our findings indicate that if anatomical evidence of brain "damage" does exist in this group its documentation must await the application of newer diagnostic techniques, such as positron emission tomography or nuclear magnetic resonance.

1527 INEFFECTIVENESS OF CARBAMAZEPINE (CBZ) FOR FEBRILE SEIZURE PATIENTS REQUIRING PROPHYLAXIS BUT INTOLERANT TO OR UNCONTROLLED BY PHENOBARBITAL (Ø). Peter R. Camfield, Carol S. Camfield, and John A. R. Tibbles. Spon. by John F. Crocker. Dalhousie Medical School, I.W.K. Hospital for Children, Department of Pediatrics, Halifax, Nova Scotia.

Selected children with febrile seizures who are at increased risk of epilepsy are candidates for daily phenobarbital (Ø) prophylaxis. Some of these children become Ø failures due to adverse behavioral side effects or recurrent febrile seizures despite adequate Ø serum levels. For 30 months we have used carbamazepine (CBZ) for consecutive patients with Ø failure: 10 for adverse behavioral effects, 5 for recurrences on Ø. None had previous afebrile seizures, epileptiform EEG, or neurologic abnormality except 2 with mild developmental delay. CBZ was started at an average age of 33 months. After an average of 6.7 months, 12/15 had recurrent febrile seizures, 8/10 with adverse behavioral effects from Ø, and 4/5 with recurrences on Ø. Compliance was excellent by history in all 12, documented by preceeding therapeutic levels in 4 (0.6-1.1 mg/dl). In 5 others CBZ levels at the time of recurrence ranged from 0.4-0.7 mg/dl. The 3 without recurrences have therapeutic levels but have only received CBZ for 2-4 months.

We estimate a complete population of 12 million is required to compare two drugs for treatment of Ø failure patients. Therefore, data from consecutively treated patients will likely provide rationale for alternate anticonvulsants. CBZ appears to be ineffective for Ø failures.

1528 SENSORINEURAL HEARING LOSS IN CHILDREN FOLLOWING RADIATION THERAPY James Coplan, Charles T. Grimes, Robert A. Richman, and Ernest M. Post. SUNY-Upstate Medical Center, Department of Pediatrics and Otorhinolaryngology, Syracuse

To determine the prevalence of hearing loss following radiation therapy (RT), we studied six children who had previously undergone RT for treatment of intracranial tumors. Mean age at RT was 8.5 yr (range 2.3-10yr), mean dose of RT to the inner ear was 3,800 rad (range 1,450-5,000 rad), and mean postirradiation interval prior to audiologic evaluation was 5.6 yr (range 1-12 yr). Indications for RT were: eosinophilic granuloma(2), optic glioma(1), brainstem glioma(1), astrocytoma (1), and ectopic pinealoma(1). At formal audiologic evaluation, four of six children had sensorineural hearing loss (SN HL). One child had received unilateral irradiation of the mandible and temporal bone; ipsilateral severe SN HL above 3,000 hertz was found. One child has asymmetric radiation-induced cerebral calcification following bilateral irradiation of the sella and temporal fields. She had bilateral SN HL, moderate in one ear, severe in the other, with greater hearing loss on the side more prominently manifesting the other radiation effect. Two children had unilateral moderate SN HL following symmetrical irradiation of the sella and temporal fields. One child had received a brief course of gentamicin prior to audiometric evaluation; medical and family histories revealed no other obvious causes for SN HL. Middle ear function (tympanometry) was normal in all subjects. We conclude that the prevalence of SN HL following cranial RT of solid tumors is sufficiently high to warrant routine pre and post-RT audiometrics, with annual re-evaluation for at least 5 years.

1529 MITOCHONDRIAL ABNORMALITY WITH DEFICIENT CYTOCHROMES aa_3 AND B, PRODUCING FATAL MITOCHONDRIAL MYOPATHY AND LACTIC ACIDOSIS IN AN INFANT AND FATAL HEPATOPATHY IN A SECOND COUSIN. G. Robert DeLong, Rosemary Boustany, June Aprille, John Halperin and Harvey Levy. Harvard Medical School, Massachusetts General Hospital, Pediatric Neurology Unit, Boston.

Fatal infantile mitochondrial myopathy with lactic acidosis, morphologically abnormal mitochondria (mito), deficient cytochromes aa_3 and b, and a Fanconi-like aminoaciduria has been reported previously. We report two infants, second cousins, with a similar fatal disorder of mito, but limited to skeletal muscle in one child, and to liver in the other. The first presented at 3 mos. with weight loss, hypotonia, external ophthalmoplegia, and progressively severe lactic acidosis with high lactate/pyruvate ratio ($\sim$50). EM of muscle biopsy showed increased numbers of enlarged mito containing concentric rings of cristae. Spectroscopy revealed no detectable cytochrome aa_3 or b, but normal cytochrome c. Cytochrome oxidase activity was $<$ 1% normal. In autopsy kidney, heart, lung, liver and brain, cytochromes were normal. Liver mito were normal by EM. The second cousin, related through maternal grandfather, presented at 5 mos. with persistent vomiting and liver failure without lactic acidosis. Mito in a liver biopsy were abnormal by EM. In autopsy liver, cytochrome aa_3 and b were barely detectable by spectroscopy; cytochrome oxidase activity was $<$ 10% normal. Kidney was normal; muscle was not studied. The mito abnormality in the two children is presumably related, but unexplained are the mode of genetic transmission and the involvement of a single different organ in each child.

● 1530 CEREBROVASCULAR RESPONSE TO HYPOXIA DURING BARBITURATE COMA IN NEWBORN LAMBS AND ADULT SHEEP. Judith H. Donegan, Richard J. Traystman, Raymond C. Koehler, M. Douglas Jones, Jr., and Mark C. Rogers. Departments of Anesthesiology/Critical Care Medicine and Pediatrics, Johns Hopkins Medical Institutions, 600 N. Wolfe St., Baltimore, MD 21205

The cerebrovascular response to isocapnic hypoxia during barbiturate coma was compared to the awake response in 16 newborn lambs [L] and 11 adult sheep [S]. Cerebral blood flow (CBF), cerebral O_2 consumption ($CMRO_2$) and cerebral O_2 delivery (OD) were obtained in awake, lambs and sheep at normoxia (CaO_2 = 14.8 ± 0.6 [L], 14.1 ± 0.6 [S] vol % [mean ± SE]) and at moderate (CaO_2 = 10.9 ± 0.5 [L], 10.5 ± 0.5 [S] vol %) and severe (CaO_2 = 8.0 ± 0.6 [L], 7.4 ± 0.5[S] vol %) hypoxic hypoxia. Pentobarbital (~ 90 mg/kg) was given and the measurements repeated at same CaO_2. Control $CMRO_2$ was higher in lambs than adults (5.5 ± 0.6 vs 4.1 ± 0.6 ml O_2/100g/min), and CBF and OD were higher (CBF = 86 ± 6 [L], 50 ± 11 [S] ml/ 100g/ min; OD = 12.4 ± 0.7 [L], 7.1 ± 0.7 [S] ml O_2/100g/min). Moderate hypoxia (MH) increased CBF to 138 ± 14 [L], 88 ± 7 [S] ml/ 100g/min, with a further increase at severe hypoxia (SH) (177 ± 17 [L], 146 ± 20 [S] ml/ 100g/min). $CMRO_2$ remained unchanged while OD was unchanged in lambs and rose in sheep. During coma $CMRO_2$ was reduced to 2.7 ± 0.2 [L], 2.2 ± 0.3 [S] ml O_2/100g /min, CBF to 44 ± 33 [L], 28 ± 4 [S] ml/100g/ min and OD to 6.4 ± 0.5 [L], 3.7 ± 0.4 [S] ml O_2/100g/min. $CMRO_2$ did not change with hypoxia. Any differences in responsiveness to hypoxia between sheep and lambs as well as between awake and comatose animals were proportionate to the differences in $CMRO_2$. Cerebral O_2 delivery was maintained at all times.

1531 EFFECT OF REDUCED CEREBRAL OXYGEN CONSUMPTION UPON THE CEREBROVASCULAR RESPONSE TO HYPOXIA. Judy H. Donegan, Richard J. Traystman, Raymond C. Koehler, M.Douglas Jones, Jr., and Mark C. Rogers. Depts. of Anesthesiology/Critical Care Medicine and Pediatrics, Johns Hopkins Medical Institutions, Baltimore, MD 21205

The response of the cerebral vessels to graded isocapnic hypoxia in 10 awake sheep was compared to the response following sufficient pentobarbital (~90 mg/kg) to produce electroencephalographic silence and to reduce cerebral oxygen consumption ($CMRO_2$) by 46%. Cerebral blood flow (CBF), $CMRO_2$ and cerebral O_2 delivery (OD) were determined at normoxia (CaO_2 = 14.1 ± 0.6 vol % [mean ± SE]) and during moderate (CaO_2 = 10.5 ± 0.5) and severe (CaO_2 = 7.4 ± 0.5) hypoxic hypoxia before and after barbiturate. CBF was measured with radiolabelled microspheres in chronically catheterized sheep. In awake animals CBF increased from control (50 ± 4 ml/100g/min) to 88 ± 7 and 146 ± 20 with moderate (MH) and severe (SH) hypoxia. $CMRO_2$ did not change significantly from control (C) (C = 4.1 ± 0.9; MH = 4.7 ± 0.3; SH = 5.4 ± 0.5 ml O_2/100g/min), while OD increased (C = 7.2 ± 0.6; MH = 9.3 ± 0.6; SH = 11.5 ± 1.4 ml O_2/100g/min). Following pentobarbital CBF was reduced 44%, $CMRO_2$ 46% and OD 48%. CBF increased with hypoxia (C = 28 ± 4, MH = 42 ± 4, SH = 57 ± 7 ml/100g/min), whereas $CMRO_2$ and OD were unchanged from control ($CMRO_2$ = 2.2 ± 0.3, OD = 3.7 ± 0.4 ml O_2/100g/min). While the cerebrovascular response to hypoxia was less during coma than in the awake state, the reduction in response was proportionate to the reduction in $CMRO_2$, and cerebral OD was maintained constant.

● 1532 MEASUREMENT OF REGIONAL CEREBRAL GLUCOSE UPTAKE IN NEWBORN INFANTS USING POSITRON EMISSION TOMOGRAPHY. Lex W. Doyle, Claude Nahmias, Gunter Firnau, David B. Kenyon, Stephen Garnett and John C. Sinclair. Departments of Nuclear Medicine and Pediatrics, McMaster University Medical Centre, McMaster University, Hamilton, Ontario, Canada.

We have used positron emission tomography (PET) with ^{18}F-2-fluoro-2-deoxy-D-glucose (2-^{18}FDG) to investigate regional cerebral glucose uptake in newborn infants. 2-^{18}FDG was synthesized from accelerator-produced ^{18}F. The tomograph is a high-efficiency, single-slice, stationary instrument with a resolution of 7 mm in the plane. 2-^{18}FDG in normal saline was injected intravenously. After one hour, tomographic slices of the brain were obtained at several levels. The levels at which the tomographic slices were taken were defined relative to the cerebral ventricles whose position had previously been determined by ultrasound.

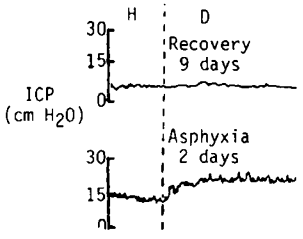
Using PET, we can differentiate clearly between the glucose uptake of grey and white matter structures. We have identified areas of high glucose uptake that correspond to thalamus, caudate nucleus, striatum and cortical mantle. We are using PET to determine regional variations in cerebral glucose uptake in babies with birth asphyxia, cerebral hemorrhage or seizure disorders.

● 1533 THE INFLUENCE OF INOSIPLEX TREATMENT ON THE NEUROLOGICAL DISABILITY OF SUBACUTE SCLEROSING PANENCEPHALITIS PATIENTS. Robert H. DuRant, Paul R. Dyken, Andrea V. Swift (Spon. by Alex Robertson), Medical College of Georgia, Departments of Pediatrics and Neurology, Augusta.

Subacute sclerosing panencephalitis (SSPE) is a central nervous system degenerative disease of children that rapidly progresses to death in most untreated cases. Using a specially devised neurological disability index (NDI) this study compared the level of NDI longitudinally in a group of SSPE patients receiving inosiplex treatment (n=12) to a group of intreated SSPE controls (n=15). Based on t-tests, mean NDI did not differ between the groups from onset of SSPE through 21 months. From 2 years through 4½ years the inosiplex group had significantly ($p<0.01$) lower NDI than the non-treatment group. The subjects were then divided into four sub-groups: Group 1 (N=7) rapidly progressing SSPE, non-inosiplex treated; Group 2 (N=8) slowly progressing SSPE, non-inosiplex treated; Group 3 (N=6) rapidly progressing SSPE, inosiplex treated; Group 4 (N=6) slowly progressing SSPE, inosiplex treated. Based on analysis of variance and Tukey multiple comparison tests, the rapidly developing groups (Groups 1 and 3) did not differ in the progression of NDI at any follow-up period. However, the slowly developing inosiplex group (Group 4) had significantly ($p<0.01$) lower NDI than the slowly developing non-treatment group (Group 2) from 2½ years to 4½ years after onset of SSPE. The findings indicate that inosiplex was effective in reducing the NDI of SSPE. However, insoiplex appears to be more effective in patients with the slowly developing or chronic form or SSPE.

1534 HEAD POSITION IS CRITICAL TO INTRACRANIAL PRESSURE IN ASPHYXIATED INFANTS. Janet R. Emery and Joyce L. Peabody. (Spon. by June P. Brady). Children's Hosp. and Cardiovasc. Res. Inst. Univ. of Ca., Dept. of Ped., S.F.

Attention to head positioning of asphyxiated newborns to minimize intracranial pressure (ICP) has been neglected. We tested the effect of head position on ICP in 6 asphyxiated (BW 1200-3970 g; mean age=2 days) and 6 non-asphyxiated infants (BW 1830-3460g; mean age=3 days). We measured transfontanel ICP, thoracic impedance, blood pressure, heart rate, transcutaneous PO_2 (tcP_{O_2}),and transcutaneous PCO_2 (tcP_{CO_2}) and compared the results in the horizontal (H), elevated 30°, and dependent 30° (D) positions. There were no significant changes in thoracic impedance, blood pressure, heart rate, tcP_{O_2}, or tcP_{CO_2} with changes in position. ICP in the dependent position was higher than in the horizontal position in all infants. However, asphyxiated infants had a greater increase in ICP, (mean±SE), 8 ± 2 cmH_2O compared to 3 ± 1 cmH_2O in the non-asphyxiated infants ($p<0.05$). One infant was studied following asphyxia and again after recovery (Fig.). ICP decreased in both groups with head elevation but there was no difference between the groups (mean± SE) 4 ± 3 and 4 ± 1 cmH_2O.



We conclude that head position is critical in infants with asphyxia. We warn against the use of the dependent position and suggest that head elevation may be beneficial in these infants.

1535 HYPOXIA ALONE INDUCES INTRACRANIAL HEMORRHAGE (ICH) IN NEWBORN RATS. Rochelle C. Feldman, W. Donald Shields, Cynthia T. Barrett, Jo Anne Nakagawa. UCLA School of Medicine, Center for the Health Sciences, Department of Pediatrics, Los Angeles

Hypoxia has been associated with ICH in experimental animals and newly born infants, but as a single insult has not produced ICH in published reports. We have established a model in which hypoxic insults reliably produce hemorrhages in the cerebellum (ICeH) and 4th ventricle in newly born rats. Daily 1 or 2 hour exposures of rats to 8% O_2 on days 3,4,5 resulted in ICeH in 18/28 compared with 0/12 ICeH in control rats exposed to 21% O_2 for the same time periods ($p < 0.005$). No differences in incidence (I) or severity (S) were present between animals exposed daily for 1 hour (7/10) or 2 hours (11/18). Hemorrhages were located in 4th ventricle, cerebellar folia, vermis and less commonly in external granular and molecular layers. When rats were exposed to 8% O_2 for 1 hour at varying postnatal ages (0-6 days), the highest I and S occurred when insults were delivered beginning at day 3 ($p = .048$). Rats with major hemorrhage weighed significantly more prior to hypoxic exposure than those without hemorrhage (8.7g ± 0.51 vs 8.1g ± 0.57, $p < .01$).

The model described above employs hypoxic insults alone with pathology, gestational timing and relationship to growth similar to that of ICH in the human. It establishes that an hypoxic insult in an unanesthetized animal can cause significant ICH and provides a basis for further studies on modification of ICH.

1536 CENTRAL NERVOUS SYSTEM (CNS) LESIONS AND CRITICAL HEART DISEASE (CHD) IN THE NEWBORN. Rochelle C. Feldman, W. Donald Shields and William F. Friedman, UCLA School of Medicine, Center for the Health Sciences, Department of Pediatrics, Los Angeles.

Studies of the association between congenital heart disease and cerebral lesions have focused on older infants and children. Lesions have been attributed to longstanding hypoxia and/or post-surgical cardiac catheterization complications. To define the risk of cerebral lesions in the newborn, we reviewed all neonatal autopsies which included brain examination of babies with CHD between 1971-1980. Nineteen of 32 babies (59%) with CHD had CNS lesions, 89% of them hemorrhagic (Group I). Babies without CNS lesions were designated Group II. The lesions are shown below:

TYPES OF BRAIN LESIONS

Intraventricular Hemorrhage:	9	Infarction and/or Cerebromalacia:	6
Subarachnoid Hemorrhage:	10		
Subdural Hemorrhage:	4	Other brain lesions:	2

Differences were sought, but not found, between Group I and II babies with respect to gender, gestational age, birth weight, intrauterine growth, Apgar scores and brain weight. The average age at death of Group I babies was 102 hours, contrasted with 239 hours in Group II ($p < .05$). Cardiac catheterization was performed with equal frequency in the two groups. Thus, significant brain lesions are associated with CHD in newborns substantially more often than was previously recognized, and are present regardless of invasive studies. Definition of their presence and severity may be a critical element of clinical management and follow-up.

1537 A CONTROLLED TRIAL OF DEANOL FOR TOURETTE SYNDROME. Jack W. Finney, Edward R. Christophersen, and Dewey K. Ziegler. University of Kansas College of Health Sciences and Hospital, Depts. of Pediatrics and Neurology, Kansas City, Kansas.

Recent studies have suggested a relationship between cholinergic hypoactivity and the Tourette syndrome (TS). We have evaluated, using a time series design, the effects of deanol for a six-yr-old male with vocal and eye-blinking tics. Two raters (one "blind") scored vocal tic rates from videotapes made in the home during parent-child interactions (academic and game tasks). Vocal tics decreased during

		Conditions			
Task		Baseline	Deanol	Reversal	Deanol + Diazepam
Academic	x rate/min	0.40	0.06	0.38	0.07
Game	x rate/min	0.42	0.05	0.78	0

the deanol only (200 mg/day) and the deanol plus diazepam (200 + 6) conditions, and increased during the reversal condition. Diazepam was prescribed due to increased irritability and emotional behavior. Effects and trends were similar for both measurement situations and were at zero rates at a two-month follow-up. Throughout the 25 weeks of the study numerous new tics waxed and waned, confirming the diagnosis of TS and suggesting a lack of generalized suppression of tics. However, the data suggest that the vocal tic, the most disruptive for school and social situations, was controlled by deanol. Further clinical trials and controlled studies appear warranted given the mild side effects of deanol and possible benefits for undesirable tics. The effectiveness of deanol supports the relative cholinergic hypoactivity hypothesis for TS.

1538 EFFECT OF ACUTE METABOLIC ACIDOSIS ON BILIRUBIN AND ALBUMIN IN RAT BRAIN. Masahisa Funato, William Oh, and William J. Cashore. Brown University, Women and Infants Hospital, Dept. of Pediatrics, Providence, RI.

This study was designed to explore two questions 1) does acute metabolic acidosis (AMA) enhance entry of bilirubin (BR) into the brain? and 2) if so, what is the mechanism? 16 pairs of awake young adult white rats were infused with 25 mg/kg/hr of BR for 180 mins. Experimental AMA was induced by infusion of HCl (4 mEq/kg/hr); controls received equal volumes of saline. At 180 mins., plasma BR levels were 13.8±2.5 vs 14.5±4.3 mg%, albumin (ALB) levels 3.6±0.4 vs 3.8±0.5 gm%, pH 7.28±0.09 vs 7.06±0.11 ($p<0.001$), and Base Excess -3.8±1.9 vs -16.6±3.7 mEq/L ($p<0.001$) in control and experimental animals, respectively. Whole brain BR by chloroform extraction was 2.25±0.40 µg/gm wet weight in controls and 3.25±0.53 µg/gm in acidotic animals ($p<0.005$). In 8 pairs, plasma ALB was labeled with ^{125}I-albumin and brain ALB content derived from plasma was calculated from the specific activity. Despite a 50% increase in brain BR, brain ALB content was similar in control and experimental animals, as shown:

	N	Brain BR, µg/gm	Brain ALB, µg/gm	BR/ALB Molar Ratio Plasma	Brain
Control	8	2.23±0.41	68±24	0.43±0.04	4.2±1.7
Experimental	8	3.34±0.68	70±20	0.45±0.05	6.1±2.3
p value		<0.005	n.s.	n.s.	n.s.

The data suggest that AMA increases the entry of BR into the brain and that the increase in brain BR is probably a result of dissociation of BR from ALB rather than a breakdown in the blood brain barrier to albumin.

● **1539** LIDOCAINE THERAPY FOR INTRACRANIAL HYPERTENSION Terry L. Furgiuele (Spon. by Stanley Porter), Eastern Virginia Medical School, Children's Hospital of The King's Daughters, Department of Pediatrics, Norfolk, Virginia.

Intravenous Lidocaine was prospectively evaluated for effectiveness in reducing elevated intracranial pressure (ICP). Five children (ages 11 mo-14 yr) with diffuse cerebral edema were studied. Underlying etiologies for ↑ICP included head trauma, Reye's Syndrome and Herpes encephalitis. All children had continuous subdural pressure monitors in place with ICP values of >20 torr for 5 minutes which were unresponsive to hyperventilation or osmotherapy.

All patients received a single dose of 1.5 mg/kg of Lidocaine over 1 min for a total of 10 clinical trials. ICP values, mean arterial pressure (MAP), heart rate, central venous pressure and ECG rhythm were monitored and recorded and duration of effect noted. Periodic blood samples were collected and serum frozen for future assay.

ICP was lowered in 100% (10/10) of clinical trials. Reduction in ICP from base-line values varied from a high of 80.9% to a low of 14.2%. Those patients not on continuous barbiturate infusion had a more favorable response. MAP was not affected and thus cerebral perfusion pressure (MAP-ICP) was also improved in all patients studied. No adverse clinical effects were seen. Mean duration of effect was 20 minutes.

We conclude that intravenous Lidocaine may be a useful medication for the treatment of intracranial hypertension, particularly in patients with a compromised cardiovascular system.

● **1540** REVERSIBLE SEPARATION OF TIGHT JUNCTIONS IN CULTURED BRAIN CAPILLARY ENDOTHELIAL CELLS. Gary W. Goldstein, Phillip D. Bowman, and A. Lorris Betz, University of Michigan Hospitals, Department of Pediatrics, Ann Arbor, Michigan 48109.

Endothelial cells in brain capillaries are sealed together by continuous tight junctions. This feature combined with a low level of transcellular pinocytosis produces a blood-brain barrier which limits the movement of polar molecules into the brain. To study barrier function at a cellular level, we prepared capillaries from a homogenate of bovine brain cortex, isolated the endothelial cells by collagenase treatment and gradient centrifugation and maintained the cells in tissue culture using a fibronectin-coated substrate and 10% plasma derived bovine serum. The cultured cells contained Factor VIII antigen and angiotensin converting enzyme--the two best accepted markers of endothelium. By electron microscopy, the cells formed a continuous monolayer sealed together by tight junctions. Incubation in a calcium-free buffer for 2 minutes resulted in separation of the tight junctions and retraction of the cell bodies. Cell contact was re-established when calcium was added back to the medium. Brain capillary endothelial cells in tissue culture provide a new way to study reversible opening of the blood brain barrier and should be a useful tool for learning more about the pathogenesis of brain edema and hemorrhage.

1541 HYPERLEXIA: PROGNOSIS AND VARIABILITY IN IQ SCORES Leonard Graziani, Karen Brodsky, Jeannette Mason, Ruth Zager. Thomas Jefferson University, Departments of Pediatrics and Neurology, Philadelphia, Pa.

The interrelationships between early development, IQ scores and prognosis were studied in 16 boys and 3 girls with hyperlexia (unexpectedly high word recognition skills in association with impaired language comprehension). All children were examined during the pre-school period and subsequently at least once during school age. During the pre-school period all disclosed abnormally low language development although non-verbal abilities ranged from normal to severely retarded; perseverative and other atypical behavior complicated the evaluation in all, and 6 were considered non-testable. Of the 7 children with normal full scale WISC-R IQ scores at school age, 3 previously had tested in the retarded range, 2 had been non-testable and 4 eventually entered regular classes. Despite the good prognosis in some, persisting deficits in social and emotional maturity prevented most from entering a fully mainstreamed educational program. IQ scores were highly correlated with reading comprehension and correlated less well with word recognition. Thus hyperlexia is a non-specific finding in some children with developmental language disorders or with mental retardation and indicates neither a normal academic potential nor a primary emotional disturbance. Recognition of hyperlexia in a child with a severe behavioral disturbance permits the examiner to focus on the language disorder as the primary dysfunction. The hyperlexic child must be assessed periodically, and a long term prognosis should not be attempted until school age and only when IQ scores are noted to be stable.

1542 ULTRASOUND MEASUREMENTS OF VENTRICULAR WIDTH AND BRAIN GROWTH IN PRETERM INFANTS. Leonard Graziani, John Steban, Christian Stanley, Hemant Desai, Paul Branca, Pam Foy, Larry Waldroup, Matthew Pasto, Barry Goldberg. Departments of Pediatrics, Neurology and Ultrasound. Thomas Jefferson University, Philadelphia, Pa.

Serial ultrasound imaging was used to measure the ratio of ventricular width (VW) to intracranial diameter (ID)in 110 preterm infants of less than 33 weeks gestation in order to determine the effects of intracranial hemorrhage (ICH)on brain and ventricular growth. Based on the presence or absence of major perinatal complications and ICH,the infants were classified as follows: low risk (no ICH or complications,Group I); high risk (perinatal complications but no ICH, Group II); and very high risk (ICH,Group III). The correlations between the VW/ID ratios (at the level of the foramen of Monro in coronal and horizontal sections)and post conceptional age / (PCA); range 25 to 75 weeks /were compared in the 3 risk groups. Eight infants with progressive post hemorrhagic hydrocephalus were omitted from further analysis. The linear regressions of VW/ID ratios and ID measurements were negatively and positively correlated,respectively,with PCA in all 3 groups of infants. Differences in the linear regressions of VW/ID ratios (but not the ID measurements or head circumferences)were noted between group I and group III. The differences suggest that ICH in preterm infants is associated with decreased brain growth and cerebral atrophy. The cause of the decreased brain growth in infants with ICH is uncertain,and may be related to multiple factors, the most important of which may be partial destruction of the glial anlage in the germinal matrix.

1543 LATERAL VENTRICULAR ASYMMETRY IN THE HUMAN NEONATE. Jeffrey D. Horbar, Kathleen Leahy, Jerold F. Lucey, University of Vermont College of Medicine, Department of Pediatrics, Burlington, Vermont

Left-right asymmetries have been described in fetal and adult human brains. We reviewed the real-time ultrasound brain scans of 129 neonates examined between December 1979 and June 1981 in an attempt to identify asymmetry in the sizes of the lateral cerebral ventricles. Scans were performed in coronal and sagittal planes using a 7.0 mHz linear array transducer applied over the anterior fontanel. Seventy-five infants (GA 28 to 44 weeks) had no ultrasound evidence of intracranial pathology. The scans of each of these infants were reviewed independently by two examiners who compared the sizes of the bodies of left and right lateral ventricles by inspection. Their assessments agreed in 66/75 cases (88%). The body of the left lateral ventricle was larger than the right in 21/66 infants (31.8%), the right was larger than the left in 4/66 infants (6.1%) and the ventricles were equal in size in 41/66 infants (62.1%), ($p<0.001$, sign test). Asymmetry was detected as early as the 28th week of gestation and on the first postnatal day. Ventricular asymmetry probably represents a normal developmental pattern but may result from intrauterine or postnatal deformation of the skull and brain. Follow-up neurologic and psychometric testing will be required to determine if there is a relationship between ventricular asymmetry and the functional specialization of the cerebral hemispheres.

●1544 IMPAIRED TRANSPORT OF ORGANIC ACIDS BY CHOROID PLEXUS: A POTENTIAL FACTOR IN REYE'S ENCEPHALOPATHY. Chung S. Kim, Lorcan A. O'Tuama, John D. Mann and Charles R. Roe. Univ. of N.C. and Duke Univ., Neurology and Pediatrics, Chapel Hill and Durham.

Elevations of medium chain fatty acids (MCFA) in serum and brain are associated with a model of Reye's syndrome (RS). Clearance of organic acids from brain via choroid plexus (CP) may critically influence the clinical course. In this study we examined the interactions of a series of organic acids with translocation mechanisms of the CP.

Lateral and fourth ventricular CP of young albino rabbits were incubated for 10 minutes in media containing ^{14}C-2,4-dichlorophenoxyacetic acid (2,4-D) as a marker of organic acid transported by CP. Addition of octanoate (C_8) to the media resulted in marked inhibition of 2,4-D uptake in a dose related manner (66% and 89%, at 0.1 and 1.0 mM). Valproate, an isomer of octanoate, had no significant inhibitory effect (13% at 0.1 mM). Of the dicarboxylic acids tested, succinic (C_4), adipic (C_6) and suberic (C_8), the omega-oxidation product of octanoate, caused no significant inhibition of the CP carrier. The inhibitory effect of other dicarboxylic acids increased with chain length, e.g. dodecanedioic acid (62% at 0.1 mM). Lack of cross inhibition with glycine or tyrosine supported the specificity of the carrier system for organic acids.

Hence, octanoate substantially inhibited the CP organic acid transport system. Impaired acid transport by CP may result in accumulation of short and MCFA in brain and thereby contribute to the encephalopathy of RS.

1545 VENTRICULAR DILATATION: A PROGNOSTIC FEATURE OF CONGENITAL MYOTONIC DYSTROPHY. A. Lazzara, P. Ahmann, P. Fernhoff, F. Dykes, M. Horder. (Spon. by A.W.Brann). Emory Univ. Sch. of Med., Grady Mem. Hospital, Depts. of Peds. & GYN/OB, Atlanta, Georgia.

Ventricular dilatation (VD) has been described in congenital muscular dystrophy, Duchenne muscular dystrophy, and adults with myotonic dystrophy (MD). Abnormalities of cerebral architecture (polymicrogyria, neuronal heterotopia, neuronal loss) have also been described in such patients. This could explain the known association between MD and mental dysfunction. We have recently evaluated four patients with congenital MD in the immediate postnatal period with CT scan or cranial ultrasound. Three demonstrated varying degrees of VD. All had head circumferences normal for gestational age. One infant (preterm) had moderate to severe VD, was severely affected clinically, required mechanical ventilation (MV) in the neonatal period, had poor psychomotor development and expired as a consequence of the myopathy at age two years. Two patients (both preterm) demonstrated mild VD, had severe myopathy necessitating MV and eventually expired in the neonatal period as a consequence of the myopathy. One patient (term) had no ventricular dilatation, was mildly affected clinically, did not require MV and survives to this day (6 months) with normal psychomotor development.

Central nervous system involvement appears to be common in congenital MD. Ventricular dilatation with normal head circumference may indicate a dysmorphic process involving cerebral parenchyma. Its presence appears to be associated with early death or severe psychomotor retardation.

1546 HYPERBILIRUBINEMIA AND INTRACRANIAL HEMORRHAGE IN LOW BIRTH WEIGHT INFANTS. Jerold F. Lucey, Marykay Pasnick and Jeffrey D. Horbar. Dept. of Pediatrics, University of Vermont, Burlington, Vermont 05405.

Hyperbilirubinemia is suspected of causing brain damage in low birth weight infants. Controversy exists over the serum concentration thought to be toxic. Exchange transfusions have been recommended for serum concentrations as low as 8-15 mg% in infants of 800-1500 grams birth weight. Hemorrhages into closed spaces are known to cause hyperbilirubinemia. Recent studies using ultrasound to detect intracranial bleeding indicate that at least 40-50% of infants less than 1500 grams birth weight have intracranial hemorrhages (ICH).

In all previous studies which have attempted to relate serum bilirubin concentrations to development, infants with ICH (Gr. 1-4) have not been identified.

A preliminary retrospective study of 90 infants with ultrasound diagnosed ICH indicates that these infants have higher average bilirubins and respond more slowly to phototherapy.

A prospective study in which phototherapy is controlled is underway to test the hypothesis that infants with ICH have higher average serum bilirubins. Our hypothesis is that ICH results in hyperbilirubinemia and that hemorrhage is a more likely cause of brain damage than mild hyperbilirubinemia.

In the light of this new information all previous studies comparing outcome or therapies for hyperbilirubinemia must be reexamined. An elevated serum bilirubin may only be an indicator of a previously undetected hemorrhage.

1547 IPSILATERAL ACOUSTIC REFLEX THRESHOLDS (IART) IN INFANTS. P.M. McMillan, C.D. Marchant, S.A. Schupp, P.A. Shurin. Case Western Reserve Univ. Sch. Med., Cleveland Metropolitan Gen. Hosp., Dept. of Pediatrics, Cleveland.

The stapedius muscle contracts reflexively in response to intense sound. Threshold testing for acoustic reflexes may be useful in evaluating hearing acuity, middle-ear status and brainstem auditory function. We have studied IART in 24 ears of 14 infants 2 weeks to 12 months of age who had normal middle ears as determined independently by pneumatic otoscopy and tympanometry. IART were measured using an otoadmittance meter. Stimulus tones were supplied intermittently at a rate of 9.1 tones per second and duration of 46 msec per tone. Responses were measured in the intervening 64 msec with a 660 Hertz (Hz) (85 dB SPL) probe tone. Stimuli of 500, 1000, 2000 and 4000 Hz were presented in 5 dB increments beginning at 70 dB HL. Maximum stimuli were 90 dB HL at 500 and 4000 Hz, 100 dB HL at 2000 Hz, and 110 dB HL at 1000 Hz. A threshold was defined as the lowest intensity producing a $\geq$.036 millimho change in acoustic admittance at the probe tip.

All subjects had a detectable reflex in one or both ears.

Frequency (Hz)	No. of reflexes present/ No. of ears tested	IART (dB HL) Median	Range
4000	16/24	85	70-90
2000	21/24	85	70-95
1000	22/24	85	70-95
500	20/23	85	75-90

IART are readily determined in infants and have potential use in detecting deafness, the effects of ototoxic drugs, and middle-ear effusions.

1548 MATURATION OF VISUAL EVOKED RESPONSES IN THE NEONATE. David L. McPherson and Bharti Ghosh (Spon. by Beverly Morgan). Univ. of California, Irvine, Dept. of Peds., Coll. of Medicine, Irvine, CA.

The visual flashed evoked potential (VER) was studied to follow maturation of the VER in neonates. 85 neonates were studied and they ranged in age from 26 weeks to 623 weeks postconception. P_1 through N_3 waves were examined as a function of gestational age, chronological age, and conceptual age. A Nicolet Med-80 minicomputer was used for data collection and analysis of 64 averaged flashes presented monocularly at the rate of 1.8 flashes /second. Silver disc electrodes were placed at O_2 and C_z, with the common electrode placed at A_1. A 500 msec window was used to collect the VER. P_1 latency matures up to approximately term, while P_2 continues maturation beyond term. A significant difference between P_1 and P_2 waveforms were found ($p < .05$). Although significant differences were not found between left P_1 and right P_1, and left P_2 and right P_2 waves, it was found that there was a significant correlation ($p < .05$) for P_1 and P_2 as a function of left or right eye stimulation. Three distinct maturation curves were seen, with the steepest growth segment between 36 and 58 weeks postconception. This suggests that the flash evoked waveforms of P_1 and P_2 arise from separate sensory neuronoal populations in the cortex. However, the observation that there was not a significant difference between left monocular P_2 and right monocular P_2 waveforms indicates that the scalp distribution of P_1 and P_2 are diffused enough not to demonstrate concise distribution of the scalp potentials up to 400 weeks post conception.

1549 ALTERATIONS IN THE AUDITORY BRAINSTEM EVOKED POTENTIALS IN PRETERM INFANTS WITH VENTRICULOMEGALY. David L. McPherson, Feizal Waffarn, T. Glatz and Robert F. Huxtable. College of Medicine, University of California Irvine, Dept. of Pediatrics, Irvine, CA.

Auditory brainstem evoked responses (ABR) have mainly been used to evaluate hearing in the preterm infant. This study explores the use of ABR to evaluate the neurophysiologic effects of ventriculomegaly. Twenty-six observations were made in 10 preterm infants. Birthweights ranged from 600-1500 gm; gestational age ranged from 27-31 wks. Ventricular size was determined by cranial ultrasonography using a 5 mHz linear-array transducer. The ratio of the width of the lateral ventricle at the level of the occipital horn to the width of the subadjacent cerebral cortex was measured in the axial plane. Ratios $>.5$ represented ventriculomegaly. ABR recordings were obtained using a Nicolet Med 80 Minicomputer. Acoustic clicks were presented at 11.1/sec for intensities of 30-80 dB HTL in 10 dB increments, monaurally, to both left and right ears. A series of 1024 averages were taken using a band-pass filter of 150-3000 Hz. Latency of the 5 predominant wave forms were measured and central conduction times (CCT) computed. Normal ABR thresholds were found for all cases evaluated. Normal CCT for waves I-V for both right and left ear stimulation were observed. However, the CCT for waves III-V were abnormal in those infants with ventriculomegaly. The CCT for waves III-V for left ear stimulation was significantly prolonged ($p < .03$) when compared to infants of similar gestational age. The results suggest that infants with ventriculomegaly may show normal ABR recordings for hearing and I-V CCT, with abnormal prolongation of the III-V CCT, which may be of physiologic significance.

1550 DIETARY RESTRICTION OF VERY LONG CHAIN FATTY ACIDS IN ADRENOLEUKODYSTROPHY AND ADRENOMYELONEUROPATHY. H.W. Moser, J.D. Schulman, W.B. Rizzo, M.A. Van Duyn, F.R. Brown III and A.B. Moser. John F. Kennedy Institute and Johns Hopkins University, Baltimore, MD and NICHD, NIH, Bethesda, MD

Adrenoleukodystrophy (ALD) and adrenomyeloneuropathy (AMN) are associated with the accumulation of saturated very long chain fatty acids (C24:0 - C26:0 and longer) in the brain, adrenal, plasma, and red blood cells, and in cultured skin fibroblasts and muscle. The accumulated fatty acids are of dietary origin at least in part (Johns Hopkins J. 147, 1980). We are evaluating the clinical and biochemical effects of dietary restriction of very long chain fatty acids in ALD and AMN. We analyzed the very long chain fatty acid content of over 100 common foods, and devised an apparently nutritionally adequate and reasonably palatable diet which restricts daily hexacosanoate (C26:0) intake to 3 mg., compared to 12-40 mg. in the average western diet. This diet has been administered to 7 patients with childhood ALD, to 3 with AMN, and to 3 asymptomatic boys who have biochemical abnormalities associated with ALD and who are related to ALD patients.

Data will be presented about the effects of this diet on the elevated plasma very long chain fatty acid levels and on clinical status. No consistent reduction in plasma very long chain fatty acid levels has so far been observed. Two patients with AMN showed subjective and objective improvement coincident with diet administration, while the clinical progression of the childhood ALD patients did not appear to be altered by this regimen.

●1551 REYE'S-LIKE SYNDROME IN RABBITS: INDUCTION BY A MIXTURE OF NATURALLY OCCURRING ORGANIC ACIDS. Jerome V. Murphy, Tsae-Fung Hwang and Joseph Harb. Medical College of Wisconsin, Milwaukee Children's Hospital, Departments of Neurology and Pediatrics, Milwaukee, Wisconsin

That certain fatty acids might play a role in Reye's syndrome (RS) is indicated by (1) the induction of a very similar disease in animals using either octanoic acid or 4-pentenoic acids and (2) elevated concentrations of other short chain fatty acids (SCFA) in the plasma of RS patients. To learn if the SCFA found in the plasma of RS patients are etiologic in the disease, rabbits were intravenously infused with a mixture of SCFA, each in proportion to the concentration reported in the plasma of RS patients. The total concentration of SCFA was 0.3 M, and this was infused at a rate of 0.2 ml/min. Eight of ten rabbits developed hyperventilation, hyperammonemia and death. Of these 8 rabbits, 4 had elevated intracranial pressure (>20 torr). Ultrastructural changes in brain and liver were identical to those found in the human disease. Animals that died had increasing levels of SCFA in plasma, and survivors had constant SCFA levels; i.e. survivors did not appear to accumulate SCFA in serum. Infusions of 0.3 M concentrations of the individual fatty acids were much less effective in producing signs of RS. These experimental observations suggest that the SCFA found in the plasma of RS patients are etiologic in the pathogenesis of RS. This mixture is probably a more physiologic agent to study RS in animals than octanoic acid. The data also suggests that the expression of RS may vary depending on the ability of the host to maintain low concentrations of SCFA.

1552 OUTCOME OF LESS THAN 1000 GRAM BIRTH WEIGHT INFANTS COMPARED TO GREATER THAN 1000 GRAM BIRTH WEIGHT INFANTS AT AGE 3 YEARS FROM AN INNER CITY POPULATION. Z. Najak, B. Sweeney, B. Dunbar, and A.W. Brann, Jr., Emory University School of Medicine, Atlanta, Georgia

The functional status of the nervous system of children at Grady Memorial Hospital(GMH)weighing ≤1500 grams is reported.Women delivering at GMH are from an urban population defined as 85%black 68% single,50% with less than a high school education.and 39% less than 20 years of age.Group(Gp.)A,≤1000 gm(n=77)were born in the years 1976-78;and Gp.B,>1000-1500 gm(n=123)born in 1978.The mean gestational age for Gp.A was 29 weeks and for Gp.B was 31 weeks. In Gp.A, there were 60% small-for-gestation(SGA)infants compared to Gp.B which had 29% SGA(TORCH infection and dysmorphisms excluded).Major neurologic deficits were identified in 11 out of 63 (17%)in Gp.A,and 11 out of 105(11%)in Gp.B.The distribution of these deficits was similar between the AGA(14%)and SGA(17%) categories of both groups.Development assessed by the Stanford-Binet (SB),2 year Bayley(2yr.-B)and Peabody scales(PB)for Gps.A and B, SGA and AGA categories and the non-sick preterms(norms)at GMH are

	Norms	n	Group A	n	Group B	n	SGA	n	AGA	n
B-2yr.	98±16	21	79±16	34	79±18	54	79±17	39	79±18	48
SB-3yr.	74±11	21	80±17	28	83±12	21	82±18	25	81±10	24
PB-3yr.	72± 8	19	77±12	28	81±15	21	78±17	24	78±10	25

1)MDI/IQ or major neurologic impairments did not differ in relation to gestational age or birth weight.
2)SGA was not associated with increased neurologic deficits or a lower MDI/IQ.
3)IQ was significantly lower($p<.05$)in Gp.A with RDS;and motor deficits were outstanding in those ventilated in both Gps.

1553 BRAINSTEM AUDITORY EVOKED RESPONSE FOLLOW-UP TO 8 MO. IN ≤ 1200 GM INFANTS. Michael N. Nelson, Mary Ellen A Bozynski, David A. Klodd, Werner A. Meier, Dennis L. Kisiel (Sponsored by Joseph R. Christian), Rush Medical College, Rush Presbyterian St. Luke's Medical Center, Departments of Pediatrics, Psychology, and Otolaryngology, Chicago.

Beginning in March, 1980, 42 of 43 consecutively born ≤ 1200 gm infants who survived to term gestational age were evaluated for auditory deficit using the Brainstem Auditory Evoked Potential (BAEP). Latencies to 85 dB click stimuli were computed based on wave I-III and wave I-V difference scores. At term, 13 infants showed an abnormality involving slowed conduction beginning at wave III (superior olives in the pons). Nine of these infants were followed-up at 8 months (corrected age) with a repeat BAEP. The other 4 infants were lost to follow-up. The 9 follow-up infants showed an average improvement in wave I-III latency of 0.54 msec, while average wave I-V (inferior colliculus) improvement was 1.16 msec. A Student t test revealed significant improvement in conduction time for wave V only ($p < .001$). The wave I-V latency difference was 4.5 msec at 8 months, with an absolute wave V latency of 6.4 msec. Results for the right and left ears did not differ. Mean wave V thresholds were 39.4 dB at term, and 30.3 dB at 8 months, but this difference was not statistically significant. Significant postnatal improvements in latency, together with the normal thresholds seen at 8 months, argue against using the BAEP as a one-time evaluation procedure in the intensive care nursery. Failure to show improvements in latency and threshold appears to be rare, even in infants who show grossly delayed waveforms in the neonatal period.

1554 INTRACRANIAL PRESSURE AS A GUIDE TO THERAPY AND PROGNOSIS IN THE NEAR-DROWNING CHILD. E. Nussbaum, S Galant, Pediatric Pulmonary Center and Intensive Care Unit, Miller Children's Hospital Medical Center/Department of Pediatrics, University of California, Irvine.

Seventeen of 45 near-drowned children presented in a flaccid stage of coma (F.C.). Intracranial pressure (ICP) monitoring by the subarachnoid bolt and cerebral perfusion pressure (CPP) served as major guidelines in the therapy of those children who were comatose. Cerebral resuscitation included: Hyperventilation ($PaCO_2$ 20-25 mmHg) with hyperoxygenation (PaO_2 >150 mmHg) in conjunction with hypothermia (86°-88°F), fluid restriction, muscle paralysis, pentobarbital and furosemide. Mannitol was employed for elevated ICP (>20 mmHg) unresponsive to manual hyperventilation. Overall survival rate was 78% (35/45) and complete recovery 71% (32/45). Of those in F.C. 41.2% (7/17) survived, 29.4% (5/17) recovered completely including normal electroencephalogram, and 11.8% (2/17) remained brain damaged. Survival strongly correlated with mean ICP and CPP during the first 24 hours following admission. Survivors had mean ICP and CPP values of 11.86 ± 2.12 and 79.00 ± 3.86 mmHg respectively compared to those expired who had mean ICP and CPP values of 32.38 ± 5.19 and 31.63 ± 5.31 mmHg respectively ($P < 0.005$ for each parameter). Subjects with mean ICP <20 and CPP >50 mmHg had a 87.5% survival rate (7/8) compared to those with mean ICP >20 and CPP <50 mmHg who expired (5/5). We conclude that ICP and CPP measurements provide valuable information regarding therapy and prognosis in these patients which is clearly superior to clinical parameters alone.

1555 MANNITOL CROSSES THE BLOOD-BRAIN BARRIER IN REYE'S SYNDROME. James P. Orlowski, Cleveland Clinic Foundation, Cleveland, Ohio

Mannitol is a commonly employed osmotic agent for the control of intracranial hypertension in Reye's Syndrome (RS). Four patients with liver-biopsy confirmed RS had intraventricular catheters placed for monitoring of intracranial pressure (ICP). Each patient had 4 or more samples of CSF and plasma obtained for mannitol levels and osmolalities during the course of their treatment for RS. Mannitol was given in 0.5-1.0 gm/kg I.V. doses for ICP elevations above 25 mmHg which did not respond to manual hyperventilation. Mannitol was detected in the CSF within 24 hours of commencing osmotherapy in all 4 cases and was present in concentrations of as high as 50 mg/dl during the course of treatment in all cases. These elevated levels of mannitol in the CSF correlated with the development of CSF hyperosmolality in 2 of the 4 cases including one patient who developed renal insufficiency. CSF mannitol levels did not parallel plasma mannitol levels. Mannitol crosses the blood-brain barrier in Reye's Syndrome and may contribute to the malignant intracranial hypertension which has necessitated craniectomy or resulted in the death of some patients with Reye's Syndrome. It would appear prudent to limit the use of mannitol osmotherapy to emergency situations where intracranial hypertension cannot be controlled by other measures such as manual hyperventilation, controlled hypothermia or intravenous barbiturates and to use the minimally effective dose, preferably 0.25-0.50 gm/kg. Furosemide may be a better drug for the control of acute ICP elevations in RS.

1556 THIN RIBS ON CHEST X-RAY: A USEFUL SIGN IN THE DIFFERENTIAL DIAGNOSIS OF THE FLOPPY NEWBORN. John P. Osborne, E. Gordon Murphy and Alan Hill. (spon. by Henry Levison) University of Toronto, The Hospital for Sick Children, Department of Pediatrics, Toronto.

The differential diagnosis of the floppy newborn is difficult on clinical grounds alone. Thin ribs have been observed on chest x-ray in infants with congenital myotonic dystrophy. However, the frequency and specificity of this finding has not been reported. We have reviewed the prevalence of this radiological finding in a variety of neuromuscular diseases which presented in the neonatal period and have related the chest x-ray findings to the clinical signs.

In a 5 year period 19 newborns with neuromuscular disease had a chest x-ray. The diagnosis of neuromuscular disease was made by a combination of electromyography, muscle biopsy and examination of the mother as appropriate.

Thin ribs on chest x-ray were observed in 3 of 7 cases with congenital myotonic dystrophy, 2 of 4 cases with myotubular myopathy and 1 of 5 patients with spinal muscular atrophy (Werdnig-Hoffmann Disease). The ribs were normal in 1 case with nemaline myopathy and 2 cases of non specific myopathy. Polyhydraminos was recorded in 4 of the 6 cases with thin ribs.

The simple observation of thin ribs on chest x-ray in the neonatal period is highly suggestive of neuromuscular disease but is not specific for, nor invariable in, congenital myotonic dystrophy. When seen in association with hypoxic-ischemic encephalopathy it suggests that neuromuscular disease was the primary cause of respiratory difficult at birth.

1557 CLINICAL KERNICTERUS (K) IN SURVIVING LOW BIRTHWEIGHT (LBW) NEONATES WITH RELATIVELY LOW PEAK BILIRUBINS (Bilis). M.J. Painter, D.R. Brown, R. David, Univ of Pitt Med Sch, Magee-Womens Hosp, Dept of Ped, Pittsburgh, PA

Autopsy-proven K occurs in LBW neonates whose peak Bilis never exceed 10 mg/dl. However, clinically evident K has not been previously described in surviving LBW neonates with low peak Bilis. Since Jan. 1980, we have cared for 4 LBW neonates who were opisthotonic and had peak Bilis <10 mg/dl. At follow-up examination, 4 were deaf, 2 had paralysis of upward gaze, 3 had developmental delay, 2 had microcephaly, 4 had hypotonia or spastic paraparesis, and 1 had stained teeth. Gestational age ranged from 29-35 wks, BW from 1.29-1.80 kg and 1-min Apgar scores from 4-6. Two patients had seizures, 2 had apnea and all were treated with added O_2 and mechanical ventilation. All patients experienced extremes in their pH and blood gases: (a) lowest pH ranged from 7.04-7.16, (b) lowest PO_2 from 28-35 torr, (c) highest PO_2 from 194-324 torr, (d) highest PCO_2 from 65-72 torr, and (e) lowest PCO_2 from 16-25 torr. The cause of the encephalopathy in these medically complicated patients is almost certainly multifactorial and not just due to their slightly elevated Bilis. Nevertheless, we feel that these 4 patients have post-icteric encephalopathy and represent the surviving counterparts to the relatively anicteric babies with autopsy-proven K. These patients are important because they demonstrate that this presumably preventable cause of morbidity can occur in surviving patients whose Bilis never exceeded 10 mg/dl, and because they highlight the continuing need to determine the appropriate management of jaundice in the LBW neonate with multiple medical problems.

1558

Withdrawn Prior to Publication

● **1559** RELATIONSHIP OF NEONATAL BRAIN HEMORRHAGE TO DEATH AND NEURODEVELOPMENTAL OUTCOME. Karen Pape, Stephen Bennett-Britton, Wanda Szymonowicz, Dilip Mehta, David Martin, Charles Fitz, Pamela Fitzhardinge. Research Institute, Hospital for Sick Children, Depts. of Pediatrics and Radiology, University of Toronto, Toronto.

Ninety-four infants ≤1250 gm birthweight, ≤30 wk gestation were studied with sequential realtime ultrasound scans (U/S) in the neonatal period. Hemorrhage was diagnosed in 44. In 26 it was confined to the germinal layer and/or the ventricles (GLH± IVH, grades 1,2,3). In 18 the blood extended into the periventricular white matter (ICH±IVH, grade 4). In 19 cases U/S could not be classified as definitely normal or abnormal due to technical limitations and these have not been considered in the analysis. Prospective follow-up has been completed to a minimum of 9 months post term in 51 of the 60 survivors. Major abnormality = hydrocephalus, cerebral palsy ± Bayley<80 (18 m).

	Normal	Equivocal	GLH±IVH	ICH±IVH	Total
N	31	19	26	18	94
Died	4	8	11	11	34
Survived (%)	27 (87)	11 (58)	15 (58)	7 (39)	60 (64)
Evaluated	23	9	12	7	51
Outcome Normal	16	7	11	2	36 (70)
Minor Abn.	4	1	1	1	7 (14)
Major Abn. (%)	3 (13)	1 (11)	0	4 (57)	8 (16)

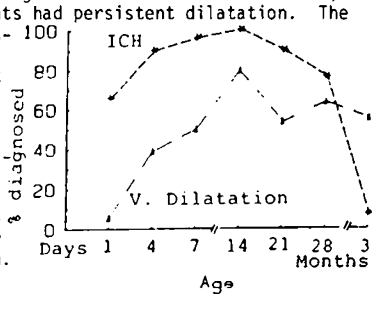
Mortality is increased in infants with GLH±IVH ($p<0.02$) and ICH± IVH ($p<0.001$). Only grade 4 hemorrhage (ICH±IVH) is closely associated with major sequelae ($p<0.01$). The results suggest that blood in the white matter has a greater prognostic significance than does blood in the ventricles.

● 1560 AUTOREGULATION OF CEREBRAL BLOOD FLOW (CBF) IN THE PRETERM OVINE FETUS. Lu-Ann Papile, Abraham M. Rudolph, Michael A. Heymann. University of California, CVRI, San Francisco and University of New Mexico School of Medicine, UNM Affiliated Hospitals, Department of Pediatrics, Albuquerque, New Mexico.

Although autoregulation of cerebral blood flow (the maintainance of relatively constant CBF in spite of changes in perfusion pressure) has been demonstrated in the term infant and near term fetus, no data is available in the preterm infant and/or fetus. To provide this evidence, 32 measurements of CBF, using the radioactive microsphere technique, were made in six preterm ovine fetuses (118-122 days gestation) over a mean carotid artery pressure (CAP) range of 20 to 90 mm Hg. CAP was altered by graduated inflation of balloons placed around the brachiocephalic artery and the aortic isthmus. To eliminate the effects of reflex changes in heart rate, aortic and carotid sinoaortic denervation was accomplished. CBF was linearly related to CAP from 20 to 45 mm Hg (15-75 ml $100gm^{-1}$ min^{-1}), constant over CAP range of 45 to 80 mm Hg (75-86 ml $100gm^{-1}$ min^{-1}) and again linear from 80 to 90 mm Hg (75-126 ml $100gm^{-1}$ min^{-1}). We conclude that 1) although autoregulation is present in the preterm ovine fetus, the range of autoregulation is narrower than that reported in term lambs and 2) the value for mean systemic arterial blood pressure lies close to the lower limit of autoregulation. This narrowed range increases the vulnerability of the preterm brain to fluctuations in blood pressure, particularly hypotension.

1561 OPTIMAL TIMING FOR CRANIAL ULTRASOUND IN NEONATES. John C. Partridge, Diane S. Babcock, Jean J. Steichen, Bokyung K. Han. (Spon. by June P. Brady).University of Cincinnati College of Medicine, Children's Hospital Medical Center, Departments of Pediatrics and Roentgenology, Cincinnati.

To determine the optimal timing for cranial ultrasound in infants at risk for intracranial hemorrhage (ICH), we studied 64 preterm infants (<1500g) by sequential cranial real-time ultrasound from birth until one year or until death. Forty-two of 64 patients (66%) demonstrated ultrasound abnormalities on one or more scans. ICH occurred in 55% of patients, usually during the first week. No new ICH was documented after 14 days of age. Twenty-eight percent of patients had significant ventricular dilatation. The peak prevalence of ventricular dilatation was at day 14. Of 46 patients with any degree of ventricular dilatation, 18 progressed. Eleven patients had persistent dilatation. The figure summarizes the diagnostic efficiency of ultrasound in the neonatal period. Peak efficiency is at days 4, 7, and 14 for ICH and at day 14 for ventricular dilatation.



We conclude that the earliest and most efficient time for ultrasound diagnosis is day 4-7 for intracranial hemorrhage with follow up at day 14 for ventricular dilatation.

1562 BRAIN DEVELOPMENT IN INFANTS OF DRUG DEPENDENT MOTHERS Matthew E. Pasto, Leonard J. Graziani, Barry B. Goldberg, Betty Leifer, Loretta P. Finnegan, Thomas Jefferson University, Department of Pediatrics and Ultrasound, Philadelphia, Pa.

Ultrasound measurements of the brain have been instituted as part of an ongoing investigation to determine the effects of psychoactive drugs taken during gestation on the developing nervous system of infants born to drug dependent women. A preliminary group of 6 passively addicted and 6 non-drug exposed infants comparable for birth weight, gestational age, 1 & 5 minute Apgar scores, sex, race and socioeconomic status, have been studied. All infants are healthy full-terms(except for abstinence). Three of the study infants were treated with phenobarbital for abstinence while the others required no treatment. All of the mothers of the study infants were on methadone maintenance with daily dosages ranging from 5 to 50 mg/day, however, all were using unknown quantities of heroin and two were using significant quantities of diazepam. In all infants, study and control, ultrasound exams at 24 hours after birth demonstrated normal cerebral structure with no evidence of hemorrhage. The ultrasound measurements did reveal very small (slit-like) lateral ventricles in all prenatally drug exposed infants but in none of the controls. This finding may be secondary to diffuse compression of the ventricles bilaterally,as may occur with generalized cerebral edema. Further evaluations are needed in order to rule out other possible etiologies. Therefore, future studies will include evaluations at 1, 2, and 6 months of age in order to determine when and if the lateral ventricles assume their expected size.

● 1563 THE EFFECTS OF SEIZURES (Sz) ON CEREBRAL BLOOD FLOW VELOCITY (CBFV), INTRACRANIAL PRESSURE (ICP) AND SYSTEMIC BLOOD PRESSURE (BP) IN THE PRETERM INFANT. Jeffrey M. Perlman and Joseph J. Volpe, Wash. Univ. Sch. Med., St. Louis Children's Hospital St. Louis, MO 63110.

The noninvasive measurement of CBFV in the anterior cerebral arteries is possible with a transcutaneous Doppler technique. From the systolic (S) and diastolic (D) amplitudes of flow, a pulsatility index (PI) is calculated (S-D/S) and is inversely related to CBFV. ICP can be measured noninvasively with a fiber-optic sensor applied to the anterior fontanel (Ladd monitor).

Six preterm infants who developed Sz were followed. In four, the Sz were subtle, and in two, generalized tonic. In each case, CBFV, BP and ICP increased markedly during Sz (Table) and returned to resting values after the Sz.

	REST			DURING SZ		
	PI	MBP(mmHg)	ICP(cmH_2O)	PI	MBP(mmHg)	ICP(cmH_2O)
1.	.65	38	6	.45	49	13
2.	.68	48	7	.48	66	25
3.	.63	28	8	.54	38	19
4.	.63	29	8	.46	41	34
5.	.65	46	7	.48	57	35
6.	.57	44	8	.44	58	21
MEAN	.63	38.8	7.3	.47	51.3	24.5

The changes in PI, BP&ICP are statistically significant($p<.001$).

The data indicate a sharp increase in CBFV, presumably a direct effect of the increase in systemic BP and reflected in an increase in ICP. Seizures may be important in the genesis of new IVH and/or exacerbation of preexisting lesions.

1564 CEREBRAL PERFUSION PRESSURE (CPP) STUDIES IN HEALTHY AND ACUTE ILL NEWBORN INFANTS. Tonse N. Raju. Usha Doshi, Dharmapuri Vidyasagar, ALSM. University of Illinois Hospital, Chicago, Illinois 60612

Using a Ladd intracranial pressure (ICP) monitor and transducer to measure ICP via the fontanel we estimated CPP in 81 infants: GROUP I: 36 healthy newborns 28-40 weeks of gestational age (GA), GROUP II: 17 infants with severe birth asphyxia (BA) (mean ± SD) G.A = 39±4 weeks). GROUP III: 28 infants with moderate to severe hyaline membrane disease (HMD) (GA 30±2.6 weeks). Recordings were performed during both acute phase and recovery. Immediate and long term outcome (9 months to 4 years) in sick infants were correlated with the least CPP during the height of illness. RESULTS: I. CPP in healthy infants increased from 28±5.9 Torr at 32 weeks GA to 37.5±4.9 Torr at term due to 10 torr increase in mean BP. II. In BA infants least CPP correlated with CNS status. 9/17 had brain damage (autopsy proved in 5, cerebral palsy in 4), 8 were normal. Least CPP in the former was significantly lower than that of the latter group. (16.7±12 vs 30±5.6 Torr, $p < 0.01$). 7/8 whose least CPP was below 3rd percentile for normal, developed brain damage; 7/9 who had normal CPP developed normally ($X^2 = 6.5 < 0.05$). III. CPP did not correlate with outcome in GROUP III: 6/28 had intracranial hemorrhage (ICH) and their CPP was similar to the CPP of 22 who did not (22±7 vs 26±9 Torr). IV. 87% of term infants whose CPP was below 3rd percentile developed brain damage. We conclude: I. Low CPP in term asphyxial infants is a risk for ischemic brain damage. 2. Since preterm infants have poor arteriolar smooth muscles, greater fraction of mean BP may be transmitted to their brain capillaries putting them at risk for ICH.

● 1565 DYNAMIC CT (dCT) SCANNING TO ASSESS INFANT BABOON REGIONAL CEREBRAL BLOOD FLOW (rCBF): A NON-INVASIVE TECHNIQUE. Tonse N. Raju, Glen D Dobben, Uday Nadkarny Dharmapuri Vidyasagar. ALSM. University of Illinois Hospital Dept. of Pediatrics, Chicago.

The dCT scanning has been used to assess forebrain and hindbrain rCBF in adults. No studies in animal or human infants have been done. The technique consists of a rapid IV injection of Hypaque(R)-76, over 2 to 5 seconds while obtaining a base line scanning at the level of lateral ventricles; this gets completed before the contrast reaches the brain. A total of 6 scans (clock and counter-clock wise) over the next 30 seconds are obtained. The display provides the architecture of cerebral vasculature for comparison and a computer generated time curve from which blood flow in ml, to any point in the brain can be computed. To explore the sensitivity of this technique and the least dose of contrast material required to obtain rCBF curves, we performed 7 studies in 3 infant baboons: a 32 week old 2.3 kg and two 5 weeks old, 1.2 kg animals. We altered baseline heart rate in 3/7 studies. We used a G.E.CT/T8800 scanner. We injected from 1 to 4 cc/kg of contrast into a peripheral vein to obtain blood flow curves. The results: (1) In each of the 7 studies excellent reproducible density flow curves were obtained. (2) The scanner was sensitive to delineate cerebral architecture even in infants baboon brain and (3) No untoward effects were noted. In one of the baboons we have rCBF by microsphere technique for comparison. We conclude that this technique is reliable to evaluate infant brain vascular architecture and to follow the evolution of ischemic process in the brain. The non-invasive nature of this method permits similar studies in human infants.

1566 ALTERATION OF VISUAL EVOKED RESPONSE IN NEONATAL POLYCYTHEMIA. RS Ramamurthy, JA Saravia, MA Hunter, MB Escobedo. Dept. of Pediatrics, Univ. of Texas Health Science Center, San Antonio (Spon. by Y Brans)

The effect of hyperviscosity (HV) and polycythemia (PC) on cerebral perfusion and oxygenation remains a major concern. The visual evoked response (VER) electroencephalogram, a noninvasive sensitive tool that has been shown to be altered in asphyxial states in neonates, was used to evaluate neonates before and after reduction transfusion aimed at reducing red cell volume. The preVER was performed immediately prior to and the post VER within 12 hrs after the transfusion. Controls with normal hematocrits had VER's recorded at the same intervels. The VER was performed using standard equipment. The latency to the beginning of the second positive wave (P_2) was measured in msec. The diagnosis of PC was made when the umbilical venous (U.V.) hematocrit was $\geq$ 63% and the U.V. Viscosity was $\geq$15cps. Nine PC and 12 control infants were studied. There was no significant difference between PC and control infants in birthweight (mean ±SD 3070 ± 771 vs 3232 ±451 gms) or gestational age (39 ±2 vs 40 ±2 wks). In PC infants there was a significant ($P < 0.005$) change in the P_2 latency associated with the reduction transfusion (224 ±54 vs 201 ±45 msec). A significant change ($P < 0.005$) in latency with reduction transfusion occurred in PC compared to control infants when the difference in latency between the 2 observations were compared (23 ±17 vs 6 ±6 msec). This observation leads us to believe that the HV state alters visual cortical functioning and is favorably affected by reduction transfusion.

1567 CHOROID PLEXUS HEMORRHAGE IN VERY LOW BIRTH WEIGHT PREMATURE NEONATES. John D. Reeder, Emmalee S. Setzer, Ralph M. Maylott, and Juri V. Kaude (Spon. by Willa H. Drummond), Univ. of Florida College of Medicine, Shands Teaching Hospital, Depts. of Radiology and Pediatrics, Gainesville, Florida.

We performed 81 cranial real-time ultrasonograms on 35 consecutive infants less than 1500 grams birthweight admitted to the Neonatal Intensive Care Unit in order to determine the incidence of choroid plexus hemorrhage. Choroid plexus hemorrhage was diagnosed only in the absence of caudate nucleus hemorrhage. Diagnostic criteria included choroid plexus nodularity, enlargement (>12 mm. in diameter), or marked asymmetry between right and left (>5 mm.). Ipsilateral intraventricular clots or occipital horn dilatation supported the diagnosis of choroid plexus hemorrhage in most cases. Intracranial hemorrhage was noted in 18 of the 35 infants (51%). Choroid plexus hemorrhage was the sole bleeding site in 11 of the 18 patients with intracranial hemorrhage (61%). Caudate nucleus hemorrhage with (n=5) and without (n=2) coincident choroidal irregularity was seen in the remaining seven cases (39%). Significant ventricular dilatation occurred in 8 of the 11 cases of choroid plexus hemorrhage (73%). This study suggests that the choroid plexus, a highly vascularized capillary bed, is the most frequent site of intracranial hemorrhage in very low birth weight premature neonates. Considering the role of the choroid plexus in cerebrospinal fluid regulation, choroid plexus hemorrhage may render the neonate at risk for serious neurologic sequelae related to ventricular dilatation.

1568 DISORDERS OF VOICE (DV) FOLLOWING REYES SYNDROME (RS). M.A. Reitman, J. Coplan, J. Casper, L.B. Weiner, R.K. Kanter. (Spon. by Frank A. Oski). SUNY, Upstate Medical Center, Dept. of Peds. and Communication Disorder Unit, Syracuse

Charts of all pts. with RS from 1971-81 (n=61) were reviewed to determine the incidence of DV during recovery and the relationship between DV and intubation, clinical staging, and peak ammonia levels. Of the 42 survivors, 23 had one or more DV:

	DV during recovery	intubated (+)	(-)	DV at discharge
aphonia	20	11	9	2
hoarseness	9	9	0	6
other DV	5	2	3	5
total pts.	23	13	10	13

Aphonia was the DV most commonly noted, occurring in 48% of survivors. Nine of the 20 aphonic pts. had never been intubated. Aphonia persisted to discharge in 2 pts., 1 of whom had never been intubated. Hoarseness was noted only in pts. who had been intubated, but was the isolated DV in only 1 case. Of the 13 pts. in whom DV persisted to the time of discharge, DV were the dominant deficit in 12. These 12 pts. were all alert, ambulatory, and followed commands; 3 had mild focal neurologic deficits. The initial and worst stages of RS correlated with the likelihood of a DV ($p < .01$) as did the peak serum ammonia level ($p < .05$):

Stage →	Initial: ≤I	≥II	Worst: ≤II	≥III	peak NH_3
DV present	(N=23) 6	17	8	15	198 µmol/L
DV absent	(N=19) 14	5	16	3	114 µmol/L

DV occur following RS and are often severe compared to other aspects of the neurologic status. DV correlate with disease severity and cannot be attributed solely to the effects of intubation.

1569 A POSSIBLE ROLE FOR OMEGA AND BETA OXIDATION IN CONTROLLING INTRACRANIAL PRESSURE. Charles R. Roe, Lorcan A. O'Tuama, Chung S. Kim, and John D. Mann. Dept. Ped., Duke Med. Ctr., Durham, N.C. and Neurology, UNC Sch. Med., Chapel Hill, N.C.

The finding of increased serum levels of short and medium chain fatty acids in Reye's Syndrome (RS) has led to an animal model in which increased intracranial pressure (ICP) develops following intravenous (IV) infusion of octanoate. In previous studies the animals were in a normal state of nutrition. To approximate more closely the clinical and nutritional conditions of RS, we studied rabbits (2.5 kg) in both the fed and fasted state. Each animal received octanoate IV at a dose of 300 mg/hr over 4 hrs (0.5 gm/kg/4hrs). Vital signs and ICP were monitored continuously. Serum and urine were collected hourly for GC-MS evaluation of the metabolism of octanoate. Fed control animals (4) receiving only saline showed no significant change in ICP. Detailed GC-MS studies showed no change in urine or serum levels of octanoate, lactate, 3-OH butyrate, adipic or suberic acids. ICP in fed animals (2) receiving octanoate increased from 3-8 fold over 4 hrs while there was no significant change from resting ICP in the two fasted animals. Average serum octanoate levels over 4 hrs were 5.6 and 11.1 mg/dl in the fed animals and 10.1 and 10.7 mg/dl in the fasted. The fasted animals showed increasing 3-OH butyrate, adipic and suberic in urine indicating active beta and omega oxidation. The absence of significant change in ICP in these animals suggests a role for omega and beta oxidation in prevention of encephalopathy.

1570 CARDIAC CONDUCTION ABNORMALITIES IN DUCHENNE'S MUSCULAR DYSTROPHY: ELECTROCARDIOGRAPHIC AND MORPHOLOGIC CORRELATES. Shyamal K. Sanyal, F.A.C.C., Warren W. Johnson, M.D., St. Jude Children's Research Hospital, Memphis, TN 38101

Twelve-lead electrocardiograms were analyzed in 50 boys, 5 to 18 years of age, who had clinical, biochemical and muscle biopsy evidence of DMD. Cardiac conduction system abnormalities were noted in 27 patients (54%). Intraatrial conduction abnormalities were most common and included: abnormal PV_1 index in 14 patients, a short P-R interval with normal QRS in 11 and coronary sinus rhythm in 2 patients. Intraventricular conduction abnormalities were noted in 7 patients; right bundle branch block in 2, left anterior hemiblock in 4 and bifascicular block in 1. First-degree atrioventricular block was seen in 1 patient. Seven patients had more than one type of conduction defect. Serial follow-up observations disclosed that the conduction abnormalities were progressive. The morphology of the cardiac conduction system was studied in 4 patients. In contrast to the heart of age and sex-matched, normal control, each DMD heart showed multifocal areas of degenerative changes characterized by vacuolization, fatty infiltration, nuclear pyknosis, variation in size and staining of myofibers, splitting and loss of myofibers and moderate-to-severe fibrosis. These dystrophic changes were similar in each patient and involved, with varying degrees of severity, sino-atrial node, atrial preferential pathways, approaches to atrioventricular node, A-V node including the upper portion, bundle of His and subendocardial as well as intraventricular right and left bundle branches.

These observations indicate a high prevalence of cardiac conduction abnormalities in patients with DMD not previously recognized. Histologic observations establish that dystrophic involvement of the cardiac conduction system provides the morphologic correlate of such EKG changes and explains persistence of infantile pattern of accelerated conduction and sinus tachycardia in some of these patients.

1571 RISK FACTORS IN THE DEVELOPMENT OF INTRAVENTRICULAR HEMORRHAGE (IVH) IN LOW BIRTH WEIGHT NEONATES. Malini Satish, Sidney Kripke, Jose Urrutia, Gerald Katzman, Venkatesan Krishnan, P.L.S. Amma, Irwin Weinfeld. (Spon. by M.G. Robinson) Medical College of Ohio, The Toledo Hospital, Dept. of Ped., Toledo, Ohio.

Computerized tomography (CT) Scan of brain was done in 106 neonates of birth weight <1500 grams in the first three weeks of life. 58 had CT proven IVH and were compared with the 48 neonates who had normal CT Scans. 8 of 27 factors analyzed were significantly associated with IVH.

	IVH		CONTROL		P Value
TABLE #1	$\bar{x}$	S.D.	$\bar{x}$	S.D.	t test
G.A. (wks.)	28.2	2.3	29.8	2.1	<.001
Birth Weight (gms.)	1004	225	1141	206	<.001
Apgar 1 Min.	3.4	1.9	4.1	1.8	<.02
Apgar 5 Min.	3.4	1.9	4.3	1.9	<.02
IMV + CPAP - (Hrs.)	950	542	735	531	<.02

TABLE #2	Yes	No	Yes	No	X^2
Prolonged rupture of membranes > 24 hrs.	12	46	23	25	<.025
Vaginal del. vs. C/S	50	8	30	18	<.025
PDA (LA/AO>1.3)	35	23	18	30	<.025
Retrolental Fibroplasia	30	21	16	30	<.025

More immature and asphyxiated babies requiring vigorous mechanical ventilation are at high risk for the development of IVH. Vaginal route of delivery poses an additional risk. Association of retrolental fibroplasia and patent ductus arteriosus with IVH is noted.

1572 PROGRESSIVE POST-HEMORRHAGIC HYDROCEPHALUS: LONG-TERM FOLLOW-UP. Howard S. Schub, Peter A. Ahmann, Margaret Patino, Francine D. Dykes, Anthony Lazzara, (Spon. by James F. Schwartz), Department of Pediatrics, Emory University School of Medicine, Atlanta

We are involved in an ongoing study of long-term outcome of infants with progressive post-hemorrhagic hydrocephalus(PPHyc). Neurologic and psychologic exams are done yearly. Outcome is analyzed according to degree of hydrocephalus and treatment mode. Group(Gp) I consists of infants with mild or moderate PPHyc that arrests or regresses spontaneously; Gp II, those with symptomatic and severe PPHyc. Asymptomatic infants with continued progression are randomized into no treatment(Gp III) or serial lumbar puncture(L.P.) treatment(Gp IV) groups. Gp III infants with continued progression are treated by L.P. Gp IV infants who fail L.P. treatment are shunted. Outcome is designated: Good-no neurologic deficit and Developmental Index(D.I.)>90; Intermediate- no or minor neurologic deficit and D.I.= 70-90; Poor-significant neurologic deficit or D.I.<70. 43 infants have been followed to a mean corrected age of 27 months (range 12-47 months). Of 23 infants in Gp I, 16 have good outcomes, 4 intermediate, 3 poor. Both patients in Gp II have poor outcomes. Of 9 infants in Gp III, 2 have good outcomes, 4 intermediate, and 3 poor. Of 9 Gp IV infants, 2 have good outcomes, 6 intermediate and 1 poor. In conclusion, Gp I (arrested or regressed PPHyc) appears to have better outcome than Gps. III and IV. No trend is apparent between the no treatment(III) and L.P. treatment(IV) groups.

1573 FOLLOW-UP OF VERY-LOW-BIRTHWEIGHT (VLBW) INFANTS: LATE DEVELOPMENTAL SEQUELAE IN GMH/IVH SURVIVORS. David T Scott, Laura R Ment, & Joseph B Warshaw, Yale Univ School of Medicine, Depts of Pediatrics & Neurology, New Haven, CT 06510.

Of the 227 VLBW (<1250g) infants admitted over a 24-month period, 143 lived at least 36hr; 139 of these were evaluated for germinal-matrix hemorrhage (GMH) or intraventricular hemorrhage (IVH) by CT, echo, or autopsy. There were 37 infants who died after 36hr; 46 infants survived with GMH/IVH; and 56 infants survived with no evidence for GMH/IVH. The 56 non-hemorrhage survivors had a significantly longer mean gestation, largely because of 4 growth-retarded infants. Comparisons of the 3 groups on birthweight and routine obstetrical factors revealed no significant differences. The 2 survivor groups had comparable Apgar scores. Among survivors, there were significant (though not necessarily causal) associations between GMH/IVH and mechanical ventilation, transfusion, and stimulants such as epinephrine, dopamine, and isoproterenol.

Of the 102 survivors, 85 (83%) were brought to follow-up for serial neurologic examinations and blind developmental evaluations with the Bayley Scales of Infant Development. Only 4 of the 85 (5%) had major neurologic impairments. However, when the Bayley Mental Indices were analyzed in a repeated-measures analysis of variance, a significant Time X Group interaction was detected: GMH/IVH survivors made poorer developmental progress, on average, during the second year of life. Thus, long-term follow-up may be required to assess adequately the prognostic significance of perinatal insults.

● 1574 MONOAMINE METABOLITES IN BRAIN AND CEREBROSPINAL FLUID IN AN ANIMAL MODEL OF HYPERACTIVITY. Bennett A. Shaywitz, George M. Anderson, J. Gerald Young and Donald J. Cohen, Yale Univ. Sch. of Med., Depts. of Pediatrics, Neurology, Psychiatry, Lab Medicine and the Yale Child Study Center, New Haven, Connecticut, 06510.

We utilized recently described assays (Anderson et al, J. Chromatog. 1980) and specially developed techniques for the collection of CSF from the cisterna magna of developing rat pups to examine the concentrations in normal rats and littermates treated with desmethylimipramine (DMI) and 6-hydroxydopamine (6-OHDA). Such treatment results in behaviors which have striking parallels to the clinical syndrome of hyperactivity observed in children. Concentrations of all the parent monoamines increased by a factor of two between 12 and 26 days in normal pups. By 26 days in normal pups, CSF HVA and 5-HIAA had declined respectively, to values 61% and 84% of those observed at 12 days. Pups treated with DMI/6-OHDA as neonates exhibited a significant reduction in CSF HVA to concentrations 30-35% of controls at all ages studied. Significant correlations emerged between CSF HVA and brain HVA and DA and also between CSF 5-HIAA and brain 5-HIAA and 5HT. Our findings indicate that it is now possible to reliably determine concentrations of monoamine metabolites in CSF samples obtained from developing rat pups. Thus, for the first time investigators may examine CSF in animal models and extrapolate these findings to similar studies of CSF in children. Future experiments should provide further insights into the relationship between CSF monoamine metabolites and central monoaminergic mechanisms.

1575 THE LOW MORTALITY AND MORBIDITY OF IVH. Shlomo Shinnar, Richard A. Molteni, Karen Gammon, Bernard J. D'Souza, and John M. Freeman, Johns Hopkins University School of Medicine, Departments of Pediatrics and Neurology, Baltimore, Maryland.

The reported mortality of severe IVH ranges up to 50-65%. Hydrocephalus occurs in over 50% of the survivors. We prospectively examined 133 consecutive infants <1800 grams birthweight. Eighteen infants died in the first 24 hours of life. The remaining 115 infants underwent CT scanning and/or ultrasonography. Evidence of IVH was found in 91% of infants 26-28 weeks gestation, 48% of infants 29-30 weeks gestation and 10% of infants older than 30 weeks gestation. The incidence, mortality and morbidity of IVH in our population are summarized in the accompanying table.

	Number	Death	Seizures	Hydrocephalus
All Infants	115	5	1	1
No IVH	75	1	1	0
IVH	40	4	0	1
Grade 1	24	3*	0	0
Grade 2	3	0	0	0
Grade 3	5	0	0	0
Grade 4	8	1	0	1

(*These 3 infants died of causes unrelated to IVH)

The incidence of significant neurological sequelae in the surviving infants is low. The improved outcomes may be due to our ability to better control perinatal events in a primarily inborn patient population.

●1576 SYNAPTIC MEMBRANE DYSFUNCTION IN FELINE GM_1 GANGLIOSIDOSIS. Harvey S. Singer, Nariko Kawamura, Joseph T. Coyle and Henry J. Baker. Johns Hopkins Univ. School of Med., Depts. of Peds., Neurol. and Neurosci., Baltimore and Univ. of Alabama-Birmingham, Dept. of Comp. Anat., Birmingham. (Spon. by John M. Freeman).

Neurochemical parameters of synaptic transmission as well as the ganglioside content and composition within synaptic membrane has been studied in brain regions of cats with GM_1 gangliosidosis, a model similar to the human juvenile GM_1 form.

Cerebellar and cortical regions in 4 GM_1 cats with advanced neurobehavioral disease were assayed for pre-synaptic synaptosomal uptake (glutamate and GABA), post-synaptic receptor ligand binding (QNB, muscimol) and synthesizing enzyme activity (choline acetyltransferase, glutamate decarboxylase, tyrosine hydroxylase). Neurotransmitter uptake tended to be impaired with glutamate 17-80% of control and GABA 42-104% of control. Receptor binding studies for muscarinic cholinergic sites was variable whereas cerebellar GABA receptors were reduced by 34%. Neurotransmitter synthesizing enzyme capability was unaltered. Synaptic ganglioside content, NANA/mg protein, was increased up to 10 fold in synaptosomes and synaptic membrane subfractions. In the affected animals, 90% of NANA was GM_1 ganglioside.

Our data suggests that an increased concentration of ganglioside within synaptic membrane is associated with an impairment of synaptic membrane related functions. These findings may contribute to the neurobehavioral symptomatology in the hereditary gangliosidoses.

● 1577 IMPAIRED OXIDATION OF VERY LONG CHAIN FATTY ACIDS IN ADRENOLEUKODYSTROPHY WHITE BLOOD CELLS. Inderjit Singh, Hugo W. Moser, Ann B. Moser, Yasuo Kishimoto Kennedy Inst. Dept. Neurol. Hopkins Univ. Sch Med. Balti. MD 21205

Adrenoleukodystrophy (ALD) is an X-linked progressive disorder associated with the pathognomonic accumulation of saturated very long chain fatty acids ($C_{24:0}$-$C_{30:0}$). We have found that CO_2 evolution from [1-^{14}C]lignoceric ($C_{24:0}$) and [1-^{14}C]cerotic ($C_{26:0}$) acids was reduced to 8 and 14% of control in fibroblasts preparation obtained from ALD patients (Biochim. Biophys. Res. Comm. 102: 1223, 1981). We now report studies in homogenates of blood leukocytes from 11 ALD patients, 3 ALD obligate heterozygotes and 17 controls in which we measured the release of CO_2 from [1-^{14}C]lignoceric and [1-^{14}C]palmitic acids. CO_2 released from lignoceric acid was 196 ± 114 cpm/mg protein/hr in ALD hemizygotes, 462 ± 282 in ALD heterozygotes, and 769 ± 399 in controls. CO_2 released from palmitic was 10,900 ± 2,300 in ALD hemizygotes, 12,000 ± 4,000 in ALD heterozygotes and 13,900 ± 5,900 in the controls. The ratio of CO_2 released from palmitate to that from lignocerate was 41.9 ± 10 in ALD hemizygotes, 29.6 ± 5 in ALD obligate heterozygotes and 18.5 ± 2.7 in controls. The differences between the controls and ALD heterozygotes are statistically significant with a p value of less than 0.01. Mean endogenous C_{24} level in total lipids was 1.33 µg/mg protein in ALD leukocytes and 0.815 in controls. In the final homogenates the exogenous C_{24} exceeded the endogenous C_{24} by a factor of 10. These data indicate that in ALD there is a specific deficit in the oxidation of very long chain fatty acids. This work was supported by grants BNS-79-23017 from NSF and NS 13513, HD 10981 and NS 13569 from NIH.

1578 INCIDENCE OF INTRAVENTRICULAR HEMORRHAGE (IVH) AS DIAGNOSED BY PORTABLE ULTRASOUND IN INFANTS WEIGHING LESS THAN 1750 GRAMS. Yolande F. Smith, Kolinjavadi Sivasubramanian, Mary K. Davitt, Edward G. Grant, David C. McCullough. Georgetown Univ. Med. Center, Washington, D.C. (Spon. by P.L. Calcagno.)

One hundred and twenty-two infants weighing less than 1750 grams were admitted to the Intensive Care Nursery between January 1980 and June 1981. Using the ATL Mark III portable real-time scanner, cranial sonography was performed on 99 infants (82%): 1) in the 1st 72 hours; 2) on day 5; and 3) at weekly intervals. 86% of the infants required ventilatory support. IVH was graded according to Papile's classification.

Birth wt. in gms.	500-749	750-999	1000-1249	1250-1499	1500-1749	Total Expired
Admissions	19	22	25	32	24	122/39
Sonograms	14	18	25	26	16	99/29
Normal scan	2	1	4	18	10	35/2
Grade I IVH	1	1	-	-	-	2/1
Grade II IVH	1	5	4	2	1	13/4
Grade III IVH	8	7	11	4	4	34/12
Grade IV IVH	2	4	6	2	1	15/10

Conclusion: The incidence of IVH in premature infants $<$1750 grams is 64%. 76% of the hemorrhages are major (Grades III & IV) and 24% minor (Grades I&II). However, infants who weigh $<$ 1250 grams are at the greatest risk with an overall IVH incidence of 88%, with the risk reduced to 33% in infants $>$1250 grams.

1579 INCIDENCE & OUTCOME OF VENTRICULO-CEREBRAL HEMORRHAGE IN PREMATURE INFANTS. Yolande F. Smith, Kolinjavadi N. Sivasubramanian, Mary K. Davitt, Edward G. Grant, David C. McCullough. Georgetown Univ. Med. Center, Washington, D.C. (Spon. by P.L. Calcagno.)

Portable cranial sonography was performed on 99 of 122 infants with a birthweight (b.w.) of $<$1750 gms admitted to the Intensive Care Nursery: 1) in the 1st 72 hours; 2) on day 5; and 3) at weekly intervals. According to Papile's classification 15 infants (15%) had Grade IV IVH. 10 infants were diagnosed on the first sonogram; 4 infants had lesser degrees of IVH (I-III) and 1 was normal on the 1st sonogram with extension to Grade IV occurring on the 2nd sonogram. 10 infants expired ($\bar{X}$ b.w. 1055 gms (580-1700) ($\bar{X}$ gestational age (G.A.) 28.4 wks). 5 infants survived ($\bar{X}$ b.w. 1110 gms (880-1385) $\bar{X}$ G.A. 28.6 wks).

Full developmental evaluation was done quarterly on 4 of the 5 survivors. Mean age at latest follow-up is 15.5 months (11-20m). 1 infant is normal for age; 1 infant is severely retarded; and 2 infants have normal mental scores, but delayed motor development.

Although 66% of infants with Grade IV IVH expired, 75% of the survivors followed have normal mental development at 1 year of age. Caution must be exercised in making drastic medical decisions on the basis of Grade IV IVH alone.

● 1580 CREATINE PHOSPHOKINASE BB ISOENZYME IN VERY LOW BIRTH WEIGHT INFANTS: RELATIONSHIP WITH INTRAVENTRICULAR HEMORRHAGE. Michael E. Speer, Ching N. Ou, Gregory J. Buffone and Vickie L. Frawley (Spon. by Arnold J. Rudolph.) Baylor College of Medicine, Texas Children's Hospital, Department of Pediatrics, Houston, Texas.

Creatine phosphokinase (CPK) is comprised of 3 isoenzymes: MM, found primarily in skeletal muscle; MB, in cardiac muscle; and BB, in brain. This study was undertaken to determine whether any difference existed in the levels of CPK BB isoenzymes in infants who developed intraventricular hemorrhage (IVH) and those who did not. Forty-eight neonates were studied with serial samples of total CPK and its isoenzymes within 12 hours of birth and every 24 hours thereafter for 5 days. All infants weighed $<$ 1400 grams and were $\leq$ 32 weeks gestation. Serial real time ultrasound evaluations and/or autopsy data were used to determine the presence or absence of IVH. Analysis of this data was by the Mann-Whitney U-test. Analysis of first sample levels demonstrated a significant difference between the amount of CPK BB found in the patients who subsequently had IVH and those who did not. (Mean $\pm$ SEM: 41.41 U/L $\pm$ 8.41 U/ L vs 9.65 U/L $\pm$ 1.63 U/L $p < 0.002$) No difference was found between the two groups when the data from the 2nd, 3rd, 4th, and 5th samples were analyzed. CPK BB isoenzyme thus appears to be an effective screening test to predict the occurrence of IVH in very low birth weight infants.

● 1581 A PROSPECTIVE NEUROPHYSIOLOGICAL STUDY OF COMA IN CHILDREN. Patricia Strickbine-Van Reet, Daniel G. Glaze, Richard A. Hrachovy. Houston, Texas 77030. (Spons. by Marvin Fishman)

Serial electroencephalograms (EEG), brainstem auditory evoked potentials (BAEPs), visual evoked potentials to diffuse flash (FVEPs), and neurological examinations were recorded in 13 children (ages 1 month to 17 years) beginning within the first 24 hours of coma and the results were correlated with outcome. Eight children survived, 6 with severe neurological deficits. Etiologic factors included trauma, hypoxia, and encephalitis, but no correlation could be made between etiology and outcome. Findings associated with a poor prognosis included an initially non-recordable FVEP (10 children died or survived with severe neurological deficits). Recordable, though abnormal, initial FVEPs were always associated with survival and mild to no neurological residua. All patients with initially normal BAEPs survived with varying neurological residua. Impaired brainstem function by initial neurological examination was associated with survival in children with normal BAEPs. All patients with intact brainstem function survived but the best outcome was seen in those patients with recordable FVEPs. This study suggests the usefulness of evoked potentials during the first 24 hours of coma for the evaluation of prognosis.

● 1582 ANTICONVULSANT BLOOD LEVELS OF PHENOBARBITAL (PB) INCREASE BRAIN GLUCOSE AND K^+ LEVELS AND PROLONG ANOXIC SURVIVAL IN NEWBORN (NB) MICE. Jean H. Thurston, Richard E. Hauhart, Elise F. Naccarato, Washington University, Dept. of Pediat., St. Louis Children's Hospital, St. Louis, MO.

At the 1981 meeting of the APS we heard that chronic PB reduced the incidence of intraventricular hemorrhage (IVH) in preterm infants from 38% to 7%. To determine mechanisms of this exciting action NB mice received PB, 10 or 20 mg/kg or 0.9% NaCl subcutaneously once daily for 7 d. No side effects were seen and weight gain was normal. Plasma PB levels (20 min after last PB dose) were 12±7 µg/ml at 10 mg/kg of PB; 25±1 µg/ml at 20 mg/kg. Both doses had similar effects on brain glucose levels, therefore results were pooled. Blood glucose levels were unchanged but PB increased brain glucose 36%, 1.20±0.06 mmol/kg (mean ± SE) (N=11) vs 0.88±0.04 in controls (N=11), $p<0.001$; the brain/plasma glucose concentration ratio increased 40%, 0.162±0.008 l/kg vs 0.116±0.005 in controls, $p<0.001$. At 20 mg/kg PB, brain $[K^+]$ increased 2%, 666±2 meq/kg dry wt (N=7) vs 655±3 in controls (N=7), $p=0.02$. Twenty mg/kg PB increased survival of the mice in 100% N_2 gas (time of last gasp) 48%, 10.80±0.86 min (N=11) vs 7.27±0.52 in controls (N=11), $p=0.003$. At 10 mg/kg PB, anoxic survival increased 19%, 6.93±0.27 min (N=7) vs 5.80±0.43 in controls (N=7), $p=0.048$.

Intraventricular hemorrhage in preterm infants usually follows some major hypoxic-ischemic event. Since glucose is the only source of ATP during anoxia and increased brain K^+ concentration may reflect increased Na^+-K^+ ATPase activity, the observed effects of chronic PB in NB mice appear highly relevant to the beneficial action of PB in prevention of IVH in preterm infants.

● 1583 REYE'S SERA: EFFECT ON RESPIRATION. James H. Tonsgard, Godfrey S. Getz (Spon. by Peter R. Huttenlocher). Univ. of Chicago, Depts. of Pediatrics, Neurology, & Pathology.

Dysfunction of liver mitochondria appears central to the pathophysiology of Reye's Syndrome (RS). Aprille reported that concentrates of RS serum added to rat liver mitochondria stimulate respiration and disrupt the ultrastructure (Science 197:908,1977). Subsequently, the incremental consumption of O_2 was attributed to metabolism of uric acid in microbodies contaminating the mitochondrial preparation (Ped. Res. 15:702, 1980). We have come to somewhat different conclusions. We have demonstrated that addition of RS serum to rat liver mitochondria produces 1.) A brief (1-2 min.) consumption of O_2 and 2.) A sustained increase in O_2 consumption. The transient increase is proportional to the amount of uric acid present in the samples (3-7 mg/dl in RS and 1-2 mg/dl in controls). It can be reproduced by the addition of uric acid to mitochondrial preparations. The sustained effect is on State 4 mitochondrial respiration (40-200% increase with RS, N=6; 0-20% with control sera, N=4). This was confirmed using chincilla liver mitochondrial preparations which lack microbodies, as well as by inhibiting the metabolism of uric acid with oxonic acid and by oxidizing the uric acid with uricase prior to addition of the sera to the mitochondrial preparation. Addition of uric acid (10 mg/dl) to rat or chincilla liver mitochondria had no effect on the sustained rate of O_2 consumption. There appeared to be no relationship between the increase in O_2 consumption and the presence of salicylates or other drugs in RS sera. The data support the presence of a factor other than uric acid in RS sera which produces sustained stimulation of mitochondrial respiration.

1584 FURTHER EVIDENCE FOR REGULATION OF CEREBRAL BLOOD FLOW (CBF) BY OXYGENASES. Richard J. Traystman, Gail H. Gurtner, M. Douglas Jones, Jr., Raymond C. Koehler, and Mark C. Rogers. Anesthesiology/Critical Care Medicine and Medicine, Johns Hopkins Hospital, Baltimore, MD 21205

The response of CBF to elevated carboxyhemoglobin levels before and after administration of metyrapone (M) and pargylene (P) (both O_2 substrates) was studied in 5 anesthetized, ventilated dogs. Under control conditions, reducing arterial O_2 content from 19.0 to 11.0 and 7.0 vol % increased CBF from control (23.4 ml/ min) to 160 and 250% of control respectively. Cerebral O_2 consumption ($\dot{V}O_2$) remained unchanged. Following administration of M (2 gm, i.v. or intra CSF), or P (20 mg, i.v.), the vasodilator response to carbon monoxide progressively decreased by 60-80% at each elevated carboxyhemoglobin level. To test if these data are consistent with the existence of a CSF chemoreceptor, we measured the CBF response to administration of sodium dithionite. Dithionite irreversibly reacts with oxygen and was infused into the lateral ventricle. Dithionite (2 ml isosmolar) resulted in an increase in CBF from control (17 ± 2) to 50 ± 5 ml/min, while $\dot{V}O_2$ remained unchanged. Subsequent administration of M (2 gm, i.v.) completely blocked the CBF response to CSF dithionite. Since the venous outflow technique measures CBF from areas remote from the CSF, and since the changes in CBF occurred rapidly (20 seconds), a neurogenic mechanism of action is suggested. These data are also consistent with the presence of a central chemoreceptor mediated by an oxygenase which interacts with metyrapone or imipramine, such as cytochrome P-450, monoamine oxidase, or cyclooxygenase.

1585 INTRAVENTRICULAR HEMORRHAGE IN PRETERM INFANTS. Kamtorn Vangvanichyakorn, Shyan Sun, Zanaida Aranda Richard Koenigsberger(Spon. F. Behrle) New Jersey Med. School, Dept. Neonatology & Neurology, Newark, New Jersey

During the period Oct. 1980 to Nov. 1981, 126 preterm infants (BW ≤ 2000 gm, GA ≤ 36 wks) had cranial ultrasonography daily after birth for 7 days and twice a week until discharge. Papile's classification was used for classification of intracranial hemorrhage. IVH incidence & mortality re birthweight:

B.W.	No	IVH	IVH%	Death	Mortality%
500-750	12	10	83.3	8	66.6
751-1000	16	14	87.5	8	50
1001-1500	43	15	34.8	4	9.3
1501-2000	55	8	14.5	0	0
	126	47	37.3	20	15.8

Onset of hemorrhage:

<12 hrs	<24 hrs	<48 hrs	<72 hrs	3-11 days
7/38(18.4%)	25/38(65.8%)	33/38(86.8%)	35/38(92.1%)	100%

Severity of hemorrhage:

Gr I (%)	Gr II (%)	Gr III (%)	Gr IV (%)
11 (24)	8 (18)	20 (44)	6 (13)

Time of ventricular resolution in survivors: (9 Gr III & 1 Gr IV)
50% resolution average 5 wks (3-12 wks)
100% resolution average 18.3 wks (3-28 wks)

LP's were performed intermittently in 6 cases & only when fontanells were severely distended. It was a surprise that almost all dilated ventricles returned to normal size or at least reduced in size in surviving infants by the time of discharge. No surgical shunt was needed in our experience. Follow-up study of survivors will be reported separately.

1586 DIFFERENTIAL SUBREGIONAL CEREBRAL BLOOD FLOW (CBF) RESPONSE TO HYPOXIA IN NEWBORN LAMBS: EFFECT OF ALPHA BLOCKADE. L. Craig Wagerle, Thomas M. Heffernan, David W. Herbert, Linda M. Sacks and Maria Delivoria-Papadopoulos. Univ. of PA., Depts. of Physiology and Pediatrics, Phila., PA.

Previous studies have shown that during asphyxia cerebral metabolic needs are met by increasing brain blood flow. The present study examines the distribution of blood flow within the brain in 12 chronically catheterized hypoxemic lambs ventilated at $PaCO_2$= 38. Following baseline measurements of blood gases, pH, O_2 sat, [Hb] and subregional CBF by microspheres, hypoxia to PaO_2=25 mmHg was induced. Measurements were repeated after 30 min. Six lambs were infused with the $alpha_1$ antagonist prazosin (0.5 mg/kg) prior to hypoxia, while 6 served as controls. Baseline blood flow to the cerebrum, cerebellum, caudate nucleus, hippocampus, thalamus, midbrain, pons and medulla were 113±7, 125±12, 110±8, 83±7, 123±7, 118±12, 112±8 and 112±6 ml/min·100g^{-1} respectively. Regression analysis showed a hyperbolic relationship between subregional blood flows and arterial O_2 content. The response slope, and therefore the magnitude of the increase in flow, was greatest in the cerebellum, midbrain, pons and medulla (73-112%) while caudate nucleus and cerebrum increased less (50%). Alpha blockade had no effect on the slope or elevation of the subregional CBF vs. O_2 content relationship. These data demonstrate a nonhomogeneous subregional cerebrovascular response to hypoxia, not mediated by sympathetic stimulation. The larger increase in flow observed to brainstem structures suggests either hypoxia induced increased metabolic requirements or a differential subregional vascular sensitivity to hypoxia in the newborn brain.

1587 CREATINE KINASE BRAIN ISOENZYME CONCENTRATION [CKBB] AS A SCREENING TEST FOR INTRAVENTRICULAR HEMORRHAGE (IVH). G. Worley, I.H. Gewolb*, B. Lipman, J. Green, C.R. Roe, S.J. Gross, Depts. of Pediatrics, Duke University Medical School, Durham, N.C., Yale University School of Medicine*, New Haven, Ct.

Our hypothesis was that the [CKBB] in CSF could be used to distinguish samples from infants with an IVH from those samples made bloody by a traumatic lumbar puncture (LP).

Only samples from infants with grades 2,3, or 4 IVH were included in the IVH group (the CSF is not bloody in grade 1 IVH). Samples had to be obtained within 10 days after the clinical onset of the IVH.

A sample was included in the non-IVH group if it came from an infant not suspected clinically of an IVH or one who had a normal scan. Also, the red blood cell count (RBC) had to be > 1000, the lowest RBC in the IVH group. Roughly matching for RBC avoided defining a "bloody" CSF.

[CKBB] was measured by radioimmunoassay. CSF was run against serum standards and [CKBB] is expressed in arbitrary units/milliliter. We defined a high [CKBB] as ≥ 11; this was the highest value found in CSF from infants with a normal neurological exam and no neurological insult within 3 days before the LP.

	IVH	Non-IVH	
High CKBB (≥11)	34	5	Sensitivity = 34/36 (.94)
Low CKBB (<11)	2	36	Specificity = 36/41 (.88)

The results suggest that [CKBB] may prove useful as a Screening Test for IVH.

1588 CREATINE KINASE BRAIN ISOENZYME CONCENTRATION [CKBB] IN THE CEREBROSPINAL FLUID (CSF) OF NEWBORNS. G. Worley, B. Lipman, I.H. Gewolb*, J. Green, S.J. Gross, C.R. Roe, Depts. of Pediatrics, Duke University Medical School, Durham, N.C. and Yale University School of Medicine*, New Haven, Ct.

To test the hypothesis that increased [CKBB] in CSF reflects brain tissue damage, we measured [CKBB] in 252 CSF samples from 156 infants using a radioimmunoassay. CSF [CKBB] was determined using serum standards and is expressed in arbitrary units/milliliter.

Infants at high risk for brain damage (those with an Intraventricular Hemorrhage (IVH), meningitis, Herpes encephalitis or severe asphyxia) had higher peak CKBB levels than those at low risk (normal neurological exam and no history of a neurological insult within the 3 days before the lumbar puncture).

	N	Mean [CKBB]	S.D.	
High Risk	41	40.9	65.0	$t(40) = 3.5$
Low Risk	40	5.0	1.6	$p < .001$

The mean [CKBB] from 14 infants with a grade 3 or 4 IVH (40.7) was greater than the mean from 10 infants with a 1 or 2 IVH (9.7), $t(18) = 6.4, p < .001$.

Infants with a definitely abnormal neurological exam at discharge (focal findings, tone abnormality, diminished responsiveness) have a greater peak [CKBB] than those considered neurologically normal at discharge.

	N	Mean [CKBB]	S.D.	
Normal	108	7.8	9.6	$t(19) = 4.17$
Abnormal	19	57.7	90	$p < .001$

These data are consistent with the hypothesis that CSF [CKBB] is an indicator of brain damage in newborns.

1589 RISK FACTORS AND NEUROPHYSIOLOGIC OUTCOME IN CYANOTIC HEART DISEASE. Francis S.Wright, Margaret O'Dougherty, Ruth B. Loewenson and Fernando Torres(Spon.by Grant Morrow, III), Ohio State Univ.Col.of Med., Dept. of Pediatrics, Columbus and Univ.of MN Med.Sch., Dept.of Neurology, Minneapolis.

A model of risk potential for neurophysiologic outcome was created, based on cardiac, neurologic, and surgical factors in 31 children with Transposition of the Great Arteries, who had received reparative surgery utilizing cardiopulmonary bypass at normothermia. Impact of these potential risk factors was assessed by five current measures: electroencephalogram(EEG), visual evoked response(VER), neurologic abnormalities, functional motor impairment and intellectual competence. Results indicated that neurologic abnormalities were significantly associated with failure of the Rashkind procedure to alleviate hypoxia ($p<.001$), prolonged hypoxia($p<.01$)and absence of ameliorating shunting heart defects ($p<.02$). Congestive heart failure and growth failure did not relate to current neurophysiologic function. CNS infection and cerebrovascular accident were associated with impaired outcome; seizures, duration of cardiac repair and post-operative complications were not. Analysis of cumulative risk scores indicated significantly higher risk scores in children with abnormal VER's ($p<.005$)or abnormal EEG's($p<.05$). Composite neurologic outcome scores highly correlated with this cumulative risk score($r=.62$) and related significantly to the children's current intelligence ($r=-.58$)and achievement($r=-.51$). The data support the hypothesis that chronic hypoxia and factors exacerbating it adversely relate to neurologic function, and that cumulative risk factors are associated with diverse neurophysiologic dysfunction.

1590 OUTCOME OF PREMATURE INFANTS WITH HYDROCEPHALUS (HD) 2° TO INTRAVENTRICULAR HEMORRHAGE (IVH). Dana W.Zarafu Lorna Plaza, Abbot Krieger. (Spon. Franklin C. Behrle) College of Med. and Dent. of N.J.-N.J. Med. School,Newark Beth Israel Medical Center,Dept. of Ped. Newark, N.J. 07112

From 1/78 to 6/81 21 infants developed Hydrocephalus 2° to IVH documented by ultrasound or computerized axial tomography (CAT), mean birth weight 1223gms. Eighteen survived. HD was classified: mild 5 (1 exp.) moderate 2(1 lost to follow-up) severe 14(2 exp.) Supportive treatment (Rx) was given as necessary. Mild and moderate HD didn't receive specific Rx. Rx of severe HD: 4 had repeated lumbar taps (RLT),9 had RLT+ventriculo-peritoneal shunt (VPS) 1 had no specific Rx (clinically well, CAT unchanged.)

Seventeen infants were followed between 6 mos.-2 yrs. with CAT scans,neurologic,hearing,vision and Denver Developmental screening test (DDST) corrected for gestational age. 5/5 with mild or moderate HD had normal DDST,2/5 had mild ↑ reflexes. CAT showed no change in 4, improvement 1.

Twelve infants with severe HD showed:

DDST-delay/mos.		RLT(3)	RLT+VPS(8)	ORx(1)
Normal		1	1	1
Mild	2-3	1	4	
Moderate	2-4	1		
Severe	> 6		3	

Mild ↑ of reflexes were noted in 2/3 RLT, 4/8 RLT+VPS. Severe spasticity was noted in 3/8 RLT+VPS. CAT showed no change in 8/12,improvement in 4/12. Severe hearing loss was noted in 1 infant, visual impairment in 2 of RLT+VPS. 3/21(14%) infants with HD expired,all had severe neurologic impairment. 3/17(17%) survivors had severe neurologic impairment,1/17(6%) had moderate development delay. 8/17(47%) showed mild or no delay.

PULMONOLOGY

1591 SPECTRAL ANALYSIS OF BREATHING IN PATTERNS IN NEWBORN INFANTS. S. Abbasi, S. Duara, J.G. Schwartz, T.H. Shaffer and W.W. Fox. Dept. of Peds., Univ. of Pa. Sch. of Med., Children's Hospital and Pennsylvania Hospital, and Temple Univ., Dept. of Physiology, Phila., PA., and Univ. of Maryland Sch. of Med., College Park, MD.

The majority of studies of neonatal breathing patterns have involved wave shape analysis in the time domain. These include determination tidal volume, insp. time/exp. time, and respiratory rate (RR). Because currently used ventilatory parameters do not differentiate complex breathing patterns, a more critical wave shape analysis technique may be required. Power density spectral analysis provides a quantitative method for expressing a given wave shape as a function of its frequency components. Spectral analysis of breathing patterns was evaluated in 5 spontaneously breathing infants, mean study wt. 1.8 ± 0.1 kg and study age of 35 ± 17 days. Infants were breathing room air through a face mask which was attached to a pneumotachograph to measure air flow and this signal was integrated into volume. Data was digitized and recorded on flexible disk and analyzed by HP 9845B computer. Power spectral density was used to evaluate breathing patterns for frequency range, peak frequency (f_p) and centroid frequency (f_c). Respiratory spectrum bandwidth was 50 to 202 breaths/min. (0.8 - 3.4 Hz). Mean ± SE of f_p = 66.5 ± 2.2 b/min., f_c = 68.9 ± 1.1 b/min. Resp. rate 70 ± 4 b/min. There was a significant correlation between f_p and RR. It appears that power spectral analysis provides a quantitative technique for evaluating breathing patterns. Of all various power and frequency parameters, f_p and f_c were most stable and reproducible.

1592 AIRWAY PRESSURES DURING HIGH FREQUENCY OSCILLATORY VENTILATION: N.B. Ackerman, Jr., D.M. Null, Jr., R.A. deLemos (Spon. by J.L. Robatham), Wilford Hall USAF Medical Center, Department of Pediatrics, San Antonio, Texas

The applicability of high frequency ventilation (HFOV) in patients with diffuse alveolar disease is based on the assumption that pulmonary barotrauma will be less likely. We explored the relationship between proximal and distal airway pressures during HFOV in ten mongrel dogs with normal or oleic acid injured lungs. Distal airway pressure was measured through catheters of known frequency response inserted retrograde and wedged in the distal bronchi. Alveolar mean pressures were estimated after equilibration following tracheal occlusion. Both pneumatic and mechanical oscillators were used with frequencies between 2 and 16 Hz and varying I:E ratios.

In most animals studied, distal mean airway pressures and mean alveolar pressures were not significantly lower than proximal mean pressures regardless of frequency. Peak distal pressures were significantly lower at the higher frequencies (over 5 Hz) but when extremely high proximal airway pressures were required to maintain oxygenation, the distal pressures were significant. Prolongation of the I:E ratio or maintenance of distending pressure by use of a restrictive orifice resulted in circumstances where distal peak and mean pressures were higher than those at the proximal airway.

The assumption that HFOV necessarily exposes the distal airway to lower pressures is not supported by this data. Distal pressure transmission during HFOV is dependent on the I:E ratio, frequency, oscillatory volume, and physical characteristics of the lung.

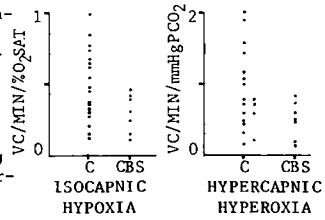
1593 APNEA IN INFANTS WITH RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION. Nick G. Anas, Christian Boettrich, Caroline B. Hall, John G. Brooks. Univ. of Rochester, Department of Pediatrics, Rochester, New York.

We studied breathing patterns during sleep of infants hospitalized with culture-proven RSV disease to determine the natural history of RSV-associated apnea, to learn whether apnea represents the extreme of a spectrum of abnormalities in control of breathing induced by RSV, and to define the characteristics of susceptible infants. During a 2-4 hour sleep period, we continually recorded heart rate, rib cage and abdominal circumference, PCO_2 at the external nares, transcutaneous oxygen tension, body temperature, and behavior. Sleep studies were repeated daily until there were no respiratory pauses ≥15 seconds. For each study, we measured the duration of the longest pause, pauses associated with bradycardia or hypoxemia, and total duration of respiratory pauses >6 seconds divided by total sleep duration ($A_6D\%$).

Five of the 32 RSV-infected infants presented with apnea requiring assisted ventilation (3) or ICU monitoring (2). All apnea was non-obstructive. Within 48 hours of admission (within 7 days of onset of clinical illness) all infants were free of pauses >15 seconds or pauses associated with bradycardia or hypoxemia. The $A_6D\%$ was <0.5 for all 5 infants. None of the 27 infants presenting without apnea developed apnea during hospitalization and none had $A_6D\%$ values >0.2 at time of admission. Apnea occurred only in prematurely born infants who were less than 40 weeks post-conception. Four of 5 had had apnea of prematurity. Apnea infants more often demonstrated radiologic evidence of pneumonia ($p<0.01$) and had greater alveolar-arterial O_2 gradients ($p<0.01$).

1594 VENTILATORY RESPONSES IN SUBJECTS WITH A HISTORY OF CHILDHOOD CYANOTIC BREATHHOLDING SPELLS (CBS). Nick G. Anas, John T. McBride, Christian Boettrich, John G. Brooks. (Intr.by David H. Smith). University of Rochester, Dept. of Pediatrics, Rochester, NY.

CBS occurs in 3% of children 3-36 months of age. We tested the hypothesis that the ability of these children to breathhold until cyanotic and unconscious relates to blunted ventilatory sensitivity to hypoxemia or hypercapnia. We measured ventilatory responses to progressive hyperoxic hypercapnia and isocapnic hypoxia by rebreathing techniques in 4 males and 3 females (ages 11-55 years) who had physician-documented CBS in early childhood. Responses were compared to those of a group of 12 males and 5 females (ages 18-40 years) with no cardiopulmonary or neurologic disease. Responses were expressed as vital capacities per minute (VC/min) as a function of mmHg PCO_2, or O_2 saturation. For each individual, responses in 3 consecutive runs were averaged. Data for control (C) and CBS groups are presented. The trend toward lower responses in the CBS group does not reach statistical significance; many individuals with CBS demonstrate normal responses. These data suggest that if an abnormality of ventilatory control explains CBS in children, it does not persist into adulthood or involves pathways other than those controlling the ventilatory response to hypercapnia and hypoxia.



1595 RESPIRATORY COUPLING, CA^{++} AND MG^{++} LEVELS, AND AGING IN CYSTIC FIBROSIS AND NORMAL FIBROBLASTS. Cynthia F. Bearer , Pamela M. Mattes , John W. Littlefield and Peter L. Pedersen. Johns Hopkins Univ. School of Medicine, Baltimore, MD 21205.

We measured the rates of O_2 consumption of a patient age-and doubling number-matched pair of cystic fibrosis (CF) and normal fibroblast cultures, by both intact cells and digitonin-permeabilized cells in the presence and absence of oligomycin or oligomycin and 2,4-dinitrophenol (DNP). Basal O_2 consumption did not differ between the CF and normal cultures, and gradually increased with culture age from about 3.5 to 8.0 natoms O_2/min/10^6 cells. Respiratory control ratios (DNP-stimulated rate/oligomycin-inhibited rate) with Na^+ succinate as substrate remained relatively constant at 2.5 to 4.0 throughout each culture's lifespan. Total cellular Mg^{++} and Ca^{++} contents increased 3.5 to 5.0-fold during the aging of both lines. Although both Ca^{++} and Mg^{++} levels seemed higher for CF than for control cells, the ratio $(Ca^{++})/(Mg^{++})$ was higher at all points in the lifespan of CF fibroblasts, suggesting elevated Ca^{++} in CF cells. Since CF cells grew significantly more slowly after only 4 doublings and stopped growing after 26 doublings compared to ~50 doublings for the control cells, cation differences may reflect early senescence in CF cells. The findings of increased Ca^{++} in CF cells but normal respiratory control suggest a defect in Ca^{++} efflux from CF cells at the mitochondrial or plasma membrane. (Supported in part by a Cystic Fibrosis Foundation Fellowship).

1596 THE USE OF TRACHEAL BREATH SOUNDS (TBS) FOR APNEA DETECTION (AD). Robert C. Beckerman, Joan M. Tonglet, Michael Wegmann; Department of Pediatrics and the Constance Kaufman Center for the Study of Breathing Disorders in Infants and Children, Tulane University School of Medicine, New Orleans, Louisiana. Spon. by Emmanuel Shapira.

Impedance pneumography (IMP) and airflow (AF) sensing devices are the standards for detection of central (CA) and obstructive apnea (OA) in hospitalized patients. We have studied a system that detects normal breaths and periods of CA and OA by using a miniature microphone coupled to the chest wall. We evaluated 10 sleeping infants and children (ages 2 months-8 years) who were referred because of symptoms of severe sleep disturbance. The TBS system was compared to IMP using AF (thermistor, CO_2 catheter) as the standard technique.

% Breath Detected		% Breath Detected		% CA		% OA	
TBS		IMP		TBS	IMP	TBS	IMP
$\bar{x} \pm$ 1SD		$\bar{x} \pm$ 1SD		$\bar{x} \pm$ 1SD		$\bar{x} \pm$ 1SD	
95 ± 2.62		98.2 ± 3.61		99.4±1.67	100±0	95.2±5.95	0

There were no statistically significant differences among the methods of breath or apnea detection. We found TBS to be as good a method as IMP or AF in detection of normal BS and periods of CA and OA in closely observed children. TBS had several advantages over the other techniques. It was easier to measure the apneic interval and was less easily dislodged by movement. Filtering of heartsounds and background noise and more efficient coupling of the TBS detector will allow even greater sensitivity. We feel that TBS may have practical application in hospital and home monitoring for apnea.

1597 FAMILIAL INCREASED AIRWAY REACTIVITY (AR): ITS ROLE IN LATER PULMONARY FUNCTION TESTS (PFT) OF PREMATURELY BORN CHILDREN AND POSSIBLE RELATIONSHIP TO PREMATURE LABOUR, Jean Marie Bertrand, Judith A. Popkin, Patricia Riley, Allan L. Coates (spon. by Harvey Guyda) The McGill Univ.-Montreal Children's Hospital Research Institute, Montreal, Que. Canada.

In order to assess the role of RDS, premature birth and familial AR on follow-up PFT, we studied 4 groups of children, aged 5 to 14 yrs. Gp1 consisted of 11 prematurely born children (GA 32.5±3.6 wks) who developed RDS in the newborn period and Gp2 were their paired sibling controls. Gp3 consisted of 11 healthy prematurely born children (GA 33.4±2.5 wks) and Gp4 were their paired sibling controls. The PFT consisted of spirometry, lung volumes and flow-volume curves by plethysmography and AR assessment by histamine challenge. AR was also evaluated in 18/22 of the mothers. The only significant difference was that Gp1 had a lower FEV1 and a higher RV/TLC than Gp2 ($p<.01$ for both). Flows at 25 and 50% of vital capacity (overall mean .43±.18 and .89±.26 TLC/s respectively) were not significantly different among the 4 groups and were similar to those reported previously for prematurely born children with and without RDS. An incidence of increased AR, at least 5 times normal for this laboratory, was found in all groups: 8/11 Gp1, 5/11 Gp2, 9/11 Gp3, 7/11 Gp4 and in 12/18 mothers. These results suggest that previously reported low flow rates in prematurely born children might be due in part to an unexpected high incidence of familial increased AR. There are known pharmacological and physiological similarities between uterine and airway smooth muscle which lead to the speculation that familial smooth muscle hyperreactivity may play a role in the etiology of premature labour.

1598 PULMONARY VASOCONSTRICTOR RESPONSE TO SEROTONIN IN THE NEWBORN LAMB. Rex G. Bickers, Stephen H. Bennett, Jay M. Milstein, and Boyd W. Goetzman, Univ. of Cal., Davis, School of Medicine, Dept. of Pediatrics, Davis, CA.

Serotonin (5HT) is a potent endogenous vasoconstrictor which may play a role in regulation of the pulmonary circulation. In order to characterize the pulmonary vasoconstrictor response (VCR) to 5HT in the newborn, we have determined their dose-response relationship (D-R) in lambs. We performed rapid bolus pulmonary artery (PA) injections of 5HT (0.02-2.0 mcg/kg) in 10 anesthetized open-chest lambs (age 0-3 d), instrumented for measurement of PA pressure (Pp), PA flow (Qp), left atrial pressure (Pa), and aortic pressure (Ps). Pulmonary vascular resistance (Rp) was calculated as (Pp-Pa)/Qp, and the D-R was determined by nonlinear regression analysis. Pulmonary VCR (% rise in Pp or Rp) was reproducible at all doses, and no rise in Ps occurred below 1.2 mcg/kg. In each experiment, the D-R exhibited two sets of receptor constants. A zero-threshold receptor had a greater peak effect (Ep) = 37.8 ± 13.5 % increase (mean ± SD) and a lower ED50 (dose required to produce Ep/2) = 0.504 ± 0.304 mcg/kg than the "second" receptor whose threshold = 0.477 ± 0.168 mcg/kg, Ep = 21.4 ± 11.5 % increase, and ED50 = 1.75 ± 1.01 mcg/kg . Co-treatment with methysergide, a serotonin antagonist, completely blocked any response to 5HT, but phenoxybenzamine, an alpha adrenergic antagonist, blocked only that portion of the VCR attributed to the zero-threshold receptor, suggesting that two 5HT receptors can be pharmacologically differentiated. There may also be cross-reactivity among various biogenic amine receptors in the pulmonary circulation.

1599 PSEUDOMONAS EXOPRODUCTS RELEASE MUCINS FROM GOBLET CELLS IN RABBIT TRACHEA. Thomas F. Boat and Jeffrey D. Klinger, Case Western Reserve University, Rainbow Babies and Childrens Hospital, Dept. of Pediatrics, Cleveland.

We investigated the hypothesis that exoproducts of P. aeruginosa (PA) stimulate the secretion of mucus by tracheobronchial epithelium. The assay system employed rabbit tracheal mucosa-submucosa explants which contain no mucous glands but secrete mucins from goblet cells in surface epithelium. Mucins were labeled to equilibrium with $^{35}SO_4$ and their secretion followed by quantitation of counts associated with chromatographically isolated, high molecular weight mucins in harvested secretions. 1:16 to 1:4 dilutions of filtered 24 hr culture supernatants of either mucoid of nonmucoid PA colony types stimulated mucin release up to 4-fold in a dose-dependent fashion. Supernatants from mucoid strains were not more active. TCA-purified type 6 lipopolysaccharide and exotoxin A from PA had no effect on this secretory system at concentrations up to 100 µg/ml. However, over the same concentration range, highly purified PA elastase effected a dose-dependent response, maximal at 3.5 times the basal secretory rate. Alkaline protease from PA had a more modest, but dose dependent effect. Proteinases from PA (and perhaps other organisms) may promote the secretion of mucus in vivo as well as in vitro, and through this mechanism may play a pathophysiologic role in pseudomonas lung infections, especially in cystic fibrosis (CF). It is also possible that PA proteinases enter the circulation from infected lungs and account, at least in part, for the mucus-stimulating effect which is characteristic of CF serum.

1600 LUNG, LIVER AND SERUM VITAMIN E CONCENTRATIONS IN VITAMIN E DEFICIENT RATS EXPOSED TO HYPEROXIA. Mary Ellen A. Bozynski (Spon. by Joseph R. Christian) Rush Med. Coll., Rush Pres. St. Luke's Med. Ctr., Dept. of Peds., Chicago and Mohammed Mazharuddin, William Boyle, Steve T. Koeff, Alicia Edick, Daisy S. McCann, Univ. of Mich., Sch. of Med., Wayne Cty. Gen. Hosp., Dept. of Peds. and Med., Wayne, Mich.

There is little data on serum, liver, and vit. E conc. for deficient animals exposed to hyperoxia. Thirty adult male rats were divided into two groups. One was fed a vit. E deficient and the other a control diet for three weeks. Weights were obtained weekly. Half then received vit. E and half placebo (0.5 mgm s.c. x 6 days, Hoffman-LaRoche, Nutley, N.J.). Equal subgroups were placed in oxygen (O_2+) or non-oxygen (O_2-) enriched environments, making a total of four groups. Oxygen exposure was: FiO_2 0.6 x 4 days, FiO_2, 0.75-0.80 x 2 days. Rats were weighed. Serum, liver, and lung vit. E conc. were determined. Serum vit. E conc. in deficient placebo treated rats (DP) was 26.9% of those treated (DT): 127 ug% vs 460 ug%. Liver vit. E: DT 4.1 ug/g, DP 1.7 ug/g, control treated (CT) 6.1 ug/g, and control placebo treated (CP) 6.2 ug/g. Lung vit. E conc. in DP (< 0.16 ug/g) was undetectable and < 5% of DT (3.04 ug/g). Oxygen exposure did not affect liver vit E. Since lung vit. E conc. was undetectable in DP rats, no difference in DPO_2+ and DPO_2- groups could be shown. Serum vit. E conc. was paradoxically higher in DPO_2+ than DPO_2- rats: 148 ug% vs 106 ug%. All rats experienced weekly weight gain except DPO_2+ which lost weight during the last week of the study. Lung is more severely depleted than liver or serum in vit. E deficiency. Serum vit. E conc. does not reflect lung. (Supported by M.S.R.E.)

1601 INFANT PNEUMONITIS ASSOCIATED WITH CMV, CHLAMYDIA, PNEUMOCYSTIS AND UREAPLASMA: 12-month followup Dana M. Brasfield, Sergio Stagno, Richard J. Whitley, Ralph E. Tiller

University of Alabama School of Medicine The Children's Hospital, Department of Pediatrics, Birmingham, Alabama

In a prospective study performed between July 1976 and June 1980, 104 infants younger than three months were identified with infant pneumonitis. Sixty-five infants (63%) were infected with the above named organisms either singly (74%) or in combination (26%). Seventy-eight (75%) of these infants were followed a minimum of 12 months. The percent distribution of patients with single, mixed or unknown etiology is equal within this group of 78 patients. Sixty-one episodes of wheezing occurred in 25 (32%) of these patients. Five patients (6%) were hospitalized 7 times for respiratory illnesses. Of 36 patients who grew at or above the 10th percentile prior to the pneumonitis only 25 (69%) continued to grow at that rate after the episode. Initially there was no specific radiographic pattern for any of the infectious agents. Fourteen patients (18%) had persistently abnormal chest roentgenograms 12 months after the initial infection. There was no significant difference in morbidity between etiologic groups. Available retrospective data suggests an association between lower respiratory tract illness in childhood and increased respiratory symptoms in later life. Our prospective data indicate an increase in respiratory symptoms, abnormal growth and abnormal roentgenograms in a group of infants followed 12 months after a episode of pneumonitis.

1602 NEUTROPHIL MYELOPEROXIDASE DEFICIENCY IN CYSTIC FIBROSIS. John D. Bray, Jacob Hanker, Alexander Spock, Duke University Medical Center, Department of Pediatrics, Durham, North Carolina.

Myeloperoxidase, a lysosomal enzyme of the neutrophil, in the presence of H2O2 and a halide constitutes a potent bactericidal system against certain micro-organisms. This study investigated the role of the neutrophil myeloperoxidase in patients with cystic fibrosis in an attempt to explain the recurrent pulmonary infection in these patients. We utilized the improved techniques of Hanker for the cytochemical demonstration of the leukocyte peroxidase. The following results were secured.

		Staining for Peroxidase Deficiency		
Patient Group	Total Patients	0	1-2+	3-4+
Allergic	32	30	2	0
Chronic Lung Disease	3	0	3	0
URI	8	6	2	0
Cystic Fibrosis	56	12	16	28

50% of the patients with cystic fibrosis had marked deficiency in cytochemical demonstration of leukocyte peroxidase and one patient had severe deficiency on repeated examinations. The deficiency did not appear to be related to the severity of the disease or age of the patient; there was a slight increase of the deficiency in males. The relationship of the observed deficiency to cystic fibrosis remains unclear; however, we are currently investigating the relationship of the neutrophil myeloperoxidase level to infection, phagocytosis and genetic aspect of cystic fibrosis.

1603 THE EFFECT OF A TRIGGERING MODIFICATION ON THE SENSITIVITY OF A PEDIATRIC VOLUME VENTILATOR John D. Bray, Robert L. Stephenson, Mark C. Rogers, and Frank R. Gioia, Department of Anesthesiology and Critical Care Medicine, Johns Hopkins Hosptial, Baltimore, MD 21205

During assist-mode ventilation of infants and small children discordance between spontaneous respiratory efforts and the delivery of positive pressure breaths is frequently noted. We performed a simple modification of a volume ventilator (Servo 900B, Siemens-Elema Co.) fitted with pediatric tubing to enchance the sensitivity and thereby diminish the asynchrony between the patient's inspiratory effort and the ventilator's assist. Rigid tygon tubing (1/4" diameter) was connected to the ventilator circuit near the patient adapter and attached to the pressure transducer in the ventilator.

The amount of volume needed to be withdrawn from the circuit to cause the ventilator to fire 90% of the time was determined with and without the modification. In addition, the maximum negative pressure in the circuit and the response time of the ventilator were determined from pressure-time tracings. Results from ten determinations the modification were compared using the t-test for unpaired data.

The withdrawal volume necessary to cause the ventilator to fire decreased from 7.5 ml. to 3.0 ml. with the modification. Maximum negative pressure (mean + SEM) decreased from 3.76 + 0.13 cm. H_2O to 2.77 + 0.15 cm. H_2O ($p<0.05$). In addition response time was decreased from 135 + 1.5 msec to 125 + 3.3 msec ($p<0.05$). We conclude this modification of the Servo improves sensitivity and response time for assist mode ventilation of infants.

1604 EVALUATION OF BRONCHOPULMONARY DYSPLASIA BY CARDIAC CATHETERIZATION. Rochelle L. Burstein, Terrence Dillon, Steven M. Yabek, P. Sue Corlew, William Berman, Jr. University of New Mexico School of Medicine, UNM Affiliated Hospitals, Department of Pediatrics, Albuquerque, New Mexico.

Nine infants, 10-28 months, were evaluated for bronchopulmonary dysplasia (BPD) by cardiac catheterization. Mean estimated gestational age = 29 wks; mean birth weight = 1280 gms. All infants required oxygen and diuretic therapy. Measurements at F_IO_2 of 0.21, 0.40 and 0.88 included oxygen consumption ($\dot{V}O_2$), oxygen capacity, oxygen saturations, pulmonary artery (PA) and wedge pressures, and high fidelity recordings of right ventricular dp/dt (RV dp/dt) and right sided systolic time intervals. Mean values in room air were: mean PA pressure, 39mmHg; peak RV dp/dt, 729mmHg/sec; RPEP/RVET, 0.336; $\dot{V}O_2$, 139 ml O_2/min/M^2; pulmonary flow index, 3.4 L/min/M^2; pulmonary vascular resistance (PVR), 8.6 units•M^2; PO_2, 54 torr; PCO_2, 40 torr; pH, 7.40. Three of 9 children responded to oxygen with a significant fall in PA pressure and PVR. The 3 children who responded had mean PA pressures, PCO_2's and PVR's of 59mmHg, 50 torr and 12.1 units•M^2, respectively. Echocardiographic measurements of RPEP/RVET correlated well with the high fidelity recordings, but neither measurement reflected PVR or PA pressure accurately. LV function studies and pulmonary wedge angiograms were normal. Invasive studies may aid in management of children with BPD by determining hemodynamic status and defining the response tc oxygen therapy.

1605 TRANSCUTANEOUS PCO_2 DURING HYPERCAPNIC STUDIES OF PREMATURE INFANTS WITH APNEA. Luis A. Cabal, Abel Chaves, Toke T. Hoppenbrouwers, Enrique I. Cardenas, Manuel Durand, Bijan Siassi and Joan E. Hodgman. Univ. of So. Calif. School of Med., LAC-USC Med. Ctr., Dept. of Ped., Los Angeles.

The findings of altered hypercapnic ventilatory responses in premature infants with apnea are controversial. We studied the ventilatory responses to 4% CO_2 + 40% O_2 and 4% CO_2 + 16% O_2 in 6 healthy preterm infants and in 4 infants without cardiopulmonary disease who developed after the first week of life 3 or more episodes of idiopathic apnea, $\geq$ 20 sec. in 24 hours. All studies were performed during active sleep using a nosepiece and a pneumotachograph and measuring end-tidal and transcutaneous PCO_2 while the infants were on a radiant heat warmer. There were no differences in minute ventilation, tidal volume, respiratory frequency, or CO_2 sensitivity. However, transcutaneous PCO_2 was higher ($P< 0.001$) in infants subject to apnea during both hypercapnic challenges. The findings of this study suggest that: 1) The ventilatory responses to hypercapnia do not differentiate healthy prematures from those with apnea of prematurity and 2) Tissue PCO_2 measured by transcutaneous sensor is a sensitive measurement that, during ventilatory studies, differentiates premature infants at risk for apnea from normal prematures. These results are consistent with differences in tissue metabolism or in CO_2 storage between the groups studied.

●**1606** ENHANCED ACTIVATION OF ALAE NASI(AN) DURING ACTIVE SLEEP(AS) IN PRETERM INFANTS. W.A.Carlo, R.J.Martin, E.Abboud, E.N.Bruce, C.R.Shivpuri, K.P.Strohl, A.A. Fanaroff. Dept. Peds., Case Western Reserve Univ., Cleveland, O.

The AN may influence the nasal passage size, thus the resistance to airflow and consequently affect ventilation. Our objective was to determine factors that modulate AN activity and its role in airway resistance. AN electromyogram(EMG) was recorded by surface electrodes in 9 healthy preterm infants (GA 33±1 wks, BW 1.7±0.2 kg, postnatal age 16±6 days) during AS and quiet sleep(QS) both before and during 4% CO_2 inhalation. Airflow was measured with a nasal mask pneumotachograph and in 4 infants nasopharyngeal pressure was used to calculate transnasal resistance. Phasic AN EMG was calculated as percentage of breaths with AN activity; tonic AN EMG as percentage of time with elevated baseline AN activity. Prior to CO_2 both phasic and tonic AN EMG occurred more frequently during AS than QS.

	Phasic(PreCO_2)	Phasic(4% CO_2)	Tonic(PreCO_2)	Tonic(4% CO_2)
AS	43±30%	82±23%	10±7%	24±26%
QS	13±19%	82±27%	2±6%	2±6%
	p<.005	NS	p<.05	p<.05

When breathing 4% CO_2, the incidence of phasic EMG increased in both AS and QS while tonic EMG did not change. The presence of phasic or tonic AN EMG resulted in a reduction of transnasal resistance of 28±21% in AS and 14±12% in QS. We conclude that both sleep state and chemical respiratory drive affect AN activity in preterm infants. Furthermore, AN activation maintains patent nasal passages thereby decreasing nasal resistance and thus may facilitate ventilation especially during AS.

1607 PHOSPHOLIPID INVOLVEMENT IN ESTROGEN STIMULATION OF CHOLINEPHOSPHATE CYTIDYLYLTRANSFERASE IN FETAL RABBIT LUNG. Arthur J. Chu and Seamus A. Rooney. Yale Univ. School of Med., Dept. of Pediatrics, New Haven, Connecticut.

Cholinephosphate cytidylyltransferase (CYT) may be important in the regulation of lung phosphatidylcholine and surfactant biosynthesis. We examined the effect of 17β-estradiol (E) on CYT activity in fetal rabbit lung. E (2.2 μg/kg) or vehicle was administered i.m. to pregnant does on day 26 of gestation and the fetuses were delivered on day 27. E increased CYT activity in fetal lung 100,000 x *g* supernate by 57% from 324 pmol/min/mg protein in controls to 509. Delipidation of supernate with butanol/acetone (BA) reduced the activity to approx. 60 pmol/min/mg in both control and E-treated groups. Addition of a chloroform/methanol (CM) extract from a 3-fold excess of supernate restored the activity. Thus, CYT activity in BA-extracted control supernate was 287 pmol/min/mg when CM extract from control supernate was added and 55% higher (444 pmol/min/mg) when the same amount of CM extract from E-treated supernate was added. The stimulatory effect of E was, therefore, entirely restored on addition of lipids. Fractionation of CM extracts on silicic acid columns showed that the stimulatory factor was entirely recovered in the phospholipid fraction. Neutral lipids and glycolipids as well as non-lipid fractions were not stimulatory. The same results were obtained on addition of CM extracts of control and E-treated supernate to unextracted control or E-treated supernate. These data clearly show that the stimulatory effect of E on fetal lung CYT is mediated by phospholipid(s).

Supported by NIH grant HD-10192.

1608 EFFECT OF RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION ON AIRWAY EPITHELIAL TRANSPORT. Michelle M. Cloutier, David T. Wong, Pearay L. Ogra, SUNY, Children's ›spital, Department of Pediatrics, Buffalo, New York.

The effects of RSV infection on the water and ion transport :operties of the cotton rat trachea were studied in a whole :gan perfusion system previously described (Ped Res 15:817-821,)81) with measurement of transepithelial potential difference /ms), short-circuit current (Isc) and resistance (R). Two)nth old cotton rats were infected with $4x10^7$ PFU of aerosolized SV and sacrificed 72 h later. Uninfected littermates served as)ntrols. Lungs were cultured for RSV and only tracheas from ›imals with 10^2-10^3 PFU of RSV/gm lung tissue were used. All :acheas were grossly normal, had 100% viability by trypan blue taining and normal tracheal histology. Control tracheas had a ms (mV) -6.7 ± 1.5 (n=6, mean±SEM), Isc ($\mu A/cm^2$) 40 ± 4 and R $\Omega \cdot cm^2$) 134 ± 27. In RSV-infected tracheas ψms was unchanged at 5.7 ± 1.3 (n=5); however, Isc was decreased at 29 ± 2 (p <.01) ad R was increased at 266 ± 15 (p <.001). To further character-ze the change in R, the diffusion potential for NaCl was easured. ψms decreased 10.7 ± 1.8 mV in control tracheas and .8 ± 1.2 mV in RSV-tracheas. These differences suggest changes n ion fluxes and backfluxes in RSV and possibly other respira-ory viral-infected airways and may result in changes in water ransport even in the absence of histologic damage. These bservations may explain the development of the increased secre-ions seen in viral infections.

1609 EFFECTS OF BETA-CAROTENE DEFICIENT DIETS ON MORPHOMETRIC MEASURES OF PULMONARY OXYGEN TOXICITY IN MICE: A CONTROLLED TRIAL. Nicole E.)hen-Addad, Robert O. Bollinger, and Ronald L. Poland, New ersey Medical School, College Hospital, Newark and Wayne tate Univ., Children's Hospital, Detroit, Depts. of Ped.

40 mice were divided into 4 groups; each group was given ne of the following diets for 6 weeks: 1 Standard diet, 2 eta-carotene deficient, 3 Beta-carotene and vitamin E eficient, 4 Beta-carotene and vitamin A deficient. Three ice from each group were sacrificed and lungs were evaluated / electron microscopy using the morphometric techniques of eibel. The remaining mice were placed in 65% oxygen and acrificed as above after 3 or 6 days of exposure to oxygen. ne arithmetic and harmonic mean thicknesses of the alveolar-apillary membrane were measured along with its individual)mponents (epithelium, interstitium, endothelium). The lungs f each animal were sampled in duplicate and mean values were)mpared using t-test and analysis of variance.

)nclusions: At the end of the six-week period, diet alone ad little effect on the morphometric components of the espiratory membrane. By the sixth day in 65% oxygen, all nimals (regardless of diet) showed lung injury (increases in armonic mean thickness of the respiratory membrane) but ifferent diets led to differing patterns of injury: diet 1, he endothelium; diet 2, the interstitium; diet 3, the pithelium; and diet 4, the epithelium and the endothelium. hus, diet and time in 65% oxygen had significant interactive ffects on the respiratory membrane thicknesses.

1610 INHIBITION BY PROPRANOLOL OF INFLATION-PRODUCED PHOSPHOLIPID SECRETION IN EQUIVALENT EXCISED LUNGS OF NEWBORN RABBITS: EVIDENCE FOR A SYMPATHETIC REFLEX. nthony J. Corbet, Jane E. Cregan and Arnold J. Rudolph (spon by eba M. Hill). Dept. of Ped, Baylor College of Med, Houston.

Alternating newborn rabbits 29.5 days gestation were given in-raperitoneal injections of d,l-propranolol 0.1mg or saline and llowed to breath for 45 min before sacrifice. After tracheostomy nd degassing the lungs were lavaged 7 times. Depending whether njection was with propranolol the lavage saline contained pro-ranolol 10^{-3}M. The lungs were inflated with room air to 30 cm 20 for 45 min and lavaged 5 times with fresh saline, the pooled avage being assayed for total phospholipid (TPL). Further lit-ers were examined after propranolol injection by lavaging with ropranolol 10^{-4}M. Other litters had no prior injection and were avaged with d,l-propranolol or d-propranolol 10^{-3}M. The data rom 60 litters were used. The results are expressed as mg TPL/m dry lung weight (±SE): 1) Prior injection studies, d,l-propran-lol 10^{-3}M 1.14+0.15 vs saline 2.22+0.24 (p<0.001), d,l-propran-ol 10^{-4}M 1.05+0.24 vs saline 0.90+0.13, 2) No prior injection tudies, d,l-propranolol 10^{-3}M 0.77+0.09 vs saline 1.31+0.12 (p< .001), d-propranolol 10^{-3}M 0.88+0.15 vs saline 1.13+0.17. Thus ,l-propranolol but not d-propranolol inhibited phospholipid re-ease at 10^{-3}M. Because d-propranolol has all properties of d,l-ropranolol but 100-fold weaker beta-adrenergic antagonism, the esults show inflation-produced phospholipid secretion is inhibi-ed by beta-adrenergic blockade. Since the circulation is absent n equivalent excised lungs, and prior injection not important, he results suggest a neurogenic sympathetic reflex.

1611 PERIODIC BREATHING: RELATIONSHIP TO STATE AND TEMPERATURE. Robert A. Darnall, (Spon. by John Kattwinkel), University of Virginia School of Medicine, Department of Pediatrics, Charlottesville.

Almost all respiratory pauses (RP) occur during periodic breathing (PB). Both sleep state (ST) and temperature (T) affect the frequency of RP. In 6 premature infants, skin T was allowed to fall to 34.9±.1 C. 4-6 times during a 6-8 hour period while we monitored sleep and respiration to determine the influence of ST and T on PB. For each 60 sec. epoch, respiration was scored as PB or non-PB, and ST was assigned (REM,NREM, IND, AWAKE). We calculated the % of time apneic (%AP), and the mean length (L) of all RPs of greater than 2 sec. duration occurring during the epoch. The amount of PB (%), and the mean %AP and L during PB for REM and NREM sleep are given below:

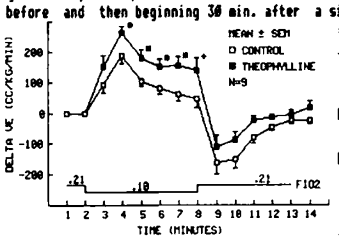
	REM (NTE)	NREM	REM (COOL)	NREM
% PB	32	38	18*	38
%AP	22.6 ± .7	28.8 ± .8#	19.7 ± 1.1	28.6 ± 1.2$
L (sec)	5.7 ± .2	6.6 ± .2#	5.3 ± .3	7.0 ± .3$

MEAN+/-SEM; * REM(NTE) vs REM(COOL) p<.001; # p<.01; $ p<.001

We conclude that 1) PB occurs during all sleep states; 2) during cooling, the amount of PB decreases only in REM; 3) during PB, pauses are shorter and the % of time apneic is less during REM compared to NREM: cooling has no effect on %AP or L in either REM or NREM sleep. We speculate that PB occurs independent of state and that afferent influences associated with REM tend to shorten respiratory pauses. During cooling, the reduction in apnea appears to reflect a decrease in the amount of PB during REM sleep.

1612 THEOPHYLLINE REDUCES VENTILATORY DEPRESSION IN HYPOXIC NEWBORN PIGLETS, Robert A. Darnall (Spon. by John Kattwinkel), University of Virginia School of Medicine, Department of Pediatrics, Charlottesville.

The ventilatory depression induced by hypoxia in newborn infants may be a contributing factor in the development of apnea. Theophylline (T) decreases the frequency of apnea in prematures. To assess the effect of T on hypoxic ventilatory depression, we induced hypoxia in 9 newborn piglets < 72 hours of age by decreasing FiO2 to .18, before and after treatment with T. Each animal was anesthetized with ketamine and xylazine, intubated, and the femoral artery catheterized. Recordings of EKG, HR, BP, expiratory flow, and integrated expiratory volume were obtained during three, five minute hypoxic trials, first before and then beginning 30 min. after a single bolus of aminophylline (15 mg/kg). The results are given below:



	CONTROL		THEOPHYLLINE	
FiO2	.21	.18$	.21	.18$
PaO2	56±3	25±3$	66±3	24±2$
PaCO2	29+2	25+1	27+2	22+2
pH	7.46±.03	7.48±.03	7.52±.02	7.51±.05+
HR	127±6	153±6$	148±6	179±8$

$ values obtained after 5 min. of hypoxia
MEAN±SEM; $ p<.001; $ p<.005; + p<.01

We conclude that theophylline significantly reduces ventilatory depression during hypoxia. This mechanism may contribute to the clinical success of theophylline in the treatment of apnea of prematurity. Xanthines are competative inhibitors of adenosine, a neural depressant, which has been shown to be released from brain cells within seconds after the onset of hypoxia. Our results suggest that during hypoxia theophylline may be competing with a rapidly acting respiratory depressant, such as adenosine, resulting in a reduction of ventilatory depression.

1613 POSSIBLE AUTONOMIC INSTABILITY IN NEAR-MISS SIDS INFANTS AS DEMONSTRATED BY CEPSTRAL ANALYSIS. A. Davis* J. V. Aranda. McGill University-Montreal Children's Hospital Research Institute, Montreal, Quebec, CANADA.

Seven babies being investigated for apnea were studied using spectral analysis of EEG, EMG, ECG, nasal air flow(AF) and respiratory movement(RM). Sleep recordings were made over a 1-3 hr period and spectra calculated over successive 4-second epochs within this period. Active (AS) and quiet sleep (QS) were determined by simultaneously recorded polygraph. Spectra of the spectral amplitudes (cepstra) were then calculated for AF, RM and AF over 128 epochs or 8.4 minutes of AS and QS. This gave phase relationships between AF, RM and heart rate (HR) occurring over frequency ranges 0 - 7.5 cycles/min. Phase shifts between RM and AF were small and near 0 for babies with central or mixed apnea, or periodic breathing and large and near ±180° for babies with obstructive apnea. Phase shift between AF and HR was small for babies with bradycardia and large for those whose HR increased when AF decreased. In addition, phase shifts between RM, AF and HR all increased in active sleep. SPECULATION: Phase shifts may represent the action of the autonomic system in responding to changes in AF. In a normally compensating system, large (±180°) phase shifts indicate that as AF decreases, RM and HR increase. However, in babies with central apnea, phase shifts are small so AF and RM decrease simultaneously. In addition, babies with small phase shifts between AF and HR may respond to decrease AF with a nearly simultaneous drop in HR; leading to decreased circulation and further decreases in AF and HR, in a vicious cycle, to complete cessation of activity. This effect would be greatest in QS when phase shifts and hence, compensation or feedback control, are at minimum.

● 1614 HYPOTHYROIDISM (HYPO) AND GLUCOCORTICOIDS (GLUC) MODULATE THE DEVELOPMENT OF THE LUNG INSULIN RECEPTOR. Sherin Devaskar, Supriya Ganguli, Uday Devaskar, and Mark Sperling, University of Cincinnati, Dept of Peds, Children's Hospital Medical Center, Cincinnati.

Lung glycogen provides precursors for surfactant, synthesis of which may be modified by hyperinsulinemia, HYPO or GLUC. Since glycogen formation is mediated by insulin, while glycogenolysis is mediated by cAMP,we investigated the characteristics of insulin receptors (IR) in membranes of fetal (F) rabbit lung and their cAMP production during normal ontogeny; the effect of GLUC and HYPO on IR characteristics also was examined. Specific binding of ^{125}I-insulin (n=6 pools at each F age) increased to a peak at 29d gestation, but declined by 30d. Scatchard analysis revealed an increase in IR ($10^{10}mg^{-1}$ protein) from 129±7 (mean±SE) at 22-24d to 574±16 at 29d, declining to 467±12 at 30d, term=31d; IR in adults were significantly lower than F. EPI and PGE_1 (10^{-4}M) doubled basal cAMP production of ∿ 100 pM/mg prot/min until 29d. However, with the fall in IR at 30d, cAMP in response to EPI and PGE_1 increased 5-fold. Administration to mothers of PTU, 200 mg with T4,20 µg, induced F HYPO since PTU but not T4 crosses the placenta; IR at 28d was reduced by 50% from control ($p< 0.001$) In contrast,GLUC administration to mothers increased F lung IR by 50% ($p< 0.001$). Affinities did not change during ontogeny or with HYPO or GLUC. Conclusions: 1) Normal ontogeny of the F lung IR is characterized by an abrupt decline before birth. 2) With decline in IR there is a sharp increase of cAMP responsivity. 3) Acting in concert,these harmonious changes could favor surfactant synthesis. 4) HYPO and GLUC modulate normal development of the F lung IR.

1615 OPTIMUM POSITIVE END EXPIRATORY PRESSURE (PEEP) IN RESPIRATORY DISTRESS SYNDROME (RDS). Jack L. Dolcourt (Spon. by Lowell Glasgow),Univ. of Utah School of Medicine and Primary Children's Med. Cntr., Dept. of Pediatrics, Salt Lake City, Utah

Selecting the level of PEEP for ventilation of newborn infants with RDS is largely empiric and not based upon individualized measurements of lung mechanics. Ventilation at the "best PEEP", determined by maximum pulmonary compliance, has been used in adults. We applied this concept to the ventilation of newborn infants with RDS.

A microprocessor-based instrument was developed and then used to measure dynamic pulmonary compliance (Cdyn) and tidal volume (V_t) in 6 newborns requiring ventilator support for severe RDS. Birth weight was 1652±612 grams (mean ±SD). Cdyn and V_t were averaged over 50 breaths at 2, 4, 6 and 8 cm PEEP. These results show that, when normalized for weight, Cdyn declined at the rate of 0.02±.01 cc/cm/kg per cm PEEP and V_t declined at the rate of 0.56±.37 cc/kg per cm PEEP. No unique PEEP could be identified which maximized Cdyn or V_t. These data demonstrate that PEEP actually interferes with the mechanics of ventilation, as measured by Cdyn and V_t and fails to support the concept of "best PEEP" as determined by maximization of Cdyn in newborns with severe RDS.

● 1616 TRIIODOTHYRONINE(T3) PLUS DEXAMETHASONE(DEX) ELIMINATE SEX DIFFERENCE IN FETAL RAT LUNG SURFACTANT PHOSPHATIDYLCHOLINE. Kimberly E. Dow, John S. Torday Spon. by Barry T. Smith, Harvard Medical School, Department of Pediatrics, Boston, MA.

In both human and rabbit fetuses, male lungs contain less saturated phosphatidylcholine (SPC) than do female lungs. Female fetal lung maturation is also more responsive to glucocorticoid stimulation. Since thyroid hormone augments the surfactant response to glucocorticoids in vitro, we tested the effect of T3 on SPC synthesis in combination with Dex in vivo. Fetuses from time-mated rats were given saline, T3 (1µg) and/or Dex (1µg) intra-amniotically on day 17 (term=21days); fetuses were sacrificed on day 20 and lung slices were incubated with ^{3}H-choline.

^{3}H-SPC Produced (cpm/100µg protein; $\bar{x}$ ± SEM)

	Control	Dex	Dex + T3
Male	91 ± 7	115 ± 15	151 ± 24
Female	123 ± 8	135 ± 15	189 ± 13

Female lung synthesized 30% more ^{3}H-choline than male lung under control conditions ($p<.01$). Treatment with T3 and Dex together caused a marked increase over controls in both males ($p<.01$) and females ($p<.01$). There was no significant difference between males and females treated with both hormones. This is in contrast to the greater response in females which is often seen when glucocorticord is used alone.

Based upon these observations and those of others we speculate that a similar combined treatment regime would provide effective prenatal prophylaxis for respiratory distress syndrome in male fetuses who seem to be refractory to glucocorticoid alone.

● 1617 COLD AIR CHALLENGE IN ASTHMATIC CHILDREN. Allen J. Dozor, F. John McLaughlin, Mary Ellen B. Wohl. Harvard Medical School, Children's Hospital Medical Center, Department of Pediatrics, Boston, MA.

Eucapneic hyperventilation with cold, dry air is a sensitive test for reactive airways in adults. We studied the response of 6 asthmatic children, mean age 13 yrs (range 11-15 yrs) with uncomplicated, non-steroid dependent asthma. None had received medication for at least 12 hours.

Baseline lung function tests expressed as percent of predicted value were: total lung capacity (TLC) 104% (range 79-135%), vital capacity (VC) 93% (range 80-114%), forced expiratory volume in 1 second (FEV_1) 83% (range 71-100%), peak flow rate (PFR) 76% (range 55-107%), and maximum mid-expiratory flow rate (MMFR) 67% (range 54-80%).

Each subject, seated comfortably and wearing noseclips, hyperventilated for 4 minutes breathing dry (0 mgm H_2O/L air), cold (mean temperature -19°C, range -15 to -30°C) air. The subjects were instructed to fill a target balloon which was emptied at a rate adjusted for each subject (25xFEV_1L/min). CO_2 was added to the inspired gas and end-tidal CO_2 was monitored to assure eucapnea. All subjects responded at 4-8 minutes post hyperventilation. Mean fall in lung function expressed as percent decrease from baseline values was VC 14±2.8% SEM (range 6-20%), FEV_1 31±3.6% (range 19-41%), PFR 36±3.8% (range 22-47%), and MMFR 69±4.8% (range 53-83%). The subjects performed the test well. Although none developed clinically significant bronchospasm, all were treated with isoproterenol. This technique appears to be an easy and safe means of testing for airway reactivity in children.

1618 INDIVIDUALIZED AMINOGLYCOSIDE DOSAGES IN PEDIATRIC PATIENTS. Lisa M. Dunkle, Lawrence S. Martin, Richard M. Reichley and Daniel J. Westrich (Spon. by Thomas Aceto, Jr.), St. Louis University School of Medicine, Cardinal Glennon Memorial Hospital for Children, Department of Pediatrics/Adolescent Medicine and Pharmacy Department, St. Louis, Missouri.

Variability in distribution and clearance of aminoglycosides dictates modification of dosing regimens based on serum concentrations. A calculator program utilizing a one-compartment model was used to adjust dosages for 19 courses of gentamicin (G) and 12 of tobramycin (T) in 19 pediatric patients. There were 13 males: 6 females; 16 white: 3 black; mean age 7 5/12 years (range 1 day-17 years). Thirteen patients had cystic fibrosis (CF); the remainder, infections with various gram-negatives. A conventional IV dose (mean 2.23 mg/kg G and 1.94 mg/kg T) was followed by 3 or 4 accurately timed determinations of serum levels. Program calculated volume of distribution (V_D), half-life ($T_½$) and appropriate dosing to achieve desired levels. $T_½$ of G was mean 1.42 hr in CF patients and 1.95 hr in non-CF ($p<.005$). V_D of G was mean 0.385 L/kg in CF and 0.258 L/kg in non-CF ($p<.0005$). Resulting dosage recommendations were mean 16.1 mg/kg/day G in CF (range 9.1-34.4) and 8.2 mg/kg/day G in non-CF (range 5.1-14.4). Dosing interval range 3-12 hours. Mean recommended dose of T in CF was 12.2 mg/kg/day (range 6.3-17.7) Achieved serum levels of both drugs in 17 pts. was mean peak 7.85 µg/ml (range 5.0-11.4) and mean trough 1.2 µg/ml (range <1-2.9). Calculator program is a simple means to appropriate dosing regimens of aminoglycosides, particularly in CF and neonatal pts. whose $T_½$ and V_D differ markedly from average. Followup serum levels are mandatory.

●1619 NATURAL AND ARTIFICIAL SURFACTANT REPLACEMENT IN PREMATURE LAMBS by E.A.Egan, R.H.Notter, and D.L.Shapiro. Depts. of Peds. and Physiol., SUNY-AB, Buff., NY 14222 Dept. of Peds., Univ. of Roch., Roch., NY 14642.

The efficacy of exogenous lung surfactant replacement was studied in premature lambs of 126-134 days gestation. Lambs were exteriorized from anesthetized ewes and ventilated with 100% O_2 following tracheal instillation (>15mg/kg) of 7:3 dipalmitoyl phosphatidylcholine (DPPC):egg phosphatidylglycerol (PG) or of extracted mixed lipids (<1% protein) from cow lung lavage (CLL). Ventilation was for 2 hours with umbilical circulation intact, and a further 11-13 hours after separation. We measured arterial blood gases and at 2 and 13-15 hours alveolar phospholipid content (PL) and in vivo quasi-static lung pressure-volume curves. The CLL animals had lower A-a DO_2, higher FRC and more PL than controls; a larger A-a DO_2 was the only way DPPC:PG animals differed from controls.

		2 hours			13-15 hours		
Group	N	PaO_2	FRC(ml/kg)	PL(mM)	PaO_2	FRC(ml/kg)	PL(mM)
Control	5	210±61	9±2	10±5	313±69	11±1	14±2
CLL	3	309±65	21±2	121±8	374±35	27±4	55±4
DPPC/PG	3	118±58	13±3	14±4	28±9	16±2	13±2

Both CLL and DPPC:PG mixtures gave good surface tension lowering in vitro (∿1-2 dn/cm at 22°C), but CLL adsorption facility was significantly greater than DPPC:PG for the dispersion methods used prior to instillation. CLL animals maintained adequate PL content and normal lung function, but use of an ineffective surfactant resulted in rapid loss of instilled phospholipid and compromised gas exchange (HL25170, HL22552).

1620 ENZYMES OF PHOSPHOLIPID SYNTHESIS IN FRESHLY ISOLATED TYPE II ALVEOLAR EPITHELIAL CELLS by J.N. Finkelstein and C. Kramer (Spon: D.L. Shapiro), Univ. of Roch., hester, New York 14642.

The specific activity, substrate specificity and subcellular ation of three key enzymes in pulmonary surfactant phospho- id biosynthesis were measured in subcellular fractions pre- ed from whole lung (W), alveolar macrophages (M), unpurified persed lung cells (C), and purified type II cells (TII) from lt rabbit. Glycerol-3-phosphate acyltransferase (GPAT),chol- phosphotransferase (CPT), and lysophosphatidylcholine acyl- nferase (LPCAT) were localized primarily in the endoplasmic iculum (> 50% of recovered activity).

	GPAT*	CPT*	LPCAT*	
W	5.2	8.1	62	*Enzyme Activity
M	6.4	17.9	71	(nmol/min/mg)
C	---	13.1	214	
TII	8.9	31.2	308	

T was slightly enriched in fraction TII, while CPT and LPCAT e increased 4-5 fold. Type II cell GPAT showed little acyl specificity; oleoyl CoA was incorporated equally as well as nitoyl CoA. In contrast, LPCAT was highly selective for palm- yl CoA. Under optimum assay conditions, palmitoyl CoA was d 6-10 fold more effectively than oleoyl CoA. These enzyme ults are consistent with active phospholipid synthesis in e II cells from adult lung. Further, the dramatic enrichment substrate specificity of LPCAT in type II cells supports the ortance of the deacylation-reacylation cycle in the synthesis dipalmitoyl phosphatidylcholine by type II cells.

1621 INDICATIONS FOR FLEXIBLE FIBEROPTIC BRONCHOSCOPY IN PEDIATRIC PATIENTS. Sherahe Fitzpatrick, Bernard Marsh Ko Pen Wong, Dennis Stokes(spon by Jerry Winkelstein) Johns Hopkins Hospital,Balto;MD,Dept Ped/Otol/Med

Although the availability of the flexible fiberoptic broncho- pe (FFB) has been a major advance in adult pulmonary medicine, role of FFB in pediatrics has remained less well defined. refore, a 2 yr retrospective study was undertaken to determine indications for FFB in pediatric patients (pts). Ninety-five atients (age range 4 days-21 yrs; X=6.9 yrs) underwent 129 FFB cedures in either an OR or ICU setting. Topical anesthesia ldeocaine only) was given in 46% of cases and a transnasal ap- ach was utilized in 74% of cases. Olympus 3.8mm scope was used 50% of cases. Rigid bronchoscopy was done concomitantly in 16% cases. Diagnostic (dx) procedures during FFB included: trans- achial biopsy(11), bronchial brushings(5), bronchial lavage(5), alized bronchogram(2) & biopsy of endobronchial lesion(1). In- ations for FFB included: stridor(41); abn. CXR [37-persistent ltrates(15), atelectasis(14), mass(3), other(5)]; evaluating way in trach. pts(13); airway obstruction(11); hoarseness(7); urrent pneumonia(7); chr. cough(4); suspect foreign body(3); led extub(3); tracheal injury(2) & hemoptysis(1). Presumptive was confirmed in 67% of cases but was revised in 14%. In 12% cases, preop dx was uncertain but was obtained by FFB. A nor- exam was noted in 10%. Overall, a specific dx was made in 88% cases of which 46% involved a lower airway disorder. Minor plication rate of 2% was observed [transient hemoptysis(2) & oxia(1)] with no major complications. This study demonstrates safety & value of FFB in selected pediatric pts when performed skilled endoscopist in an optimal setting.

1622 REMEMBRANCE OF THINGS PAST: NEWBORN RATS TREATED WITH ENDOTOXIN AND EXPOSED TO HYPEROXIA FOR THE FIRST WEEK OF LIFE ARE SUBSEQUENTLY TOLERANT TO O_2 TOXICITY ON EXPOSURE TO HYPEROXIA AS ADULTS. Lee Frank and Donald Massaro (Intr. by Eduardo Bancalari, Pediatrics), V.A. Hospital and Dept. Med., Univ. of Miami Sch. of Med., Miami.

It is known that endotoxin (ENDO) confers marked protection inst acute pulmonary O_2 toxicity in adult rats (97% survival 25% for controls); and also improves survival in neonatal s exposed to >95% O_2 (Peds. Res. 13:533, 1979). We now report rprising "memory" effect (in the lung) of adult rats that e treated with ENDO while exposed to O_2 for the first week of e. When subsequently allowed to grow up in room air, and then allenged with >95% O_2, these adult 300g rats which had been ted with ENDO during neonatal O_2 exposure were found to be stent to pulmonary O_2 toxicity (3/3 survival, lung wet/dry = 5.2 ± 0.2) compared to similar rats exposed as neonates to O_2 while receiving saline and rechallenged with O_2 as adults survival). Survival in O_2 of age-matched adult rats not -exposed as neonates to O_2 was 1/8 (wet/dry lung wt = 5.8 ± . Thus, in a small group of rats (a 2nd and 3rd group are rway), adult rats which had received ENDO during early life sure to O_2 appear to exhibit a "memory" of tolerance to hy- oxia, in adult life, without re-treatment with ENDO. We know in adult rats ENDO has stimulatory effects on lung protein, and DNA synthesis and on the antioxidant enzymes. But the t mechanism to explain this peculiar "memory" effect is sently) unknown. (Supported by V.A. Research Funds and NIH t HL26029).

●1623 HIGH FREQUENCY VENTILATION (HFV) DOES NOT AFFECT PULMONARY SURFACTANT, LIQUID OR MORPHOLOGY IN NORMAL CATS. I.D. Frantz, A.R. Stark, J.M. Davis, P. Davies and T.J. Kitzmiller. Harvard Medical School, Children's Hospital Medical Center, Boston, MA.

To assess the effects of HFV on the lung, we examined lung water (wet/dry weight), surfactant and morphology in normal adult cats with no intervention, conventional ventilation (CV) or HFV. There were 10-12 cats in each group. The CV and HFV animals were ventilated for four hour periods maintaining equal blood gases and mean airway pressure. Peak tracheal pressure on CV was 16.5± 0.9 cm H_2O, compared to 8.5±1.1 cm H_2O on HFV ($p<0.00001$). After sacrifice, pressure-volume curves were performed and surfactant in lung lavage was quantified biochemically and on a surface balance.

Measurement (mean±SE)	Control	CV	HFV
Lung wet/dry weight	5.1±0.4	4.6±0.3	4.7±0.4
Disaturated phosphatidyl choline (mg/g wet lung)	0.27±0.04	0.21±0.03	0.21±0.03
Surfactant (area in cm^2 at 12 mN/m/g wet lung)	271±48	309±53	244±65
Min surface tension (mN/m)	5.1±1.1	5.9±1.3	5.3±0.7
Vol. at 10 cm H_2O (% total)	89.1±1.0	88.3±1.1	89.3±1.0

No difference is statistically significant. No difference in light or electron microscopic morphology was seen. These data confirm that equivalent blood gases can be maintained during HFV at equal mean, but lower peak tracheal pressure than with CV. Under these conditions, HFV has no effect on lung liquid, surfactant or morphology.

●1624 UNILATERAL PEEP AND PULMONARY BLOOD FLOW. Bradley P. Fuhrman, John Everitt, James E. Lock (Spon. by James H. Moller) Univ. of Minnesota, Dept of Pediatrics, Mpls.

To test the theory that moderate levels of PEEP raise pulmonary vascular resistance(PVR) directly in normal infant lung, 11 (2-4 wk) lambs had EM flow probes placed on R and L pulmonary arteries (PA). 6 had L atrial lines. 1 wk later, under chloralose, an endobronchial tube was placed. Probes were exteriorized. PA, femoral artery, and R atrium(N=6) were catheterized. An esophageal (ES) balloon was inserted(N=9). Lungs were synchronously ventilated by 2 Servo900B volume ventilators. Control(CON) periods (PEEP=2cmH_2O) were alternated with 10 minute studies(ST) in which PEEP was applied to R, L or both lungs at 5, 10 and 15 cmH_2O. Unilateral PEEP (UPEEP) reduced pulmonary blood flow†(PBF) and raised PVR$^{\rho}$ of the ipsilateral(IP) but not of the contralateral(CLT) lung. At all levels of UPEEP, total PBF fell* promptly and reversibly due to reduced stroke volume†(SV). This fall was not due to changes in R or L ventricular transmural filling pressure, for ES pressure increased as much as RAP or LAP with UPEEP. Total PVR rose only moderately with UPEEP, and PAP rose minimally.

	IP PBF(cc/min)		CLT PBF(cc/min)		PAPmmHg		LAmmHg		SV(cc)	
UPEEP	CON	ST	CON	ST	CON	ST	CON	ST	CON	ST
5	500±230	450±220*	510±250	510±250	22	22	9	9	6.8	6.5†
10	490±240	350±200†	490±220	540±230*	21	22	8	9	6.9	6.2†
15	500±230	280±190†	510±240	570±280*	21	24	9	11	7.2	5.9†

PEEP raises PVR directly. In the infant lamb, UPEEP can reduce SV without reducing ventricular filling pressure or increasing mean PAP. This suggests that PEEP causes myocardial depression.
$^{\rho}p<.05$ *$p<.01$ †$p<.001$ (ST vs CON by paired t)

1625 GLYCOGEN METABOLISM DURING MATURATION IN CULTURE OF THE A549 TYPE II PNEUMOCYTE CELL LINE by R.L. Gallo, J.N. Finkelstein, R.H. Notter, W.M. Maniscalco, and D.L. Shapiro, Univeristy of Rochester, Department of Pediatrics, Rochester, New York 14642.

Glycogen may be an important intracellular substrate for phospholipid synthesis in late gestation fetal lung. We examined glycogen metabolism during maturation in culture of A549 cells, derived from a human lung adenocarcinoma, which retain several characteristics of type II cells. Glycogen content of the cells, grown in F12K medium containing 10% fetal bovine serum (inoculum 3×10^4 cells/cm^2), decreased during exponential growth to a minimum at confluence (day 7-10). Following this, glycogen content increased to peak at 14-16 days in culture. Cellular glycogen declined rapidly between days 16-21, coincident with a 2-3 fold increase in the rate of incorporation of choline into phosphatidylcholine. Total glycogen synthetase activity peaked at 7 nmol/min/mg protein by 12 days in culture. The activity of glycogen phosphorylase a was low during this time (1 nmol/min/mg) but increased 3.5 fold between 14 and 18 days in culture. This increase was accompanied by a decrease in cellular glycogen content. The observed patterns of enzyme activity, glycogen content, and phospholipid synthesis in the A549 during maturation in culture mimic those of rat lung during cellular differentiation and active phospholipid synthesis. These data suggest that the A549 cell cultures may be a useful model of certain aspects of type II pneumocyte differentiation.

1626 DISTRIBUTION OF VENTILATION IN NEWBORNS WITH CHRONIC LUNG DISEASE (CLD). Tilo Gerhardt, Steve L. Goldman, Dorothy Hehre, Rosalyn Feller, Eduardo Bancalari. University of Miami, Department of Pediatrics, Miami.

Distribution of ventilation was measured serially in 20 preterm infants (BW±1200±370 gms, GA 30.6±2.4 weeks) with CLD. All infants required mechanical ventilation for >3 days because of severe HMD, were still O_2 dependent by 4 weeks of age and their chest radiographs showed haziness and increased interstitial markings. A helium oxygen gas mixture was used for the nitrogen washout and pulmonary clearance delay (PCD) was calculated from the endtidal N_2 values.

Age (weeks)	2	4	8	12	26
PCD %	34.6±10.3	29.9±11.6	35.1±15.6	31.5±13.2	44.8±20.0

PCD was not abnormally prolonged in any of the infants studied. However, some patients while breathing the nitrogen free gas mixture, showed a sudden increase in endtidal N_2 after a sigh. This suggests airway opening and washout of previously unventilated areas. Based on this observation FRC was determined in 15 of these infants under baseline conditions and while breathing 4% CO_2 which increased tidal volume by 35%. FRC was determined by measuring the amount of exhaled N_2, while breathing a N_2 free gas mixture. FRC was 14.3±3.3 ml/kg under basal conditions and increased to 16.7±3.7 ml/kg while breathing with a larger tidal volume. ($P < 0.001$). The results suggest that FRC is reduced in newborns with CLD probably secondary to airway closure. Breathing with a larger tidal volume may open airways so that portions of the lung which had trapped gas before, become ventilated. FRC in infants with CLD is considerably below closing volume (funded by NIH#1RO1-HL/HD-25023-01A1).

● 1627 INCREASED TIDAL VOLUME IMPROVES DISTRIBUTION OF VENTILATION IN INFANTS WITH HMD. Steven L. Goldman, Tilo Gerhardt, Dorothy Hehre, Rosalyn Feller, Eduardo Bancalari. University of Miami, Department of Pediatrics, Miami.

To determine the effect of tidal volume (V_T) on distribution of ventilation, we performed nitrogen washouts on 9 preterm infants with HMD. To avoid hyperoxia, an oxygen-helium mixture was used as the washout gas. Each infant was studied using a "large" and "small" V_T. In 6 infants requiring mechanical ventilation, the V_T was adjusted by changing the peak inspiratory pressure; in 3 spontaneously breathing infants, the V_T was altered by adding 2-4% O_2 to the inspired gas mixture. Washout results are given in terms of "percent Pulmonary Clearance Delay" (PCD); the smaller the PCD, the more uniform the distribution of ventilation. f_1 is that fraction of total lung volume which is ventilated more quickly and f_2 the more slowly ventilated compartment.

	Small V_T (mean ± SEM)	Large V_T	P
V_T (ml/kg)	6.8 ± .8	10.3 ± 1.8	<.001
f_1	.925 ± .013	.88 ± .015	<.01
f_2	.075 ± .013	.118 ± .015	<.01
PCD (%)	40.1 ± 5.7	19.5 ± 2.9	<.01

There was more uniform distribution of ventilation with the large V_T, but paradoxically f_2 was proportionally larger. Because both slow and fast compartments were ventilated more efficiently with the larger V_T, the net result was a significant decrease in PCD. We speculate that with a larger V_T, some poorly or non-ventilated areas of lung are recruited, adding to the FRC, increasing the proportion of the slower ventilated compartment.

●1628 ABNORMALITIES IN HR AND RESPIRATORY POWER SPECTRUM IN SIDS. David Gordon, Dorothy H. Kelly, Solange Akselrod, Andrew Ubel, Robert Kenet, Richard J. Cohen and Daniel C. Shannon. Harvard-MIT School of Health Sciences and Technology, Massachusetts General Hospital, Children's Service, Boston, MA 02114.

In order to test the hypothesis that autonomic imbalance contributes to the sudden infant death syndrome (SIDS), we analyzed the power spectra of heart rate and respiration (Resp) during 256 sec of quiet sleep (QS) in SIDS (autopsy) and control (C) infants. Eight controls were studied at 1-4 wks, 10 at 5-12 wks and 12 at 13-44 wks. Eight SIDS (10 records) were studied, 4 at 1-4 wks and 6 at 5-16 wks. Data were recorded by pneumogram at home. We played tapes through an Oxford PMD-12/Mingograph and selected the most regular epoch of QS. Epochs with a sigh or a trend in HR of > 2% were excluded. We transferred data from cassette to reel (HP 3968A) FM and sampled at real time (8085 microprocessor) at 360Hz (ECG) and 4Hz (Resp). We computed power spectra of HR and (Resp) from 0.02 to 1.0Hz. Stationarity was confirmed on consecutive epochs; spectral peak areas varied by < 10%. HR fell with age in 3 C groups 144.6, 131.9 and 111.8/min ($p < .001$) but not in SIDS 124.6, 129.3/min. Variance in HR (HR var) at resp frequency (f), increased with age in C and in SIDS ($p < .001$). HR var at .02-.09Hz increased with age by 480% ($p < .001$) in C. HR var in SIDS was 2,200% >C in this peak at 1-4 wks and 450% at 5-12 wks. Mean f fell 32.4 to 24.2/m in C and was higher (45.7/m, $p = < .03$) at 1-4 wks in SIDS. Var in f (band width of resp power spectrum) was greater in SIDS ($p < .001$). These data reflect instability in the control of fluctuations in both the cardiovascular and respiratory system in babies who died of SIDS.

1629 METABOLISM OF ^{14}C-ARACHIDONIC ACID BY TYPE II ALVEOLAR EPITHELIAL CELLS IN PRIMARY CULTURE. Janet E. Graeber, Ronald W. Walenga, Rodney E. Ulane, Marie J. Stuart, NICHD, National Institutes of Health, Bethesda, MD, and SUNY, Department of Pediatrics, Syracuse, NY.

Primary cultures of adult rat alveolar Type II cells were prepared by the method of Dobbs et al., (B.B.A., 618:510, 1980) and purified to >90% by differential adherence. Cells plated at $5x10^6$/flask were pre-labelled with 5μM ^{14}C-arachidonic acid (AA) ($2.05x10^6$ cpm/5 ml MEM + 10% FBS) for 18 hours at which time cellular uptake was essentially complete (< 4500 cpm remaining/5 ml media). The label was distributed among all phospholipid classes. When the cells were washed free of exogenous AA and maintained for 6 hours in media and either 10% FBS, or 10% FBS + thrombin (1 U/ml), A23187 ($3x10^{-6}$M) or epinephrine (10^{-5}M) + ascorbic acid (10^{-3}M), AA was released into the media with no significant differences in the percent of prelabel observed in the various experimental situations (.77 ± .09%, 1SD). Conversion of AA to metabolites of both the cyclooxygenase (6-keto $PGF_{1\alpha}$, the stable end product of PGI_2; PGF; PGE_2) and lipoxygenase (HETES) pathways occurred as identified by comigration with authentic standards and autoradiography. Metabolite production equalled 0.05 ± 0.01% (1SD) of the total AA previously incorporated by the cells. No production of thromboxane B_2 was observed. Our findings suggest that adult rat primary Type II cells possess enzymes for the uptake and metabolism of AA.

● 1630 CORTICOSTEROID RECEPTOR-RESPONSE RELATIONSHIPS IN CULTURED FETAL RABBIT LUNG. Ian Gross, Philip L. Ballard and Roberta A. Ballard. Yale Univ. School of Medicine, New Haven, CT; Univ. of California, San Francisco and Mt. Zion Hospital, San Francisco; Departments of Pediatrics.

We have studied both binding of corticosteroids and their effect on choline incorporation into phosphatidylcholine (PC) in explants of 24 day fetal rabbit lung cultured for 48 h. Stimulation by dexamethasone (dex) 10^{-7}M was first observed after 12 h of exposure; it increased in a linear fashion for 36 h and then began to plateau. Fetal sex had no effect on dex induced PC synthesis or nuclear binding of dex. There was a striking similarity between the K_D values for specific nuclear binding of dex and cortisol (0.6 ± 0.1 and 7.3 ± 0.1 nM, resp.) and the concentrations at which half maximal stimulation of PC synthesis occurred (0.7 ± 0.1 and 6.8 ± 0.5 nM, resp.). The relative potency of steroids (10^{-7}M) for nuclear binding and stimulation of PC synthesis were the same: Dex>cortisol>cortisone>corticosterone>dehydrocorticosterone, with no effect by progesterone, testosterone or estradiol at this dose. Cortisone was rapidly converted to cortisol in culture. Both actinomycin D and cycloheximide, inhibitors of RNA and protein synthesis resp., blocked dex induced PC synthesis in a dose dependent fashion. Actinomycin D had a marked effect if added at the initiation of dex exposure, but little effect when added after 24 h, whereas cycloheximide was effective whether added at 0 or 24 h. These data support the theory that corticosteroid induced stimulation of PC synthesis in fetal lung is mediated by binding to specific receptors with subsequent de novo synthesis of RNA and protein.

● 1631 OXIDANT AND LIPID INDUCED PULMONARY VASOCONSTRICTION MEDIATED BY ARACHIDONIC ACID METABLITES. Gail H. Gurtner, Philip L. Smith, Andreas Knoblauch, Hassan Makhzoumi, Richard J. Traystman, N. Franklin Adkinson, Depts. of Anesthesiology/Critical Care Medicine and Medicine, Johns Hopkins Medical Institutions, Baltimore, MD 21205 (Spon.: Mark C. Rogers)

We have previously reported that lipid and hydrogen peroxides cause a marked pulmonary vasoconstriction in the isolated perfused rabbit lung (Am Rev Respir Dis 134(4): 246, 1981). Unsaturated lipids, such as linoleic acid or the mixture of fatty acids used in intravenous hyperalimentation (Intralipid®) caused a similar but smaller effect at higher concentrations. Animals which were pretreated with the antioxidants butylated hydroxyanisole (BHA) or Vitamin E had no pressor response. The vasoconstrictor response could be completely abolished by administration of indomethacin. Measurement of arachidonic acid metabolites in the effluent perfusate revealed that both peroxides and lipids elicited thromboxane (TxB_2) production but that Intralipid® caused marked increases in production of 6 keto $PGF_{1\alpha}$, a metabolite of prostacyclin. The pressor response was closely correlated with the concentration ratio TxB_2/6 keto $PGF_{1\alpha}$. Thus administration of peroxides or lipids, which can undergo peroxidation, activate the arachidonic acid pathway leading to production of vasoactive products. The differential ability of peroxides and lipids to elicit prostacyclin production may be related to inhibition of prostacyclin synthetase by the peroxides which are more potent oxidants. The lack of pressor response in the antioxidant treated animals could be due to the ability of the antioxidant to directly scavenge arachidonic acid hydroperoxides.

1632 PULMONARY RESPONSE TO FENOTEROL IN CHILDREN USING TWO DIFFERENT AEROSOL DEVICES. D. Gurwitz, C. Mindorff, H. Levison, Research Institute, The Hospital for Sick ;ildren, Toronto, Ontario, Canada.

The addition of a new device, an aerochamber (A), described Newhouse (Am. Rev. Resp. Dis. 121:123, 1980), to the conven-onal metered dose inhaler (MDI) has been proposed to improve stabilize pulmonary response to aerosol sympathomimetics in ;ildren who may have difficulties learning proper aerosol tech-que. We compared the response to 200 ug fenoterol in 12 asth-tic children after delivery from a MDI with delivery from the ıl plus A in a single dose, double-blind, crossover trial. The ıme treatments were then compared in an open 6 week crossover udy in 12 subjects. Assessments of pulmonary function was rried out for 4 hours following a dose of drug under each con-tion. In the long-term trial, these tests were performed at ıe end of each phase. Ten males and 2 females with a mean age 10.8 years entered the double-blind study. Mean baseline FEV_1 ›r the MDI and MDI plus A, respectively were 1.58 and 1.48 .tres. Both treatments result in a significant increase in ılmonary function. The peak change in FEV_1 was 0.428 ± 0.105 .tres with A and 0.443 ± 0.091 litres with MDI. The magnitude response over 4 hours was not significantly different for the treatments. After long term use, the peak changes of FEV_1 ;re 0.361 ± 0.078 litres with A and 0.432 ± 0.092 litres with ›I, which were not significantly different. We conclude that ıe addition of an aerochamber to the conventional MDI offers › particular advantage in treatment of children with asthma.

1633 MYOINOSITOL (INO) PREVENTS N-NITROSO-N-METHYLURETHANE (NMU) INDUCED FATAL RESPIRATORY FAILURE. Mikko Hallman and Benita L. Epstein. University of California, San ;go, Department of Pediatrics, La Jolla, California.

Alveolar phospholipids (PL) are similar in RDS and in adult RDS. wever, in adult RDS, lung effluent phosphatidylinositol and asma INO are low. In this study rabbits were treated as follows ;roup 1:7.5/mg/kg NMU subcutaneously; Group 2:NMU, followed by IO, 3-5g/kg/day; Group 3:INO; Group 4:Normal treatment; Group 5: IO-deficient diet, starting 15 days before NMU; Group 6:INO-de-cient diet +3-5g/kg/day INO, starting 15 days before NMU. The ›rtality: Group 1:10/10 dead, 6.4±7 days after NMU; Group 2:2/11 ;ad (day 8 & 12, 2 weeks observation); Group 5:9/9 dead, 3.4±.3 ıys after NMU; Group 6:0/9 dead. In another experiment, animals ;re sacrificed, when Group 1 had respiratory failure (5.6±.7 days ›om NMU). Alveolar lavage was analysed for PL (mean±SEM, n=8 each ›oup):

saturated lecithin (DPC):	1) NMU	2)NMU+INO	3) INO	4)Normal
DPC/sphingomyelin	3.3±0.3	12.8±1.0	26.4±1.8	28.5±1.5
µmoles/kg	2.0±0.4	5.0±0.4	8.5±0.6	6.7±0.4
ıosphatidylinositol (%PL)	4.1±0.5	12.6±0.8	11.1±0.5	4.3±0.3
ıosphatidylglycerol (%PL)	2.0±0.4	0.2±0.2	0.6±0.1	7.8±0.5

ı Group 1, minimum surface tension of alveolar lavage (at 37°C, ırface concentration 13 nmoles PL/cm^2) was 15.8±2.2 dyn/cm where-; the minimum surface tension of lavages from groups 2-4 was <5 ›n/cm. INO supplementation increased serum and lung INO, and INO :arvation decreased INO. Present results demonstrate the impor-ınce of dietary INO in lung damage. INO may be useful in treat-ːnt of adult RDS and bronchopulmonary dysplasia. Grant: NIH HD10622.

1634 HYPOPROTEINEMIA AND LUNG FLUID BALANCE IN AWAKE LAMBS. Thomas A. Hazinski, Thomas N. Hansen, Gunnar E. Sedin, Robert B. Goldberg, and Richard D. Bland. Cardiovasc ːs Inst, Dept Pediatrics, Univ California, San Francisco

Respiratory distress from lung edema often occurs in babies .th hypoproteinemia, which reportedly facilitates edema either by ːducing the protein osmotic pressure difference between plasma ıd interstitial fluid (lymph) or by increasing lung microvascular ːrmeability to protein (Circ Res 43:925, 1978). To see how hypo-ːoteinemia affects fluid balance in the newborn lung, we measured ılmonary arterial and left atrial pressures, lung lymph flow, and ›ncentrations of protein in lymph and plasma of 8 2-wk-old lambs ːfore and after protein depletion. Studies included a 2-h control ːriod, followed by 4 h of increased lung microvascular pressure, ːoduced by inflation of a balloon in the left atrium. Each lamb ıd 2 studies, between which we drained protein-rich systemic ›mph through a thoracic duct fistula for 3 days and replaced .uid losses with feedings of a protein-free solution. This de-ːeased plasma protein concentration from 5.8 ± .2 to 3.6 ± .4 g/dl ıd it increased lung lymph flow from 2.6 ± .1 to 4.1 ± .2 ml/h. ›dy weight and vascular pressures remained constant, and the .fference in protein osmotic pressure between plasma and lymph ːcreased by less than 2 torr. Left atrial hypertension, which ›ould accentuate differences in lymph flow that occur as a result ː increased permeability to protein, increased lung lymph flow / 97 ± 10% during normoproteinemia and by 67 ± 8% after protein ːpletion. We conclude that hypoproteinemia increases net trans-ıscular filtration of fluid without influencing endothelial ːrmeability to protein in the lungs of lambs.

1635 GASTROESOPHAGEAL REFLUX DURING SLEEP IN ASTHMATICS D. Hughes*, S. Spier, J. Rivlin and H. Levison Research Institute, The Hospital for Sick Children, Toronto, Ontario, Canada.

Considerable controversy surrounds the role of gastroesopha-geal reflux (GER) in the production of night time symptoms in asthma. We have previously observed increased diaphragmatic muscle activity and abdominal excursions during REM sleep in adolescent asthmatics. We speculated that these changes may predispose to GER by increasing transdiaphragmatic pressure. We studied 8 moderately severe asthmatics (6M, 2F) mean age 15.4 yr. and 7 normal adolescents (4M, 3F), mean age 15.9 yr overnight in the sleep laboratory. Sleep was monitored by EEG, EOG and EMG. Esophageal pH was recorded with a pH electrode, the tip positioned 87% of the distance from Nares to GE junction. Ventilation was monitored with a respiratory inductive plethys-mograph and oxygen saturation with a Hewlett-Packard ear oximeter. There were a total of 9 episodes of GER (pH < 4.0 longer than 15 sec) in 3 patients in the asthma group and 6 in four of the controls. Mean duration of reflux was 122 ± 107 sec (±S.E.) in the asthmatics and 223 ± 84 sec in the controls. Oxygen saturation and ventilation did not change during or following the episodes. None of the reflux episodes was preceded or accompanied by stage REM sleep. Asthmatics do not appear to reflux more than normal controls and the reflux is not sleep state related.

*Canadian Lung Association Fellow

●1636 THEOPHYLLINE(T) NORMALIZES BREATHING PATTERN ABNORMALITIES IN NEAR-MISS(N-M) SIDS. Carl E. Hunt, Robert T. Brouillette and Donna Hanson. Northwestern Univ., Children's Memorial Hosp., Dept. of Pediatrics, Chicago.

Home monitors have been both advocated and maligned for infants at risk for SIDS. To determine the efficacy of T as an alternative treatment, we obtained 24-hour Pneumograms(Pg) in 57 infants on T in whom the pre-T Pg was abnormal, 39 previously healthy infants with symptomatic sleep apnea (N-M SIDS) and 18 asymptomatic SIDS siblings. Abnormal Pg criteria were: total duration of all respiratory pauses ≥ 6 sec. exceeding 0.5% of sleep time ($A_6/D\%$), ≥ 1.5 episodes of periodic breathing (PB) per 100 min. of sleep, or prolonged sleep apnea (> 20 sec.). The initial Pg was obtained at 7.8 ± 9.3 (± SD) weeks and the repeat Pg 14 ± 11 days later, at which time the T plasma level was 11.7 ± 2.9 ug/ml. T treatment resulted in comparable and highly significant decreases in $A_6/D\%$ and PB/100 min. in both groups (Table, $\bar{X}$ ± SD, $p < .001$, two-tailed, paired t test). As a percent of

Group	$A_6/D\%$		PB/100 min.	
	Pre-T	Post-T	Pre-T	Post-T
N-M SIDS	1.3 ± 1.6	0.3 ± 0.6	2.0 ± 1.9	0.4 ± 0.8
SIDS SIBLINGS	1.9 ± 1.3	0.3 ± 0.2	3.0 ± 2.5	0.2 ± 0.3

those infants abnormal initially, $A_6/D\%$ normalized in 41 of 50 (82%) and PB/100 min. normalized in 31 of 32 (97%). Among the 50 of 57 infants in whom the PG completely normalized with T (87.7%), further symptomatic apnea did not occur and none died of SIDS. In summary, T normalizes abnormal breathing patterns in most infants at risk for SIDS and appears to prevent further symptomatic sleep apnea and SIDS.

1637 SURFACTANT POOL SIZES, INHIBITORS AND THE SEVERITY OF RESPIRATORY DISTRESS SYNDROME (RDS) IN PREMATURE LAMBS Machiko Ikegami, Alan H. Jobe, Harris C. Jacobs, and Sally J. Jones, UCLA School of Medicine, Harbor-UCLA Medical Center, Department of Pediatrics, Torrance, CA.

15 premature lambs at 134-136 days gestational age (term-150 days) were delivered by C-section. Each lamb was paralyzed and supported on a ventilator for 10 hours with constant settings (rate=20/min, IT=1 sec, PEEP=2 cm H_2O, FiO_2=1.0) except for peak inspiratory pressure (PIP) which was varied between 23 and 51 cm H_2O to keep the pCO_2 between 30-40 torr whenever possible. The PIP and compliance measurements were used to reflect the severity of RDS. At sacrifice a thorough alveolar wash (AW) was collected and phosphatidylcholine (PC) and saturated phosphatidylcholine (SPC) pool sizes were measured. PC pool size/kg correlated non-linearly with PIP (r=0.87) and compliance (r=0.88) measurements made at sacrifice; SPC and PC pool size measurements correlated well (r=0.99). We then assayed the total surfactant inhibitor content of the AW by a titration of surface activity of AW associated protein versus natural sheep surfactant (Ikegami et al, J Appl Physiol 51:306, 1981). The AW contained 137±12 mg protein and from 95 to 481 units of inhibitor. The amount of inhibitor did not correlate with the amount of AW protein. We combined the PC pool size and inhibitor units into a ratio (PC pool size/inhibitor units) that correlated extremely well with the severity of RDS (PIP and compliance vs pool size/inhib. units, r=0.95 and r=0.93, respectively). The study documents an important role for both surfactant pool size and surfactant inhibitors in the severity of RDS.

●1638 THE EFFECT OF NATURAL SURFACTANT THERAPY ON ALVEOLAR PERMEABILITY IN PREMATURE LAMBS WITH RDS. Alan H. Jobe, Machiko Ikegami, Harris C. Jacobs and Sally J. Jones, UCLA School of Medicine, Harbor-UCLA Medical Center, Department of Pediatrics, Torrance, CA.

We delivered 35 lambs by C-section at 135-136 days gestational age. 5 lambs were sacrificed at birth; 6 lambs were treated with 50 mg/kg natural surfactant at birth (+NS) and sacrificed at 3 hours of age; 24 lambs were sacrificed without treatment (-NS) at times from 20 min to 3 hrs of age. Each lamb received I^{125} albumin ($I^{125}A$) mixed with fetal lung fluid at birth and subsequently received I^{131} albumin ($I^{131}A$) by arterial injection at 7±0.5 min of age. Following sacrifice, a thorough alveolar wash (AW) was used to measure the amount of alveolar protein and the flux of the labeled albumin into and out of the alveoli. The mean AW protein pool increased linearly ($r=0.982$, $p<0.01$) at a rate of 50 mg protein/kg body weight/hr in the -NS group. The % initial dose of $I^{125}A$ that left the AW decreased linearly by 10%/hr ($r=0.964$, $p<0.01$), and 1.3%/hr of initial dose of $I^{131}A$ entered the AW ($r=0.985$, $p<0.02$). A comparison of -NS (n=12) vs +NS (n=6) lambs sacrificed at 3 hrs showed no differences in mean blood pressures, heart rates, pulmonary artery pressures, pO_2, pCO_2, or pH. However, the peak inspiratory pressures used to ventilate the lambs (other settings held constant) were higher in -NS (29± 1.6 cm H_2O) vs +NS (23±1.5 cm H_2O), $p<0.01$. Less $I^{125}A$ left the AW of +NS vs -NS lambs ($p<0.01$), and less protein and $I^{131}A$ entered the AW of the +NS vs -NS lambs. These results show 1) a very large bidirectional flux of protein in the alveoli of lambs with RDS; 2) surfactant treatment decreases the protein flux.

1639 IMMUNOHISTOCHEMICAL DEMONSTRATION OF INCREASED NUMBERS OF BOMBESIN AND SEROTONIN IMMUNOREACTIVE PULMONARY NEUROENDOCRINE (BRONCHOCONSTRICTOR?) CELLS IN INFANTS WITH BRONCHOPULMONARY DYSPLASIA. Dana E. Johnson, Thomas J. Kulik, Theodore R. Thompson, James Lock. (Sponsored by William Krivit) University of Minnesota Medical School, Dept. of Pediatrics, Minneapolis, MN 55455.

We measured the number of bombesin, serotonin, and leu-enkephaling immunoreactive pulmonary neuroendocrine cells (PNEC) in the bronchiolar epithelium of 2 groups of infants: 26 infants from 1 day to 6 months of age dying during acute hyaline membrane disease (HMD) (1-7 days of age) or bronchopulmonary dysplasia (BPD) (3 weeks-6 months of age) and 36 age-matched infants dying of non-cardiopulmonary pathology. Immunohistochemistry was used to identify all 3 compounds. Bombesin and serotonin immunoreactive cells decreased in number during the acute phase of HMD, but were greatly increased in infants with BPD, compared with control infants. Though the changes in bombesin and serotonin immunoreactive cells paralleled one another in HMD and PBD, the total number of bombesin immunoreactive cells was always greater than serotonin immunoreactive cells. Cells containing leu-enkephalin immunoreactivity were identified in very small numbers only in infants with severe BPD. This study documents the presence of an increased number of cells containing potent bronchoconstrictors in the bronchiolar epithelium of infants with severe BPD. Since bombesin and serotonin appear to be secreted from PNEC toward the underlying bronchiolar smooth muscle, this study suggests that this increase in cell number may be responsible for some of the changes in airway resistance associated with BPD.

1640 ADENOSINE: A POSSIBLE MEDIATOR OF NEONATAL APNEA. John Kattwinkel and Robert A. Darnall. University of Virginia Medical Center, Department of Pediatrics, Charlottesville.

Preterm neonates frequently have idiopathic apnea and/or bradycardia which is lessened by xanthine or oxygen therapy. Asphyxiated newborns have apnea and bradycardia coincident with profound hypoxemia. Adenosine and its metabolites are markedly increased in the CSF of asphyxiated animals and adenosine has been implicated in the etiology of hypoxic bradycardia. Adenosine is also a known presynaptic neural depressant and is competitively inhibited by xanthines.

To test the hypotheses that adenosine may play a role in the pathogenesis of neonatal apnea, a catheter was placed in the cisternal space of 4 newborn piglets (< 48 hrs old) and adenosine in mock CSF was infused for 60-120 minutes. Minute ventilation (V_E) decreased to 36% and 2% of baseline in 2/4 animals and increased to 87% and 106% of baseline following parenteral theophylline. In the two adenosine non-responders, infusion of 2-chloroadenosine (a non-metabolized analogue of adenosine) resulted in a decrease of V_E to 42% and 37% of baseline. Apnea occurred in all animals. Arterial pH remained > 7.35; arterial pO_2 remained > 50 Torr except following profound apnea.

Adenosine is a neuroinhibitor which could explain many of the findings associated with neonatal apnea. More extensive studies appear warrented.

1641 TRIIODOTHYRONINE IN INFANTS SURVIVING NEAR-MISS SUDDEN INFANT DEATH SYNDROME. T. G. Keens, P. C. Dennies, and M. H. Cheng, (Spon. by G. N. Donnell). University of Southern California School of Medicine, Childrens Hospital of Los Angeles, Department of Pediatrics, Neonatal-Respiratory Diseases Division and Clinical Laboratory, Los Angeles.

Chacon and Tildon recently reported increased triiodothyronine (T3) in sudden infant death syndrome (SIDS) victims at post-mortem [J.Peds, 99:758-760, 1981]. We measured T3, Adjusted Thyroxine (Adj T4), and thyroid stimulating hormone (TSH) by radioimmunoassay in 25 infants who survived a near-miss SIDS episode (cyanosis, limpness, and apnea requiring vigorous stimulation or resuscitation, in whom no treatable etiology could be found), to see if T3 was elevated in infants at high risk for SIDS. The age at first episode was 2.7 ± 0.7 (SE) months. All thyroid studies were performed at initial hospitalization or while infants were still having apneic episodes (age 7.4 ± 1.2 months). All infants had normal Adj T4 (11.3 ± 0.7 µg/dl) and TSH (3.8 ± 0.2 µU/ml). The mean T3 for near-miss SIDS infants (239 ± 10 ng/dl) was increased compared to 8 control infants under 2 years of age (200 ± 14 ng/dl; $P<0.05$). 6 of 25 infants (24%) had mildly elevated T3 (range 283-332 ng/dl). There was an equal risk of subsequent life-threatening apnea (> 20 sec) whether the T3 was elevated (83%) or normal (68%; $P = 0.50$). There were no deaths. These results suggest that T3 may be a useful marker for detecting some infants at risk for SIDS.

1642 RISK OF SUBSEQUENT APNEA IN INFANTS SURVIVING NEAR-MISS SUDDEN INFANT DEATH SYNDROME. T G Keens, P C Dennies, C D Lew, and A C G Platzker, (Spon. by G N Donnell), University of Southern California School of Medicine, Childrens Hospital of Los Angeles, Department of Pediatrics, Neonatal-Respiratory Disease Division, Los Angeles.

76 infants surviving an episode of near-miss sudden infant death syndrome (SIDS); defined as cyanosis, limpness, and apnea requiring vigorous stimulation or resuscitation to revive the infant; were evaluated. Specific treatable etiologies were found in 14 of the 76 infants (19%): Gastroesophageal reflux 8%, Seizures 7%, and Lung disease 4%. No subsequent apneas occurred in this group once treatment was instituted. 62 infants (81%) without treatable etiologies were assumed to have a primary respiratory control disorder as the etiology of their apnea, and home apnea-bradycardia monitoring was instituted. The age of initial apnea was 2.8 ± 0.3 (SE) months (range 0.1 to 12.0 months). 51 of the 62 infants (82%) had one or more subsequent apneas at home (> 20 seconds) detected by the monitor. 40 infants (65%) had one or more subsequent apneas requiring vigorous stimulation to revive the infant. 14 infants (23%) had one or more subsequent apneas requiring mouth-to-mouth breathing or cardio-pulmonary resuscitation to revive the infant. Home monitoring was successfully stopped in 10 infants after 4.3 ± 0.2 months (3 months of no apnea or bradycardia alarms). There were no deaths among the 76 infants. These data indicate that infants surviving near-miss SIDS are at high risk for the occurrence of subsequent apneic episodes.

● 1643 THE USE OF EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO) FOR RESPIRATORY FAILURE IN TERM INFANTS. B Kirkpatrick, T Krummel, D Mueller, M Ormazabal, A Salzberg, L. Greenfield. (Spon. by H Maurer) Medical College of Virginia, Departments of Pediatrics and Surgery, Richmond, Virginia.

ECMO has had limited use in the intraoperative management of infants undergoing repair of congenital heart lesions. Previously we have reported that infants with respiratory failure (A-a DO_2 >625 torr) and who did not respond to hyperventilation and the use of vasoactive agents had a 100% mortality rate. Modifying the techniques of Bartlett, 8 infants with respiratory failure were managed with ECMO after conventional means of mechanical ventilation and pharmacologic agents had failed.

Diag.	A-a DO_2 torr 1 hr Pre ECMO	1 hr Post ECMO	Survival
Mec. Asp.	652	607	+
Pul. Hyperten.	630	610	+
Mec. Asp.	652	546	+
Mec. Asp.	646	553	+
Diaph. Hernia	654	271	+
Diaph. Hernia	631	629	+
Asphyxia	640	620	-
Asphyxia	635	545	-

7 out of 8 infants had an improvement of A-a DO_2 within one hour of starting ECMO. The eighth infant showed improvement by the third hour. ECMO can improve the survival rate of terminal respiratory failure due to a variety of pulmonary diseases in term infants.

1644 FOLLOW-UP OF PREMATURE INFANTS WITH BRONCHOPULMONARY DYSPLASIA. Beverly L. Koops, Steven H. Abman, Frank J. Accurso, (Spon. by Frederick C. Battaglia), Department of Pediatrics, University of Colorado School of Medicine, University Hospital, Denver.

Thirty premature infants, born between 1978-81 have been followed in our Special Baby Clinic with bronchopulmonary dysplasia (BPD) requiring home oxygen (O_2) therapy. The median birth weight was 1020 grams (range 540-2380), gestational age 28 weeks (range 25-36), ventilator days 19 (range 0-103) and hospital days 117 (range 54-196). All were discharged on O_2.

Follow-up at an average of 14 months (range 6-26) shows that 4 (47%) are off O_2, 16 (53%) remain on O_2. Transcutaneous oxygen monitoring, electrocardiograms and chest x-rays have been serially followed to determine length of O_2 therapy. Wheezing episodes and home altitude >8000 feet also prolonged O_2 therapy. Sixteen infants have had systolic blood pressures >113 mmHg, 4 have received treatment. Hospital readmissions occurred in 14 (47%) and serious social problems in 15 (50%). After age correction for prematurity, 16 (53%) have achieved normal weight, 19 (63%) normal height and 22 (74%) normal head growth. Bayley infant development scales have been done in 24 infants; median scores were 95 Mental (range 48-136) and 87 Motor (range 14-124).

Our impression of all 30 children is as follows: medically, 27% normal, 57% mild-moderate problems, 16% severe; neurologically, 20% normal, 44% mild-moderate, 36% severe. In this clinic population with prolonged pulmonary disease, there have been no infant deaths and all but one (who also has cytomegalovirus) have shown progress in respiratory, growth and developmental status.

1645 The Role of Tracheal Smooth Muscle in the Control of Airway Mechanics of the Newborn Lamb. Randal J. Koslo, Vinod K. Bhutani and Thomas H. Shaffer (Spon. by Lois Johnson). Dept. of Physiology, Temple Univ., School of Medicine, Philadelphia, Pa.

The relationship of tracheal compliance (C_T) and resistance (R_T) to airflow was studied in 6 term neonatal lambs (1-5 days old). All lambs were anesthetised with Nembutal® (30 mg/Kg i.p.) Airway volume, radius, pressure-volume and pressure-flow relationships were determined in in-situ tracheal segments just caudal to the criciod. Uniform lengths (3.2 ± 0.1 SE cm) were studied, while the lambs spontaneously ventilated through distal segments. C_T and R_T were calculated at transmural pressures (Ptm) of 0 to 40 cmH_2O both before and after the infusion of Bethanacol® (0.16 mg/Kg) to increase airway active tension. R_T was calculated at flows (V) of 0 to 0.5 L/sec. Control C_T (13.75 ± 2.89 SE $\mu l/cm.H_2O$) significantly decreased (50.9% $p < 0.04$) and R_T (0.07 ± 0.03 SE $cm.H_2O/L/sec$; V = 0.25 L/sec) significantly increased (204.8%; $p < 0.04$) at Ptm = 0. At Ptm = 40, R_T (V = 0.25 L/sec) significantly increased both before (1300%; $p < 0.02$) and after (578%; $p < 0.04$) Bethanacol. Therefore, the tendency for airway collapsibility at Ptm = 40 was significantly reduced ($p < 0.01$) with increased smooth muscle tone and directly correlated ($r = 0.7$; $p < 0.05$) with airway compliance. These data demonstrate that tracheal smooth muscle tone alters C_T and R_T and plays a significant role in controlling airway collapsibility. (Supp. in part HL22843)

1646 CARBON MONOXIDE AND LIPID PEROXIDATION. Linda K. Kwong, Clinton R. Ostrander, Ronald S. Cohen, Barrett E. Cowan, and David K. Stevenson (Spon. by Philip Sunshine). Dept. of Ped., Stanford Univ. Sch. of Med., Stanford, CA.

The possible generation of carbon monoxide (CO) from in vitro peroxidation of phospholipids independent of heme catabolism has been previously reported [Biochim Biophys Res Commun (1976) 73: 50], using a spectrophotometric technique to detect quantitatively the hemoglobin binding of the "extra" CO produced. We confirmed this other source of CO by demonstrating its production from in vitro peroxidation of phosphotidyl choline (PC), purified from egg white, in a gas-tight reaction vessel coupled directly to a chromatograph and a very sensitive (± 1 ppb) reduction gas detector. Using ascorbate·Fe^{+++} as the initiator of the free radical reaction, the evolution of CO was shown to occur with PC peroxidation. In the absence of PC, no CO was detected. Without ascorbate.Fe^{+++} and with a metal chelator, citrate, PC underwent slow autoxidation as shown by CO production; without O_2, no CO was produced from PC. Therefore, CO can be formed in association with the peroxidation of PC by O_2 and ascorbate·Fe^{+++}. Recent evidence suggests a direct toxicity of CO to various cellular functions in addition to damage resulting from CO-induced hypoxia. Membranes rich in polyunsaturated fatty acids are highly susceptible to oxidation, especially if the in vivo antioxidant protective systems are impaired due to immaturity, disease, or poor nutrition. Oxidative injury during O_2 therapy in neonates may be due to membrane damage as well as direct CO toxicity since local concentrations of CO might be high as a result of lipid peroxidation and tissue retention of CO.

1647 SPUTUM PENETRATION OF MOXALACTAM IN PATIENTS WITH CYSTIC FIBROSIS (CF). Celine Laferriere, Marinus Flux, John Kramer, Donald Frederick, Cathy Hopkins, Melvin I. Marks. University of Oklahoma Health Sciences Center, Department of Pediatrics, Oklahoma City and Tulsa, Oklahoma.

Much of the difficulty in eradicating Pseudomonas aeruginosa (PA) from the sputum of CF patients relates to inadequate sputum concentrations of antibiotics. We evaluated moxalactam penetration and kinetics in purulent sputum from five CF patients with pulmonary disease and chronically colonized with PA. Results were compared to those from similar patients receiving tobramycin or ticarcillin. Samples of saliva, sputum, and serum were obtained before, 5,30,60,120,180,240 and 360 min. after completion of the second intravenous dose of each drug. Dosages in mg/kg/dose were moxalactam 33, tobramycin 33 and ticarcillin 200. Concentrations were determined by bioassay with E. coli, B. subtilis and Sarcina lutea indicators for each drug, respectively. Mean peak antibiotic concentrations were usually noted within one hour of the end of the IV infusion and are listed below and compared to the MIC_{90} for 13 PA isolated from these patients.

	Moxalactam	Tobramycin	Ticarcillin
Serum(ug/ml)	155.8	9.1	121
Sputum(ug/ml)	2.15	.67	< 2
Sputum/serum	1.3%	7.3%	< 1.7%
MIC_{90} (ug/ml)	32	2	32

Moxalactam, like other antibiotics commonly used to treat PA pulmonary infection, penetrates sputum at concentrations below that expected to effectively eradicate these bacteria from CF patients.

1648 EFFECT OF THEOPHYLLINE (T) AND CAFFEINE (C) ON LUNG MATURATION IN FETAL RABBITS. Susan Landers, Jane E. Cregan, Anthony J. Corbet and Arnold J. Rudolph. (spon by Reba M. Hill). Department of Pediatrics, Baylor College of Medicine, Houston.

The effect of T and C on lung maturity in fetal rabbits was examined. Maternal rabbits of 25.5 days gestation were given 4 IM injections every 12 hrs of T 15mg/kg (n=5), C 30 mg/kg (n=7) or saline (S)(n=10). At 27.5 days gestation, 12 hrs after the last injection, pups were delivered by hysterotomy and sacrificed immediately. After tracheostomy, pressure-volume curves were performed. The lungs were weighed (WLW), homogenized, and total phospholipid (TPL) measured. Total lung capacity at 30 cm H_2O was 1.84 ± SE. 26 ml/gm WLW for T, 1.35 ± .15 for C, 1.51 ± .13 for S. Values analyzed were mean for each litter. The volume retained on deflation to 5 cm H_2O was 0.35 ± .06 for T ($p < .05$), 0.37 ± .03 for C ($p < .001$), 0.25 ± .03 for S. Lung TPL was 1.09 ± .08 mg/gm WLW for T ($p < .01$). 0.73 ± .01 for C, and 0.73 ± .06 for S. Mean litter size was 5.6 for T, 8.4 for C, 6.5 for S. There were no differences for body weight or WLW. In separate experiments, fetal rabbits had theophylline blood levels 12 ± 1.0 mg/L 1 hr after 15 mg/kg dose, 72% of maternal levels (n=3), and caffeine blood levels equivalent to maternal of 8.4 ± .16 mg/L 1 hr after 10 mg/kg dose (n=8). Improved deflation retention of air in T and C injected litters suggests improved secretion of surfactant, but lung TPL was only improved in T injected litters. This suggests T stimulates synthesis and secretion of surfactant phospholipid but C stimulates only secretion.

1649 THEOPHYLLINE AND NEONATAL CEREBRAL BLOOD FLOW. Fergus Leahy, Jorge Luz, Augusto Winter, Hans Pasterkamp, Henrique Rigatto, Dept. of Pediatrics, University of Manitoba, Winnipeg. The purpose of our study was to determine the effect of Theophylline used in the treatment of apnea of prematurity on neonatal cerebral blood flow (CBF). This is of importance for two reasons,(1)decrease in CBF has been proposed as the mechanism of action of Theophylline,(2)decrease in CBF may increase cerebral vulnerability to events such as apnea and bradycardia. We studied five preterm infants with a mean birth weight of 1600 grs ±.09 SE,mean gestational age 30 weeks ±.7,at mean postnatal age 30 days ±3. CBF measurements were made using our method of venous occlusion plethysmography with venous and arterial dopplers to assess excellence of jugular occlusion. The formula we derived was CBF ml/min/100 g: 3·51.head circumference.slope/skull volume. Theophylline was given orally in dose of 6 mgs/kg/24 hrs divided into three and serum Theophylline was measured two hours post dose by the EMIT method. CBF measurements were made at various levels of Theophylline concentration. Serum Theophylline levels ranged from 0-22 μgs/ml. We found mean CBF of 27 mls/min/100 g ±2. This was within the range previously determined (32 ml/min/100 g). Calculating change in CBF as related to changes in Theophylline level there was no correlation as statistically determined ($r=0.25$). We conclude(1)Theophylline in therapeutic doses does not decrease CBF significantly(2)Mode of action of Theophylline cannot be explained as present by changes in CBF. However, our method would not detect regional changes in CBF.

1650 SINGLE CELL ANALYSIS OF DEVELOPING RABBIT FETAL LUNG CELLS BY LASER FLOW CYTOMETRY by J.F. Leary, J. N. Finkelstein, R.H. Notter, R. Gallo, W.M. Maniscalco and D.L. Shapiro, Departments of Pediatrics and Pathology, Univ. of Rochester, Rochester, New York 14642.

Lung cells dissociated from rabbit fetuses of varying gestational ages were analyzed on the basis of phosphine-3R fluorescence and low-angle (2°-12°) light scatter using a Coulter EPICS V multiparameter flow cytometer/cell sorter. Lung cells were obtained from fetuses delivered by caesarian section at early (27 day) and late (30 day) gestational age (term=31 days) as well as from adult rabbits. Suspensions of lung cells from individual fetuses were dissociated by elastase and trypsin and subsequently stained for 30 minutes at 4°C with lipophilic phosphine-3R (1 µg/ml), which has previously been shown to stain lamellar bodies in adult rabbit type II pneumocytes. Simultaneous, correlated fluorescence and light scatter measurements were made on a cell-by-cell basis for lung cells dissociated from individual fetuses. 27 day fetuses had no clearly definable type II cell subpopulation on the basis of these two parameters; 30 day fetuses showed subpopulations of cells in light scatter and fluorescence regimes similar but not identical to those previously identified with adult type II cells. It was possible by sorter analysis to distinguish light scatter and fluorescence variations on a fetus by fetus basis. Moreover, the multiparameter nature of cell sorter analysis, and the fact that measurements can be made and correlated on a single cell basis, gives this technique the potential to define the role of individual cell populations in lung maturation.
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1651 COMPARISON OF BRONCHODILATOR EFFICACY OF ALBUTEROL AEROSOL AND ORAL AMINOPHYLLINE IN ASTHMATIC CHILDREN. Haesoon Lee (Spon. by H.E. Evans), New York Medical College, Lincoln Hospital Center, Dept. of Pediatrics, Bronx, NY

Bronchodilator effect of albuterol aerosol and oral aminophylline or both was compared in 17 children with stable asthma after withholding theophylline compounds for 24 hours and adrenergic bronchodilators overnight. Treatment consisted of either albuterol aerosol 3 puffs in a sequential manner from a canister nebulizer, or a loading dose of aminophylline orally (7.5 mg/kg body weight), or a combination of both in a double blind cross over study on 3 different days. Forced expiratory volume in 1 second (FEV_1) and peak expiratory flow rate (PEFR) were measured in duplicate before therapy and at 30, 60, 120, 180 and 240 minutes. FEV_1 response expressed as percent change over the baseline value showed significant improvement on all 3 regimens. FEV_1 response on albuterol alone was significantly greater than that on aminophylline alone in the first 2 hours ($P<0.01$); thereafter they were similar. The combination regimen produced FEV_1 response identical to that of albuterol alone in the first hour and significantly greater than either alone from 2 to 4 hours. PEFR responses were similar to that of FEV_1. Side effects of nausea, tremor, palpitation were frequent on aminophylline containing regimen (8/17 and 10/17) and infrequent on albuterol alone (3/17). Albuterol aerosol has advantages of rapid, effective bronchodilatation with few side effects.

● 1652 LIMITS OF DIAPHRAGMATIC FUNCTION IN PRETERM INFANTS. Peter N.LeSouëf, Jose M Lopes, M.Heather Bryan and A. Charles Bryan, Resp. Physiology, Research Inst. Hospital for Sick Children, Toronto, Canada.

The difficulty of measuring transdiaphragmatic pressure (Pdi) has hampered investigation of diaphragmatic function in the preterm infant. We have used a new and simplified method of measuring Pdi to study the effect of chest wall distortion (CWD) on the preterm diaphragm. Pdi = Mean pleural pressure (Ppl) minus abdominal pressure. As mouth occlusion pressure (Pmo) equals mean Ppl (Beardsmore, et al J Appl Physiol 49:735-42, 1980), and gastric pressure (Pg) estimates abdominal pressure, Pdi = Pmo-Pg Pmo can be measured with a face mask and pressure transducer and Pg with a constantly infused fluid-filled 6 Fr catheter. Using this method we have related the diaphragmatic electromyogram (Edi) to the force generated, Pdi, in four preterm infants (BW 1120 ± 190 g, age 20 ± 15 d). Edi was measured with surface electrodes and rib cage and abdominal motion using magnetometer pairs. CWD was defined as inward inspiratory motion of the rib cage magnetometer. Periods with least CWD were compared with periods with greatest CWD. We found: (1) when CWD was least, an increase in Edi produced an increase in Pdi in all infants; when CWD was greatest, large increases in Edi produced no increase in Pdi in any infant. (2) when breaths with the same Pdi from each period in each infant were compared, those from the period with greatest CWD had a significantly higher Edi in all infants (mean increase 144%, $p<0.01$) and a lower Pmo in all infants (mean decrease 26%, $p<0.05$). Thus chest wall distortion markedly limits the effectiveness of the diaphragm as a force generator.

● 1653 CIRCULATING IMMUNE COMPLEXES DECREASE DURING CORTICOSTEROID THERAPY IN CYSTIC FIBROSIS. Norman J. Lewiston and Richard B. Moss (Spon. by John J. Miller) Children's Hospital at Stanford, Palo Alto, CA.

Approximately 15% (37/250) of our patients with cystic fibrosis (CF) have symptoms which may be caused by hypersensitivity. These include recurrent fevers, arthritis, obstructive lung disease nonresponsive to usual bronchodilator therapy, and allergic aspergillosis. Sixteen of these have been treated with oral prednisone, 2 mg/kg/day during acute illness. All of these patients prior to corticosteroid therapy demonstrated increased serum ^{125}I-C1q binding activity, suggesting circulating immune complexes. Improvement in percent predicted forced vital capacity (FVC) and in Schwachman clinical score (CS, normal = 100) correlated with decrease in C1q binding activity (C1q, normal<12%) (mean±S.D.).

	C1q	FVC	CS
Pre-Rx	19.6 ± 8.1	39.7 ± 8.1	47 ± 4
Post-Rx	8.8 ± 2.9	58.3 ± 18.1	58 ± 6
P value	<.001	<.01	<.05

Ten of these patients were changed to alternate day prednisone therapy, ≤ one mg/kg/day. The others required low-dosage daily prednisone. The only unacceptable side-effect of therapy was lumbar vertebral compression in one boy. We conclude that there is a population of patients with CF who may benefit from vigorous therapy with anti-inflammatory agents. C1q binding activity or other measures of circulating immune complexes may be a useful clinical marker for this group.

●1654 PULMONARY METABOLIC FUNCTION IN THE CONSCIOUS LAMB. G. Lister and B.R. Pitt. Yale University School of Medicine, New Haven, CT 06510.

The effect of postnatal development and acute alveolar hypoxia on pulmonary metabolic function was studied in awake, intact newborn lambs. Shortly after birth (<12 hrs), under local anesthesia, indwelling catheters were placed in the right atrium, aorta and pulmonary artery of 9 lambs. Measurements of the ability of the lungs of these animals to metabolize ^{3}H-benzoyl-Phe-Ala-Pro ((^{3}H-BPAP), a synthetic substrate for angiotensin-converting enzyme (ACE)) and to remove ^{14}C-5-hydroxytryptamine (R(^{14}C-5-HT)) were made by modified indicator dilution techniques during normoxic and hypoxic (F_IO_2=0.10) conditions at 1 day, 1 week and 1 month of age. Five additional sheep (8-23 wks old) were studied as "adult" controls. BPAP metabolism in the 1 day old group was 45±3% and developed slowly to 53±2% ($P<0.05$) at one mo. of age and to 74±3%($P<0.01$) by 23 wks of age. Pulmonary R(^{14}C-5-HT) was adult-like at birth (69±2%). Except in the newborn when BPAP metabolism decreased (32±3%; $P<.05$) with hypoxia, a low F_IO_2 had no significant effect on either R(^{14}C-5-HT) or BPAP metabolism. Furthermore, these data demonstrate a selective and gradual postnatal development of pulmonary ACE which might be due to: a) increasing enzyme-substrate affinity, b) increasing amount of enzyme with endothelial cell growth, or c) increasing availability of enzyme due to alterations in distribution of pulmonary perfusion.

1655 ASSESSING PULMONARY DYNAMICS IN THE MECHANICALLY VENTILATED NEONATE: NEW METHODOLOGY. W. Andrew Litzenberger, M. Douglas Cunningham, Deborah J. Boyer, Nirmala S. Desai, Department of Pediatrics, College of Medicine, University of Kentucky, Lexington.

Knowledge of changing dynamic lung compliance (C_L) and airway resistance (R_L) would facilitate mechanical ventilation of neonates. Standardized methods for assessing pulmonary functions in sick newborn infants are not available. We describe a method for assessing C_L and R_L in mechanically ventilated neonates. Seven neonates with respiratory insufficiency were assessed for C_L and R_L while undergoing mechanical ventilation. Mean birthweight was 1197 grams; gestational age was 30 wks. A multichannel recorder with scalar and loop output was used to calculate C_L and R_L. We measured airflow ($\dot{V}$), airway pressure (P_{aw}), and esophageal pressure (P_{es}). Volume (V) was calculated from $\dot{V}$ which was taken from a pneumotachograph placed just proximal to the endotracheal tube. P_{es} was measured using a water-filled infant feeding catheter placed in the lower esophagus. The pressure used in both compliance and resistance calculations was transpulmonary pressure (P_{tp}), the absolute difference between P_{aw} and P_{es}. Our values for dynamic compliance ($\Delta V/\Delta P_{tp}$) were 0.58±0.09 S.E.M. initially, and 1.12±0.15 cc/cm$H_2$0/kg just prior to extubation. Airway resistance ($\Delta P_{tp}/\Delta \dot{V}$) was 149±38 cm$H_2$0/L/sec/kg initially, and 51±7 with recovery. Our method provided a reproducible means for bedside assessment of changing lung status in the mechanically ventilated neonate.

1656 NEONATAL PULMONARY FUNCTION TESTING DURING MECHANICAL VENTILATION: SERIAL STUDIES IN BRONCHOPULMONARY DYSPLASIA. W. Andrew Litzenberger, M. Douglas Cunningham, borah J. Boyer, Nirmala S. Desai, Department of Pediatrics, Cole of Medicine, University of Kentucky, Lexington.

Prospective pulmonary function testing from the outset of meanical ventilation was carried out to study the possible develment of bronchopulmonary dysplasia (BPD) in neonates with resratory distress syndrome (RDS). Seven infants with RDS who subquently developed radiographic and clinical evidence of BPD re assessed for dynamic lung compliance (C_L) and lung resisnce (R_L) during mechanical ventilation. They were compared with similarly treated infants who recovered from RDS. To study newrn C_L and R_L, serial measurements were made of airflow ($\dot{V}$), rway pressure (P_{aw}), and esophageal pressure (P_{es}); volume was lculated from $\dot{V}$ and transpulmonary pressure was derived from w and P_{es}. R_L values for BPD infants began to rise during week of life and peaked during week 3; non-BPD infants showed no ange of R_L during week 1 of life. Highest R_L measured in BPD tients was 2.7 times greater than in RDS infants (322±45 S.E.M. 120±40 $cmH_2O/L/sec/kg$, $p<0.01$). R_L values decreased by time of tubation, but BPD infants maintained higher R_L (117±21 vs 43±7, 0.01) even though mechanical ventilation was no longer required. did not change during the course of BPD, and was not signifintly different for RDS patients at extubation (0.90±0.32 vs 02±0.51 $cc/cmH_2O/kg$. Our method demonstrated that persistently ıcreased airway resistance is a hallmark of BPD, and suggests ıat increased airway resistance in the 1st week of life may porınd the development of BPD.

1657 THE EFFECTS OF THEOPHYLLINE ON DIAPHRAGMATIC FATIGUE IN THE NEWBORN. Jose M Lopes, Peter N LeSouef, M. Heather Bryan, A.Charles Bryan. Resp. Physiol, Hosp. r Sick Children, Research Institute, Toronto, Canada.

The xanthines are effective agents in treating apnea in the eterm infant and are thought to be central nervous system stimants. However, it has been recently shown that in adults, aminylline has a direct effect on the muscle, improving diaphragtic contractility and recovery from fatigue. As apnea in the wborn may be due to respiratory muscle fatigue, the efficacy of is drug may be explained by its action at the muscle level. We erefore studied 9 preterm infants (mean BW -1160 g)before and ter the administration of theophylline. The motion of rib cage d abdomen was monitored with magnetometers and the diaphragmac EMG (EMGdi) with surface electrodes. The EMG was analysed cording to its frequency spectrum. A fall in the Hi/Lo frequenratio below 80% control values was considered to be indicative fatigue. The number of fatigue episodes and fatigue related neas was then analysed. In 3 infants we measured mouth occlusn (Pm) pressure and the EMGdi. We compared the Pm generated ring breaths with the same EMGdi before and after theophylline evaluate the effects of the drug on respiratory muscle conactility. Theophylline significantly decreased the total mber of apneas, the number of fatigue episodes and particularly e number of severe apneas caused by fatigue. Respiratory scle contractility was improved as the Pm generated for a given lGdi was always higher after the drug. We conclude that apnea lated to fatigue can be effectively treated with theophylline & s efficacy in the preterm is significantly related to a direct fect on the muscle.

1658 PHYSIOLOGICAL APPROACH TO DECANNULATION OF TRACHEOSTOMY IN INFANTS AND YOUNG CHILDREN. George B. Mallory, Etsuro K. Motoyama, James S. Reilly, Sylvan Stool, and Frank T. Weng. Univ. of Pittsburgh School of Med., ildren's Hospital of Pittsburgh, Depts of Anesthesiology, diatrics, and Otolaryngology, Pittsburgh, PA.

In children with tracheostomy (TR), the timing of decannulation decided empirically or by direct laryngotracheoscopy (DLT). developed a method to assess upper airway function and applied to 7 patients aged 4 to 27 months before DLT for TR decanulaon. Flow and volume signals were measured during tidal breaıing by connecting a pneumotachograph to the TR tube and then peated through a face mask after the TR tube was removed and ıe stoma occluded. Analysis was made the ratio of maximum inıiratory flow through TR and mouth (MIFtr/MIFmo) and the time ıt) to reach MIF as a fraction of inspiratory time ($\Delta t/Ti$). In patients with minimal upper airway pathology by DLT, Ftr/MIFmo was less than 1.0 (mean: .65 ± .19 (SEM)), indicating eater MIF with mouth breathing. In contrast, 4 patients had ıbglottic stenosis on DLT and could not be decannulated; their Ftr/MIFmo was more than 1.0 (mean: 2.27 ± .59, $p<.05$). In 6 ıt of 7 patients flow pattern through TR was characterized by ılayed peaking of inspiratory flow ($\Delta t/Ti<.5$), a pattern of ıper airway obstruction. All 3 patients who were decannulated ıowed a decrease in $\Delta t/Ti$ with mouth breathing (mean:.71 ± .03 s. .54 ± .01, $p<.005$). In 4 patients $\Delta t/Ti$ increased in 2 and ecreased 2. Thus, flow pattern analysis provides a rational ıproach toward the evaluation of upper airway patency and TR ecannulation.

1659 A COMPARISON OF HIGH FREQUENCY JET VENTILATION (HFJV) AND CONVENTIONAL MECHANICAL VENTILATION (CMV) IN EXPERIMENTALLY INDUCED MECONIUM ASPIRATION. Mark C. Mammel, Margaret J. Gordon, Stephen J. Boros, Children's Hospital, St. Paul, and University of Minnesota, Department of Pediatrics, Minneapolis, MN

Ten adult mixed-breed cats (2.5-4.5 kg) were anesthetized with ketamine and alternatively ventilated at a constant mean airway pressure with either HFJV (rate 250) or CMV (neonatal pressure preset ventilator - rate 30) following the aspiration of 2 ml/kg of 25% human meconium in saline. Aortic, pulmonary artery, and central venous pressures were continuously monitored. Thermodilution cardiac outputs were measured, and pulmonary and systemic vascular resistances (PVR, SVR), intrapulmonary shunts (Q_{sp}/Q_t), and alveolar-arterial oxygen gradients ($AaDO_2$) were determined at regular intervals. The animals were divided into two groups. Ventilators were varied at one hour intervals in the following sequence: Group I: HFJV - CMV - HFJV - CMV; Group II: CMV - HFJV - CMV - HFJV. Pre-aspiration baseline measurements for each group showed no significant differences.

Group I (those ventilated with HFJV immediately following aspiration) developed and maintained a lower Q_{sp}/Q_t than Group II ($p < 0.05$). This may be due to the effect of HFJV on meconium dispersion immediately following aspiration. Comparing HFJV to CMV in both groups, CMV was superior. CMV was consistently associated with lower pulmonary artery pressures ($p < 0.01$), lower PVR ($p < 0.05$), lower $AaDO_2$ ($p < 0.05$), and lower Q_{sp}/Q_t ($p < 0.01$).

● **1660** DE NOVO FATTY ACID SYNTHESIS IN FRESHLY ISOLATED TYPE II PNEUMOCYTES W.M. Maniscalco and J.N. Finkelstein (Spon: D.L. Shapiro), Univ. of Rochester, Dept. of Pediatrics, Rochester, New York 14642

Pulmonary surfactant, the phospholipid mixture present at the alveolar air-water interface, is synthesized in the type II pneumocyte. A unique characteristic of surfactant phospholipids is the high content of esterified saturated fatty acids, especially palmitic acid. To determine the capacity of freshly isolated rabbit type II pneumocytes to synthesize fatty acids, we examined 1) de novo fatty acid synthesis by ^3H_2O incorporation into total fatty acids, 2) acetyl-CoA carboxylase activity and 3) glucose utilization for fatty acid synthesis. In the absence of exogenous carbon substrates, ^3H_2O incorporation into fatty acids was 9.26 ± 1.3 nmoles/10^7 cells/hr. Inclusion of glucose resulted in a concentration dependent increased ^3H_2O incorporation that plateaued with 5.0 mM glucose at 3x the baseline value. This rate was twice that of a mixed cell preparation and 4.6 x greater than alveolar macrophages. Lactate also produced a concentration dependent increase in ^3H_2O incorporation, but there was no increase over baseline values with pyruvate or an amino acid mixture. Acetyl-CoA carboxylase activity was 3.15 nmoles $^-HCO_3$/min/mg prot. in type II cells. U-^{14}C glucose incorporation into fatty acids was 5.95 nmoles/10^7 cells/hr., and at 5.0 mM exogenous glucose provided 54.4% of total C_2 units used for fatty acid synthesis. These data indicate that freshly isolated type II pneumocytes can synthesize fatty acids de novo at a high rate and that exogenous glucose can be a major source of C_2 units. (Supported by American Heart Association #81 888)

● **1661** THE EFFECT OF DEXAMETHASONE ON BETA-ADRENORECEPTORS IN FETAL RAT LUNG EXPLANTS by W.M. Maniscalco, A. Parkhurst, and D.L. Shapiro, Univ. of Rochester, Department of Pediatrics, Rochester, New York 14642.

Beta-adrenergic agonists stimulate surfactant secretion from type II pneumocytes and increase the L/S ratio of lung lavage in fetal sheep. These effects are mediated through cell surface beta-adrenergic receptors. Recent studies have suggested hormonal regulation of pulmonary beta-adrenergic receptor concentration. We measured receptor concentration in lung explants from fetal rats by measuring specific membrane binding of ^{3}H-dihydroalprenolol (DHA). In lung explants from 19-day fetal lung cultured without hormones or serum, the receptor concentration did not change during 48 hours in culture and thus, did not mimic the rise in receptor concentration seen in vivo between 19 and 21 days. Addition of 1 μM dexamethasone to the cultures resulted in an increase in receptor concentration compared to controls (138.0 ± 8.8 vs. 63.2 ± 5.0 fmoles DHA bound/mg membrane protein). The receptor concentration of treated explants was similar to that seen in vivo at 21 days gestation. Scatchard analysis indicated that the increased DHA binding in dexamethasone treated explants was due to an increase in receptor number rather than binding affinity. Inclusion of cyclohexamide, an inhibitor of protein synthesis, resulted in no significant difference between dexamethasone treated and control explants (62.8 ± 6.7 vs. 51.9 ± 2.1 fmoles DHA/mg protein). These data demonstrate a direct effect of steroid hormone on fetal lung explant beta-adrenergic receptor concentration and suggest that glucocorticoids may regulate the increase in receptor concentration in vivo.

● 1662 SURFACTANT TURNOVER IN HIGH FREQUENCY OSCILLATORY VENTILATION (HFOV). Frank L. Mannino, Ronald D. McEvoy Mikko Hallman, University of California, San Diego, Departments of Pediatrics and Medicine, La Jolla.

The effect of HFOV on surfactant release is unknown. Surfactant kinetics was studied in 32 rabbits (3.0±0.3kg), under 3 conditions: HFOV (rate 1200cpm, tidal volume (TV) <5ml), using a piston/bias flow system; conventional mechanical ventilation (CV) (rate 25cpm, TV 25-35ml), using a Harvard ventilator; spontaneous breathing (SB). All animals undergoing mechanical ventilation had normal blood gases and 2.5cm/H_2O mean airway pressure. ^{14}C-palmitate was given 12hr before and ^{3}H-palmitate at the start of ventilation. Disaturated phosphatidylcholine (DPC) was analyzed in alveolar lavage (AL) and lamellar bodies (LB). Total pool sizes and total radioactivities of ^{3}H-DPC were:

Post-^{3}H	DPC(μmoles)			^{3}H-DPC(cpm X 10^{-3})		
	HFOV	CV	SB	HFOV	CV	SB
AL 1hr	20.4±2.2	23.1±1.5	21.0±1.3	3.2± 0.4	4.7± 0.8*	2.6± 0.3
AL 4hr	15.0±1.5*	21.7±2.0#	20.4±0.7	30.3± 4.4	34.2± 2.4*	23.8± 4.2
LB 1hr	15.5±1.0	11.4±1.8#	14.0±1.4	29.4± 3.9	29.3± 7.0	31.9±10.9
LB 4hr	16.0±2.3	11.6±2.4	13.1±1.8	73.9±15.4	47.8±11.1*	94.9±17.6

*p<0.05 as compared to SB; #p<0.05 as compared to HFOV

^{14}C-DPC reflected the amount of DPC present in AL and LB. HFOV tends to decrease AL-DPC and increase LB-DPC. However, the ^{3}H-DPC radioactivity in AL is increased at four hours. This suggests that there is an increase in surfactant release (from LB to AL) and an increase in surfactant reuptake (from AL to LB). HFOV may increase the mixing of lung surfactant pools and help preserve surfactant function.

1663 SHORT-TERM PULMONARY EFFECTS OF TOTAL PARENTERAL NUTRITION IN CHILDREN WITH CYSTIC FIBROSIS. A.L. Mansell, W.C. Heird, J. Andersen, C.M. Muttart, C. Ores, Columbia U. Coll. of P&S, Babies Hosp.,Dept. of Pediatrics, N.Y.

We measured indices of lung function and respiratory muscle strength before and after a 1-month course of total parenteral nutrition (TPN) in 10 children (aged 9 to 18 years) with advanced pulmonary involvement from cystic fibrosis. Maximum inspiratory airway pressures (Pmax insp) were abnormally small (below 2 SD of normal values in 8 of the 10 patients), demonstrating weakness of inspiratory muscles before the TPN. During TPN body weight increased by 19.7±9.7 SD % and Pmax insp increased significantly ($P < 0.01$) from a mean -71±15 SD cmH_2O to -85±16 SD cmH_2O. However airflow obstruction and gas exchange worsened. Maximum mid-expiratory flow (MMEF) decreased ($P < 0.05$) from a mean 33±26% of predicted to 28±21% of predicted. Arterial oxygen saturation (SaO_2) by ear oximetry also decreased ($P < 0.02$) from a mean 93.4±2.9 SD % to 91.6±2.8 SD %. During the subsequent month without TPN, MMEF did not change but SaO_2 increased ($P < 0.05$) to near original values. Since there were no changes in pulmonary diffusing capacity, we interpret the decreases in SaO_2 and MMEF as evidence for worsening of ventilation perfusion relationships on the basis of increased pulmonary extravascular fluid during the TPN. We conclude that TPN can provide a partial correction of respiratory muscle weakness associated with malnutrition in severe chronic obstructive lung disease. The possibility of worsening gas exchange should be considered when using TPN in children with evidence for interstitial pulmonary edema from cardiac disease or bronchopulmonary dysplasia.

1664 USE OF HIGH FREQUENCY OSCILLATION (HFO) IN IMMATURE LAMBS AT BIRTH. Alan J. Mautone, Paola Iorio, Immanuela R. Moss and Emile M. Scarpelli. Pediatric Pulmonary Division, Albert Einstein College of Medicine, Bronx, New York 10461.

We used HFO to initiate and sustain breathing in 10 immature (126-134 days) lambs. Fetuses were cannulated in utero, delivered through uterotomy, and placed on HFO with lungs still in the fetal state, i.e., filled with fetal pulmonary fluid (FPF). Compressed *air* at 10-16 l/min was used with the oscillator at 15-18 Hz, VT of 1.5 ml/kg. Extrauterine survival was significantly longer with HFO than with spontaneous breathing in twin lamb controls. In addition, older neonates (>129 days) were better ventilated and survived longer than younger (<130 days). Acceptable blood gas and pH values could be sustained with intratracheal pressures (ITP) ≥ 25 torr. This often (7/10) resulted in parenchymal rupture and pneumothorax. Optimal ventilation was best achieved at the higher flow rates, but at the expense of ITP elevation. Pneumothorax produced expected cardiovascular effects plus intrapulmonary right-to-left shunting relieved by evacuation of intrathoracic air. FPF-filled *excised lungs* of 3 additional immature lambs were placed in a lucite plethysmograph and ventilated in the same way. Saccular aeration did not begin until effective ITP was >12 torr. Saccules of upper lobes became aerated before those of the lower lobes, and anterior aspects were aerated before posterior (dependent) regions. In 2 experiments, subpleural air pockets developed with time and sustained pressure. Thus, HFO appears to be adequate for overcoming the highest resistances to initial aeration of immature lungs, but the continuous high pressures produced by conventional settings cannot be tolerated. Supported by NIH research grants HL 07060 and HL 23995.

1665 SARCOIDOSIS IN CHILDHOOD: A REPORT OF 52 CASES. Michael M. McCarthy, William D. Bradford, Alexander Spock, Duke University Medical Center, Division of Allergy, Immunology, and Pulmonary Diseases, Department of Pediatrics, and the Department of Pathology, Durham, N. C.

Clinical and laboratory findings of 52 children with biopsy-confirmed sarcoidosis have been reviewed, and outcome evaluated over a mean follow-up period of 4 years. Age, sex and racial characteristics of the group were similar to those in previous American series, but, rather than systemic manifestations, cough was the most frequent presenting symptom. Organ system involvement was as observed before, including nearly universal lung disease, but evidence of renal involvement was more frequent than in prior reports. Pulmonary function and blood gas status, reported in more detail than in the past, revealed an expected high incidence of restrictive disease and hypoxemia, and confirmed, for the first time in pediatric sarcoid, prominent obstructive and small airways components. Radiographic evidence of lung parenchymal involvement did not significantly predict respiratory function status, indicating the necessity of functional parameters during follow-up. Prognosis was that of a chronic, often debilitating disease, with 21% incidence of apparently permanent sequellae and absence of total remissions. Efficacy of corticosteroids could not be supported from this retrospective analysis.

1666 PHARMACOKINETICS OF TOBRAMYCIN IN CYSTIC FIBROSIS PATIENTS. K. McCoy, W. Banner, Jr., J. Erickson, L. Taussig. Univ. of Az, Departments of Pediatrics and Pharmacology, Tucson (Sponsored by J Corrigan)

It has been suggested that patients with cystic fibrosis (CF) have unusually high renal clearance of aminoglycosides. Pharmacokinetics of tobramycin (TB) were studied in CF patients. Study patients were admitted for exacerbation of pulmonary disease. TB concentration-time data were obtained on the initial and final doses of a ten day course of intensive medical therapy. Additional studies on days 1 and 10 of this regimen include: creatinine clearance, chest X-ray, echocardiography and NIH score. Data were analyzed for a 2 compartment 1st order elimination model using the SPSS Nonlinear regression package. The following kinetic constants ($\bar{\chi}$ ± SEM) were obtained.

	Day 1	Day 10	
Elimination constant (β)	.55 ± .05	.40 ± .04	hr^{-1} ($p<.05$)
Vd-β	.27 ± .02	.34 ± .04	liter/kg
Vss	.24 ± .02	.32 ± .04	liter /kg
TB Clearance	120.1 ± 6.68	106.8 ± 6.1	ml.min/1.73M^2

The range of TB clearance was from 84.5 to 145.6 ml/min/1.732M^2 These data suggest that TB in CF patients exhibits kinetics with a "deep" tissue compartment resulting in a decreasing elimination constant as has been observed in other populations. Contrary to previous suggestions, the clearance of TB appears to be in the range predictable on the basis of glomerular filtration rates when adjusted for surface area and age. It appears that in CF patients appropriate dosing over a range of ages can be achieved using surface area method. (Supported by Eli Lilly, Syva Int'l Companies)

1667 HIGH FREQUENCY OSCILLATORY VENTILATION AS THE INITIAL VENTILATORY MODE IN DIFFUSE ALVEOLAR DISEASE. K Meredith, W Walsh, N Ackerman, R Stoddard, R Bell, D Null, R deLemos (Spon. by J Robatham), Wilford Hall USAF Medical Center, Department of Pediatrics, San Antonio, Texas

We evaluated the effectiveness of HFOV as an initial ventilatory technique in dogs with diffuse alveolar injury. Ten mongrel dogs were treated with oleic acid and placed either on IPPV or HFOV. High frequency ventilation was maintained at 5 Hz with the oscillatory amplitude and mean airway pressure adjusted to achieve optimal oxygenation and ventilation. V_T, respiratory rate and PEEP were regulated during IPPV. Each animal was maintained on the initial pattern for two hours, then the ventilatory modes were reversed. No differences in blood gases, cardiac output, cardiac index, or heart rate were observed when comparing the periods of standard and oscillatory ventilation. Mean airway pressure and pulmonary artery pressures were higher during HFOV, but the differences were not significant. The animals initially ventilated at low rates were better oxygenated throughout both experimental periods. The interval between initiation of IPPV and optimal oxygenation was shorter in animals resuscitated with IPPV.

	Fx baseline value	2hr pH	pCO_2	pO_2	4hr pH	pCO_2	pO_2
Conv-HFOV		1.0	0.8	2.9	1.0	0.9	2.9
HFOV-Conv		1.0	0.9	1.7	1.0	0.9	2.1

These studies suggest that at equivalent proximal mean airway pressures IPPV is more effective in achieving maximal oxygenation in animals with diffuse alveolar injury. The theoretical advantage of HFOV in achieving lower distal pressures may be offset by an increased exposure to oxygen.

1668 INDOMETHACIN ALTERS LUNG OXYGEN INJURY. Thurman A. Merritt, (Spon. by Louis Gluck), Univ. of Cal.-San Diego, Dept. of Pediatrics, La Jolla.

Guinea pig neonates exposed to $F_iO_2 > .9$ for 72 hours have been nown to have an increased total of polymorphonuclear leukocytes PMN) and alveolar macrophages (AM), elevated elastolytic activity easured with Succinyl-ala-ala-ala paranitroanilide and albumin n lung lavage. Directed migration of PMN and AM to 5×10^{-4} M -formyl-l-methionine-L phenylalanine is also increased 32 and 14 old, respectfully, in oxygen exposed guinea pigs compared to air xposed animals. To determine whether a non-steroidal antiinflam-atory agent influenced this response to $F_iO_2 > .9$, 0.5 mg/Kg B.W. day of indomethacin (INDO) was given to newborn guinea pigs at irth and daily while exposed to $F_iO_2 > .9$ and compared to air xposed animals likewise treated.

	Cells per mm^3	Elastase Units/100 µl	Albumin µg/ml	Chemotactic Index
2 Hr. Air	2.3×10^6	1.1×10^{-3}	57	8.5%
2 Hr. Air +INDO	1.9×10^6	0.9×10^{-3}	61	6.1%
2 Hr. $F_iO_2 > .9$	4.49×10^6	5.98×10^{-3}	599	59%
2 Hr. $F_iO_2 > .9$ + INDO	2.72×10^6	1.04×10^{-3}	271	52%

NDO resulted in a reduction in lung lavage inflammatory cells, ung elastase, and a lower lung effluent albumin in guinea pigs xposed at 72 hours $F_iO_2 > .9$. This observation suggests lung amage during oxygen exposure may be modified by prostaglandin ynthetase inhibitors. The mechanism(s) of the altered inflam-atory response in neonatal oxygen exposure remain to be deter-ined.

1669 INHIBITION OF PHOSPHOLIPASE A2 AND BETA ADRENERGIC RESPONSE OF PNEUMOCYTE TYPE II. Neal R Mettler, Bruno P Leheup, Mary E Gray, Mildred T tahlman, Virgil S LeQuire Vanderbilt University, Departments of ediatrics and Pathology, Nashville Tennessee

Surfactant production by pneumocyte type II cells is regulated by ormone-receptor mechanisms. We have shown previously that the beta drenergic agonist terbutaline, 8-bromo-cAMP or Ca^{++} transport timulation enhance choline incorporation into the phosphatidylcholine raction of type II cells in primary culture (Lab Invest 1981 45(6),Fed roc 1981 40(3) 768).These data suggested the involvement of rostaglandins and specifically phospholipase A2 in the beta adrenergic ormone-receptor response. Reported here are a series of experiments hich sought to determine if phospholipase A2 is a key-step of beta drenergic stimulation of cAMP synthesis. Type II cells from mature rats ere isolated and maintained in primary culture for two days, then reincubated 30 min with mepacrine (10^{-6}M), a phospholipase A2 nhibitor, followed by the addition of terbutaline (10^{-5}M) for an dditional 20 min. Results, shown below, are referred to 100% of cAMP ontent of the controls (n=9). Mann-Whitney rank-sum test was used for tatistical analysis.

cAMP	Mepacrine(6)	Terbutaline(5)	Mepacrine+Terbutaline(6)
% of control	74(46-115)	405(160-950)	115(75-180)
U values	15 NS	0<p .01	25 NS

We conclude that terbutaline stimulation of cAMP synthesis was nhibited by pretreatment with mepacrine. This effect could be due to a eduction of the amount of arachinodic acid available for prostaglandins ynthesis through an inhibition of phospholipase A2 activity.

1670 PROMPT REVERSAL OF BRONCHIOLITIS ASSOCIATED RESPIRATORY FAILURE WITH INTRAVENOUS AMINOPHYLLINE.

Andrew P. Mezey, Albert Einstein College of Medicine, Department of Pediatrics, 1300 Morris Park Avenue, Bronx, New York 10461

Bronchiolitis most seriously affects infants under 6 months of age in whom mortality has been estimated to be about 2%. Inability to compensate for airway obstruction may lead to respiratory muscle fatigue and respiratory failure. Since it is known that theophylline may enhance diaphragmatic contractility and relax airways, we treated 9 infants, ages 5–20 weeks, in respiratory failure (tachypnea, wheezing, radiographic hyperaeration, and $PaCO_2 > 45$ torr) with IV aminophylline. We gave 5–9 mg/kg over 20 min followed by 0.5–1.0 mg/kg/hr until the patient was stabilized. Peak serum theophylline concentrations ranged from 7 to 23 mg/L ($\bar{x}$ = 14.5 mg/L). One to 2 hr after IV aminophylline blood gases and pH had improved significantly ($\bar{x}$ given). $PaCO_2$ decreased from 53 to 42 torr ($p < 0.001$); pHa increased from 7.31 to 7.37 ($p < 0.001$); and PaO_2 from 93 to 133 torr ($p = 0.02$) as FiO_2 was lowered from a mean of 0.42 to a mean of 0.37. All clinical indices improved in parallel and there were no signs of untoward side effects or toxicity from theophylline. All patients recovered without assisted ventilation. These studies indicate that respiratory failure associated with bronchiolitis may be reversed rapidly by theophylline and that a trial of theophylline may have obviated the need for ventilatory assistance in these cases.

1671 VENTILATION AND GAS EXCHANGE IN CRYING NEONATES. J. Miranda, M.S. Schimmel, K. Schulze, M. Stefanski, J. Masterson and L.S. James. Columbia Univ.,Coll. of P & S, Div. Perin. Med., Dept. Ped., NY.

Changes in gas stores during crying may complicate blood gas interpretation. This study was undertaken to characterize the changes in minute ventilation ($\dot{V}_I$), oxygen consumption ($\dot{V}O_2$), carbon dioxide excretion ($\dot{V}CO_2$), and respiratory exchange of neonates during crying.

We measured continuously $\dot{V}_I$ (bias flow pneumotachometry) $\dot{V}CO_2$ and $\dot{V}O_2$ (open circuit indirect calorimetry), heart rate (HR) and transcutaneous PO_2 ($TcPO_2$) before, during and after 11 episodes of spontaneous crying in 11 infants ranging in weight from 650 to 3520 grams and in gestational age from 27 to 40 weeks.

$\dot{V}_I$ decreased slightly during the first 30 sec. of crying and then increased, tending to plateau after 4 mins. ($\bar{x}$ peak increase = 140%, range 36 to 302%). $\dot{V}O_2$ and $\dot{V}CO_2$ neared plateaus after 4.5 mins. ($\bar{x}$ peak $\dot{V}O_2$ = 77.4, range 38 to 155%; $\bar{x}$ peak $\dot{V}CO_2$ = 105, range 24 to 211%). HR plateaued 23% above baseline after 2.5 mins. $TcpO_2$ decreased throughout crying ($\bar{x}$ nadir = 9.5%) and increased above baseline following crying ($\bar{x}$ peak = 22%). R/Q did not increase significantly until 3 mins of crying (+.13) and the peak rise occurred following crying ($\bar{x}$ peak = +.21).

The time course of changes in ventilation and respiratory exchange during crying suggest arterial PCO_2 measured during the first 3 mins. of crying is likely to approximate or slightly overestimate resting PCO_2 whereas after 3 min.of crying measured PCO_2 may be spuriously low. Measurements of PaO_2 during crying will underestimate resting PaO_2, however measurements made during recovery from crying may significantly overestimate the resting PaO2.

1672 MATERNAL SMOKING AND THE FETAL LUNG Adrien C. Moessinger, Jorge A. Bassi, Pedro Rosso and William A. Blanc. Columbia University, Dept. of Pediatrics, Pathology and the Institute of Human Nutrition, New York, N.Y.

Cigarette smoking significantly reduces the incidence of fetal breathing movements(FBM). Since FBM are thought to promote lung growth we speculated that maternal smoking has a deleterious effect on fetal lung growth. Using the P.I.Walton Smoke Exposure machine we exposed pregnant rats to tobacco smoke for cycles of 6 min., 16X/day during the last two thirds of gestation. The animals were killed at term(day 21) and the fetuses weighed and dissected. The lungs, liver, brain and placenta were weighed to the nearest .1 mg and analyzed for DNA, RNA and protein contents. The experimental fetuses weighed 78%* of pair-fed controls. The organ/body weight ratios for lungs, liver, brain and placenta were respectively 88*, 90*, 106 and 110 percent of controls. The brain and placental cell numbers and cell sizes were unaffected. The liver contained less cells, 80%*of controls. The lungs contained less cells(DNA: 70%*of controls) and the "average" lung cell size was reduced(Protein/DNA: 90%*of controls). These results indicate that maternal smoking leads to both lung hypoplasia and hypotrophy. This phenomenon might in part explain the higher incidence of pulmonary morbidity seen in association with parental smoking.

*** p value between .05 and .001**

1673 AUTOIMMUNITY IN CYSTIC FIBROSIS: EVIDENCE AGAINST POLYCLONAL B CELL ACTIVATION. Richard Moss, Yao-Pi Hsu (Spon. by John J. Miller) Children's Hospital at Stanford, Palo Alto, CA.

Cystic fibrosis (CF) is characterized immunologically by a high prevalence of atopy, hypergammaglobulinemia, immune complex formation, and a variety of autoantibodies. Most patients are colonized with endotoxin-bearing Pseudomonas, which might be expected to stimulate a polyclonal B cell response. We looked for two markers of this, IgM and IgG rheumatoid factor (RF) production. IgM-RF was detected using a standard latex agglutination test (Hyland). IgG-RF was assayed using a microtiter solid phase radioassay employing purified human IgG Fc fragment (Cappel) as the antigen and ^{125}I-goat Fab'$_2$ antihuman IgG Fab'$_2$ as the detector ligand. Fifty six CF patients were compared to 43 children with chronic rheumatic disease and 39 healthy controls. No normals, 4% of CF, and 19% of rheumatics were IgM-RF⊕. Mean IgG-RF activity of the CF group was not higher than controls (1723±1037 vs 1642±633 net cpm, respectively). Eight of 56 CF patients were IgG-RF⊕ (activity >2 SD>normal mean) as compared to 8/43 of the rheumatic group, but levels of IgG-RF present were lower in the CF patients. The rheumatic group IgG-RF activity was elevated (2512±1875, p<.01); this was due to IgG-RF in the IgM-RF⊕ subgroup. Half of IgM-RF ⊕ but only 11% of IgM-RF ⊖ rheumatic patients had IgG-RF (p<.05). Predigestion of sera with pepsin did not alter results, indicating primary binding of IgG-RF to IgG Fc antigen. Multiple, prolonged antigenic stimulation rather than polyclonal B cell activation is the likely basis of the florid humoral immune response in cystic fibrosis.

1674 EVIDENCE OF BRONCHIAL HYPERREACTIVITY IN INFANTS WITH SEVERE BRONCHIOLITIS. Etsuro K. Motoyama, George Lister, George B. Mallory, Peter H. Mestad, Peter Rothstein, and Frank T. Weng. Univ. of Pittsburgh Sch. of Med., Children's Hosp. of Pittsburgh, Depts of Anesthesiology and Pediatrics, Pittsburgh, PA, and Yale Sch. of Med., New Haven,CT.

Acute bronchiolitis in infants may be complicated by hyperreactive airways. However, bronchodilators are not recommended in practice because of unsubstantiated belief that smooth muscles are not developed in this age group. We studied 5 infants (6 weeks to 13 months) with bronchiolitis who were in respiratory failure and were mechanically ventilated. Reproducible maximum expiratory flow-volume curves (MEFVCs) were obtained by inflation of the lung to 30cmH_2O of airway pressure followed by forced deflation with negative airway pressure (-30cmH_2O) via a pneumotachograph. Flow and volume signals were displayed on an X-Y storage oscillograph for analysis (Pediat. Res. 11:220, 1977). There was a significant ($p<.001$) reduction in FVC by deflation for 3 seconds (FVC = 35.0 ± 3.7% (SEM) pred.) and maximal expiratory flow at 25% FVC (MEF_{25} = 11.5 ± 3.2% pred.) in all 5 infants indicating volume loss due to air trapping and severe lower airway obstruction. Three patients received IV isoproterenol (0.3µg/kg/min). Two other patients received nebulized isoetharine in whom nebulized saline showed no effect on FVC and MEF_{25}. After beta agonist, MEF_{25} increased in all 5 by 151.4 ± 22.6% ($p<.05$) to a new mean of 23.2 ± 3.5% predicted. FVC increased in 3 but was unchanged in 2. The results demonstrate that young infants have functional airway smooth muscles and severe bronchiolitis is often complicated by hyperreactive airways.

1675 PROSTAGLANDINS (PG) GLUCOSE AND FETAL BREATHING MOVEMENTS (FBM). Daniel T. Murai, Chu-Ching H. Lee, Ronald I. Clyman and Joseph A. Kitterman. Cardiovasc. Res. Inst. and Dept. Peds., Univ. of Calif., San Francisco, CA.

The physiological factors that control FBM are not known. PG synthetase inhibitors (PGSI) stimulate FBM to occur continuously whereas both PGE_2 and hypoglycemia inhibit FBM. To define possible relationships between PG and fetal plasma glucose concentration ([G]) and their effects on FBM, we studied 7 chronically catheterized fetal sheep at gestational ages 126-135 days. We gave a total of 5 infusions of each of the following: (a) glucose (50 $mg \cdot min^{-1}$) for 16 h; (b) meclofenamate, a PGSI (1.2 $mg \cdot h^{-1}$), for 18 h; (c) PGE_2 (2 $\mu g \cdot min^{-1}$) for 3 h followed by (d) PGE_2 and glucose for 10 h. Results (mean ± SEM) are shown below:

	Control	Glucose	PGSI	PGE_2	PGE_2 + Glucose
Incidence of FBM (%time)	37±1	42±6	80±4	3±2	7±4
Plasma glucose ($mg \cdot dl^{-1}$)	18±1	49±3	20±3	20±3	43±5

As in previous studies, PGSI stimulated and PGE_2 inhibited FBM; neither affected [G]. Glucose infusions, alone or during PGE_2 infusions, had little effect on FBM. Thus, effects of PGSI and PGE_2 on FBM are independent of [G]. During PGSI infusions, PGE_2 concentrations decreased to < 5% of control and were similar to those in newborn lambs. These results support the hypotheses (a) endogenous PGE_2 inhibits FBM and (b) a change in PG metabolism contributes to the change in control of breathing at birth.

1676 GASTROESOPHAGEAL REFLUX & STRIDOR IN INFANCY. Dennis W. Nielson and Gregory P. Heldt (Spon. by Lowell A. Glasgow). University of Utah, Department of Pediatrics Salt Lake City, & University of California, Cardiovascular Research Institute & Department of Pediatrics, San Francisco.

We evaluated 8 infants, age 6 wks to 6 mos, who had gastroesophageal reflux and stridor to see if these 2 problems were related. Stridor began at 11 d to 2 mos, and 4/8 were in respiratory failure prior to study. None had a history of frequent vomiting, but 3 had recurrent pneumonia. Laryngoscopy and bronchoscopy done in 4 revealed laryngeal inflammation only. In 6/8, we recorded mid-esophageal pH, chest and abdominal movement, exhaled CO_2, skin surface O_2, and heart rate for 4 to 12 hrs as they slept. In the other 2, we recorded esophageal pH for 12 to 24 hrs. All had an esophageal pH <4 for > 5% of the study, and at least one episode lasted > 5 min. Of the 6 studied extensively, there were increases of 10 Torr in exhaled CO_2 (3/6), 10 bpm in resp rate (4/6), and retractions (6/6) 5-10 min after onset of reflux. After anti-reflux surgery, stridor disappeared in 48 hrs (3/4) to 3 wks (1/4). Stridor improved with medical management (upright posture and Bethanechol 8.7mg/m^2/d) in 48 hrs (4/5) and disappeared in 3 wks (2/5).

Our results indicate that reflux caused stridor and continuous airway obstruction in these patients, probably due to acute inflammation of the upper airway. Because there was no history of recurrent vomiting in any of these patients, gastroesophageal reflux should be considered in any infant with stridor, especially when there is a history of recurrent pneumonia or when there is no evidence of malacia of the larynx or trachea.

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1677 ADSORPTION PATH DEPENDENCE IN PHOSPHOLIPID DISPERSIONS by R.H. Notter, R.D. Taubold, and J.N. Finkelstein (Spon: D.L. Shapiro) Univ. of Roch., Roch., NY 14642.

The adsorption of aqueous dispersions containing dipalmitoyl phosphatidylcholine (DPPC) was studied at 34-37°C as a function of dispersion technique (e.g. sonication, vortexing, temp. control). Surface pressure-time (π-t) isotherms were measured for pure DPPC, 9:1 DPPC:dipalmitoyl phosphatidylethanolamine (DPPE), 7:3 DPPC:egg phosphatidylglycerol (PG), lipids extracted from cow lung lavage (CLL), and 5:5 DPPC:CLL. Adsorption π-t behavior for a given mixture differed significantly as a function of the method of initial dispersion in 0.15 M NaCl (5 mg total phospholipid/80 ml subphase). For example, 7:3 DPPC:PG adsorbed more rapidly after dispersion by sonication on ice than after sonication without temperature control. Heating to T=45°C (greater than the gel to liquid crystal transition temperature T_c=41°C for DPPC) was particularly detrimental to the adsorption of 7:3 DPPC:PG in terms of both quantitative and qualitative changes in the π-t isotherm. Extracted CLL (< 1% protein) exhibited the greatest adsorption capability, with small path dependence; π values of 45 dynes/cm were reached in seconds for CLL dispersions. By contrast, 7:3 DPPC:PG gave π=35-40 dynes/cm only after several hours following sonication on ice. Dispersion by sonication in an ice bath generally gave the most rapid adsorption for each mixture studied, consistent with interpretations based on maximum liposomal surface area at a given bulk concentration. Adsorption dependence on dispersion method correlates with the existence of multiple physical states in solution for phospholipid mixtures. (HL-25170;1K04-HL-00945).

1678 MEASUREMENT OF TOTAL RESPIRATORY RESISTANCE IN CHILDREN BY A MODIFIED FORCED OSCILLATION (F.O.) METHOD. E. Nussbaum, B Jeanotte, S Galant, Pediatric Pulmonary Center, Miller Children's Hospital, University of California, Irvine.

Total respiratory resistance (R_T) was measured in 20 children (11 with bronchial asthma, 2 cystic fibrosis, 7 normals) mean age 6.5 years (range 3 to 13 years) by oscillating the respiratory system from 2 to 32 Hz implementing a new microprocessor technique. Thirteen children were ≤6 years of age. This technique was also compared to airway resistance (R_{aw}) by body plethysmography both in terms of baseline values and response to bronchodilators in 3 children and 11 adults. There was an excellent correlation between both the R_T at resonant frequency ($F.O._{RF}$) and average R_T at multiple frequencies ($F.O._{AVF}$) and the childs' height with r value of -0.81 and -0.85 respectively in the 20 children studied. R_{aw} correlated very well with both $F.O._{RF}$ and $F.O._{AVF}$ r=0.79 and 0.72 respectively. Mean (±SEM) R_T at $F.O._{RF}$ and $F.O._{AVF}$ was 2.98 ± 0.22 and 3.20 ± 0.20 cm H_2O/L/s respectively compared to R_{aw} of 2.08 ± 0.23 cm H_2O/L/s. Measurements of R_T were significantly greater than R_{aw} ($P < 0.01$). Following isoproterenol aerosol inhalation (0.5%) in children and adults with obstructive airway disease R_{aw} decreased 16.64 ± 4.93% compared to 15.79 ± 2.61% for $F.O._{RF}$ and 13.88 ± 2.26% for $F.O._{AVF}$. The difference between R_{aw} and R_T changes were not significant ($P > 0.05$). R_T utilized in this study is a rapid and reproducible approximation of the R_{aw}. It requires far less cooperation than plethysmography and allows objective assessment of obstructive airway disease and its responsiveness to bronchodilators in young children.

1679 ENDORPHINS, RESPIRATORY FAILURE AND RESPONSE TO NALOXONE. James P. Orlowski, Derrick Lonsdale, Douglas S. Moodie and Susan Rose (Spon. by William M. Michener). Cleveland Clinic Foundation, Cleveland, Ohio

Two children with respiratory failure and cor pulmonale secondary to the obesity hypoventilation syndrome were found to have abnormal levels of human β-endorphin in cerebrospinal fluid and plasma. A 3.75 year old boy with Prader-Willie Syndrome (weight 48.2 kg) had a CSF β-endorphin level of 66 pg/ml and a plasma level of 14 pg/ml and a 20 month old girl with the Pickwickian Syndrome (weight 24 kg) had a CSF β-endorphin level of 47 pg/ml and a serum level of 65 pg/ml. Normal levels of β-endorphin are 110 ± 10 pg/ml in plasma and less than 15 pg/ml in CSF. A single intravenous dose of naloxone (10 µgm/kg) early in the course of respiratory failure resulted in dramatic improvement which lasted 3-4 hours. Both children failed to respond to digitalization, diuresis and a trial of progesterone. The 20 month old girl was treated with a continuous low-dose infusion of naloxone initially at 2 µgm/kg/hour and gradually increased to 10 µgm/kg/hour with a dramatic improvement in respiratory status and clinical condition. $PaCO_2$ decreased from 60-70 mmHg to 38-42 mmHg while on the continuous low-dose naloxone infusion. After five days the naloxone infusion was discontinued and progressive respiratory deterioration recurred. Both children died of overwhelming sepsis and disseminated intravascular coagulation.

Narcotic antagonist therapy may have therapeutic value in patients with respiratory insufficiency secondary to the obesity-hypoventilation syndrome.

1680 DISCORDANCES IN BIOCHEMICAL AND PHYSIOLOGICAL DEVELOPMENT OF THE FETAL PRIMATE LUNG R. Perelman, M. Engle, J. Kemnitz, R. Kotas, P. Farrell, Univ. of WI., Dept. f Pediatrics, Madison, WI.

Study of 17 fetal rhesus monkeys (Macaca mulatta) at 135, 145, 55 or 162 days gestation (term=165 days) revealed a linear progression in growth. A sequential rise was noted in lung phosphatidylcholine (PC), due to elevations in both saturated (DSPC) and nsaturated constituents. The percent DSPC was found to climb bruptly at 145 days of gestation prior to significant increases n PC or DSPC concentration but in association with improved lung eflation stability ($\%V_{10}$). This suggests that the DSPC/PC ratio ay be a sensitive biochemical indicator of surfactant phospholipid production in lung parenchyma. The proportion of saturated atty acids in PC increased from 67.5% to 77.7% between 135 and 55 days gestation consistent with rising DSPC concentrations. In ontrast to the timing of changes in PC and DSPC, phosphatidylglycerol did not increase significantly until after 155 days gestation; this was coincident with maximizing pulmonary distensibility (V_{max}). Declining levels of phosphatidylethanolamine and phingomyelin were also noted in lung tissue at 162 days, supporting the hypothesis that preferential synthesis of PC occurs during ate gestation. A serial decline in lung glycogen content with advancing gestation [inversely related to rising PC (r=0.81) and DSPC (r=0.95) concentrations] may reflect glycogen utilization as substrate for lung phospholipid production. A relationship between rising fetal blood cortisol levels and indices of fetal lung levelopment was not demonstrated. Comparison of biochemical and hysiological data indicates that discordances occur among lung aturational events.

1681 PROSTAGLANDIN D_2 PREVENTS HYPOXIC PULMONARY VASOCONSTRICTION IN NEONATAL LAMBS. Joseph Philips, Michael McDevitt, Raymond Lyrene, Celia Satterwhite, George assady. University of Alabama in Birmingham, The Division of erinatal Medicine, Department of Pediatrics.

PGD_2 dilates fetal pulmonary vessels without altering systemic ressures. Adult lung vessels constrict with PGD_2; systemic vessels constrict or dilate, depending on the species. Newborn lambs show pulmonary dilatation with low, and constriction with igh doses, again without systemic effect. However, the drug in hese studies all passes through the lung before entering the ystemic circuit, raising a question of intrapulmonary drug nactivation. We studied the effect of both pulmonary and ystemic injections of PGD_2 on hypoxia-induced pulmonary asoconstriction in 9 lambs ($\leq$ 5 days). Each received a pulmonary flow probe, left atrial (LA), pulmonary (PA), systemic (SA), and central venous (IVC) catheter. The ductus was tied. After a 1 minute control period, PGD_2 was infused at 1 or 10 $\mu g/kg \cdot min$ in the LA or IVC. Four minutes later, 5% O_2 was given for one minute, followed by return to control gas and cessation of PGD_2. Mean pulmonary vascular resistance doubled with hypoxia and no PGD_2 (31 $\pm$ 4 to 62 $\pm$ 12 mm Hg/L·min ($\bar{x}$ $\pm$ SEM)). PGD_2 in all 4 dose schedules prevented this rise. $\overline{SAP}$ was not significantly affected by any dosage schedule, or by hypoxia. Thus, PGD_2 prevented hypoxic pulmonary vasospasm while maintaining systemic pressures. These data confirm a need for further studies to probe the potential value of PGD_2 in the relief of pulmonary vasospasm in neonatal and pediatric patients.

1682 1,25-DIHYDROXYVITAMIN D LEVELS IN CYSTIC FIBROSIS (CF) J. W. Pike, S. M. Brugman, E. Reiter, M. Pitt, S. Dokoh, and L. M. Taussig. Departments of Biochemistry, Pediatrics, and Radiology, University of Arizona Health Sciences Center, Tucson; Baystate Medical Center, Springfield, MA.

Abnormalities in bone mineral status have been observed in CF. This phenomenon has been attributed to a defect in vitamin D metabolism, since recent studies suggest a depression of 25-hydroxyvitamin D_3 ($25(OH)D_3$) in CF patients. In order to examine this problem further, we measured the extent of bone mineralization (radiographic morphometry), serum Ca^{++} and PO_4, and both 25(OH)D (competitive protein binding assay) and 1,25-dihydroxyvitamin D ($1,25(OH)_2D$) (radioreceptor assay) in 20 patients from Massachusetts and Tucson during summer and winter. The CF patients had vitamin D_3 intake levels twice that of age-matched controls. Carotene levels were less than 50% of the control values. Patients, as compared to controls, demonstrated slight bone demineralization (89%), slight hypocalcemia (9.0 vs. 9.5 mg%), and normophosphatemia (4.5 vs. 4.4 mg%). 25(OH)D was significantly ($p < 0.05$) depressed only in Tucson patients (49 $\pm$ 16 vs. 68 $\pm$ 21 ng/ml), but all values were well within the normal range for this metabolite. Circulating $1,25(OH)_2D$ levels were lower ($p < 0.052$) in the CF patients (50.5 $\pm$ 15 vs. 60.8 $\pm$ 18 pg/ml), but all values were well within the normal range. Since $1,25(OH)_2D_3$ is considered to be the active hormonal metabolite of vitamin D, these data suggest that defects in bone mineral status in patients with CF are not due to alterations in vitamin D_3 metabolism.

1683 NEONATAL HIGH FREQUENCY JET VENTILATION. Thomas J. Pokora, Dennis R. Bing, Stephen J. Boros, Children's Hospital, St. Paul, and University of Minnesota, Department of Pediatrics, Minneapolis, MN

High frequency jet ventilation (HFJV) is a new form of mechanical ventilation that employs minute tidal volumes and extremely rapid ventilatory rates. HFJV has been used successfully in the treatment of respiratory failure in adults and older children. This report describes its use in a group of neonates. Ten neonates with progressive respiratory failure were ventilated with HFJV when conventional mechanical ventilation failed. Five patients survived. Following HFJV, PaO_2/FiO_2 increased in eight patients ($p < 0.05$), $PaCO_2$ values decreased in nine ($p < 0.01$), and pH values increased in nine of the ten patients (p = NS). Nine of the ten patients had intractable pulmonary air leaks - either bronchopleural fistulas or pulmonary interstitial emphysema. Following HFJV, x-ray evidence of pulmonary air leaks decreased in seven of the nine. Six patients were exposed to HFJV for more than 20 hours. Three developed significant tracheal obstructions - one was fatal. From this experience, we conclude: HFJV can successfully ventilate certain neonates with respiratory failure refractory to conventional therapy; in its present form, long-term neonatal HFJV carries the risk of airway obstruction and/or damage.

1684 MEASUREMENT OF ESOPHAGEAL PRESSURE IN NEWBORN INFANTS USING A BALLOON CATHETER SYSTEM. Thomas J. Pokora, Mark C. Mammel, Theodore R. Thompson, Gerald D. Ebert, Stephen J. Boros, Children's Hospital, St. Paul, and University of Minnesota, Department of Pediatrics, Minneapolis, MN

Esophageal balloon catheter systems have long been used to measure esophageal pressures (Pes) in adults. There is little experience with, and few standards for, neonatal Pes measurements. This report describes a standard technique for Pes measurements in mechanically ventilated neonates using a new neonatal esophageal balloon catheter system. The esophageal balloon is positioned in the distal esophagus and inflated with a volume of air previously determined by static pressure volume curves. Serial measurements are then made in one position. Measurements made in three different positions differed significantly from one another. Measurements made in the supine position were higher than those made in either the right or left lateral position ($p < 0.005$). Four different Pes wave forms associated with cardiac contractions, mechanical respiration, skeletal muscle activity, and esophageal peristalsis were observed. Neonatal Pes measurements made using this technique and this new balloon catheter system were accurate and reproducible.

1685 TREATMENT OF SEVERE NEONATAL BRONCHOPULMONARY DYSPLASIA WITH DEXAMETHASONE. Jeffrey J. Pomerance and Asha Puri. UCLA School of Medicine, Cedars-Sinai Medical Center (CSMC), Department of Pediatrics, Los Angeles.

Between 1974-1980, 13 infants at CSMC with severe bronchopulmonary dysplasia (SBPD) were treated with dexamethasone (D). Mean birth weight was 1075 grams (range 740-1660) and mean gestational age was 28.3 weeks (range 25-30). Diagnosis of SBPD was made on the basis of a need for increasing ventilatory support plus radiographic changes. A parenteral dose of D (0.2-0.6 mg/kg), was given every 8 hours for a planned short course of 3 days to infants ranging in age from 7-50 days.

Eleven of 13 infants showed a decrease in PCO_2 within 3-14 hours of initiation of therapy, thus permitting a decrease in peak inspiratory pressure by an average of 9 cm of H_2O (range 3-14) within 72 hours. FiO_2 requirements decreased by an average of 0.12 (range 0-0.36). Three of the 11 responders were extubated following a short course of D therapy. Seven infants regressed after D was stopped, and were given a second course of D treatment lasting 17-68 days.

Complications of therapy included: pneumothorax -5, hyperglycemia -4, sepsis -4, necrotizing enterocolitis -3, hypertension -1, and osteomyelitis -1. Nine of 13 infants died (age 3-40 weeks). Five died of respiratory failure; 4 deaths could be attributed, in part, to complications of D therapy.

D may be an important adjunct to therapy in infants with SBPD. Mechanism of action and optimal dose are unknown. The decision to use D in the treatment of SBPD should be weighed against the serious complications of therapy.

1686 SOME DIFFICULTIES WITH HIGH FREQUENCY OSCILLATOR (HFO) AND INTERRUPTOR (HFI). Tonse Raju, Bert Braverman, Won Dong Kim, Uday Nadkarny, Dharmapuri Vidyasagar, ALSM, University of Illinois Hospital, Department of Pediatrics, Chicago.

We evaluated two protypes of Emerson HF ventilators: HFO, a compact oscillator with a displacement volume of 25 ml and a fixed oscillation of 28 HZ/min and HFI, which interrupts high airflow at rates 5-500 HZ/min. Anesthetized adult rabbits (#6) and cats (#4) were used. In all rabbits, vital signs and blood gases were monitored and in 2 mean airway pressure (MAP) of 4-6 Torr at the tracheal carina, was maintained. In cats, in addition, $TcPO_2$ and $TcPCO_2$, cardiac output (CO) by a thermodilution technique, intracranial pressure (ICP) via the cisterna magna and pulmonary artery and right atrial pressure (PAP and RAP) were monitored. RESULTS: I. In rabbits: HFI with 28 HZ produced progressive hypoxia, hypercapnea and mixed acidosis by 25-48 mins.($\bar{x}$ values: PO_2 38.7 and 15.2 Torr, PCO_2 47.9 and 53 Torr and pH 7.22 and 7.19 respectively). HFO did not produce hypercapnea, but a drop in PO_2 was noted by 60 minutes (PO_2 45.7, PCO_2 26.3 Torr and pH 7.5). 3/6 rabbits developed pneumothorax and 1 had pneumoperitoneum. II. In cats: With MAP of 4-6 Torr both HFO and HFI produced identical results. For up to 2 hours PO_2 in room air remained between 98 to 125 Torr, PCO_2 dropped progressively from 30 to 19 Torr and pH rose from 7.36 to 7.47. Because of severe hypocapnea $\Delta TcPO_2$-PO_2 was from 50-80, $\Delta TcPCO_2$ and PCO_2 dropped from 43 to 30. ICP (6-8 Torr), PAP (14.5-16.5 Torr), RAP (6.5-7.5 Torr) and CO (0.46-0.52 L/min) remained constant through the 2 hour period. We conclude that although HFO and HFI are hailed as panacea, several problems have to be dealt with in laboratory animals before clinical use; in general cats proved to be superior models than rabbits.

1687 OXY-HEMOGLOBIN DESATURATION DURING SLEEP IN BOYS WITH MUSCULAR DYSTROPHY(MD) Gregory J. Redding, Robert D. Guthrie, Jerrold M. Milstein, Gary A. Okamoto (Spons. by David E. Woodrum) Univ. of Washington School of Medicine, Children's Orthopedic Hospital, Dept. of Pediatrics, Seattle.

We studied 4 wheelchair-bound boys, 13-17 years old, with Duchenne's MD during sleep to see if nighttime oxy-hemoglobin desaturation(S_aO_2) occurs in those children with severe restrictive lung disease. All had scoliosis(spine curves=40±15°) but none were obese. All had a reduced vital capacity(39±26% pred.), FEV_1(31±15% pred.), and Peak Expiratory Flow(29±19% pred.), as well as respiratory muscle weakness (Peak inspiratory pressure= -50±9 cmH_2O and Peak Expiratory Pressure=54±17 cmH_2O). 7.5±0.5 hours of sleep were studied using ear oximetry, end-tidal capnography, nasal and oral thermistors, impedance pneumography, EEG, electro-oculograms, ECG, and observation. S_aO_2=97.5±1% and end-tidal CO_2 pressure($P_{ET}CO_2$)=42±2torr for the group while awake. During sleep, all 4 boys had 1 or more falls in S_aO_2 of >4%, to an average of 92±1%; the lowest S_aO_2=88%. However, periods of S_aO_2<95% lasted 56±11 seconds and constituted 1.7±1.1% of total sleep time. During these periods, $P_{ET}CO_2$ rose by 8±2torr, chest wall excursion fell to 70±18% of awake levels, and airflow at the nose and mouth fell by 55±15%. No periods of central or obstructive apnea were identified. We conclude that intermittent hypoventilation occurs during sleep in boys with severe MD but that oxy-hemoglobin desaturation is neither frequent nor severe enough to constitute a pathophysiologic feature at this stage of the disease.

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● **1688** ROLE OF INSPIRATORY SUCTION AND MUSCLE HYPOTONIA IN OBSTRUCTIVE SLEEP APNEA (OSA). William R. Reed, John L. Roberts, Bradley T. Thach. Washington University Sch. of Med., Department of Pediatrics, St. Louis.

We used an experimental model to evaluate two current theories for the mechanism of pharyngeal closure during OSA. According to one view, the combined effects of inspiratory suction and genioglossus muscle (GG) flaccidity force the tongue backward against the posterior pharyngeal wall. However, clinical observations during OSA show not only posterior movement of the tongue, but also, inward movement of the lateral pharyngeal walls suggesting contraction of pharyngeal constricting muscles causes the closure. To see how negative airway pressure effects the tongue and lateral pharyngeal walls in the absence of muscle tone, we used endoscopy to study 12 infant cadavers. Suction was produced using a catheter and syringe; results were documented with photography and water manometry. Negative pressure (-1.5 to -12cm H_2O), simulating inspiration, caused a pattern of pharyngeal closure similar to that observed during clinical episodes of OSA; inward movement of the lateral walls as well as posterior movement of the tongue caused the closure. We also simulated GG contraction by applying force on the hyoid bone with a suture; this caused increase in both the lateral and A-P airway dimensions, indicating that GG tone and airway suction have opposite effects. These studies support the hypothesis attributing pharyngeal airway closure during clinical apnea to GG flaccidity and negative inspiratory pressure, since the pattern of closure produced by simulating these conditions experimentally is similar to that observed clinically.

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1689 EFFECT OF 3% CO_2 AND ABDOMINAL LOADING ON DIAPHRAGMATIC EMG IN PRETERM INFANTS DURING SLEEP. Francisco Reis, Don Cates, Leanne Horvath and Henrique Rigatto. Dept. of Pediatrics, University of Manitoba, Winnipeg, Canada.

To determine the effects of CO_2 and abdominal loading on diaphragmatic EMG during sleep, we studied 10 preterm infants (BW 1.6 to 2.1 kg; GA<37 wks). We measured surface (D_S) and esophageal (D_E) diaphragmatic EMG, $\dot{V}_E$, V_T, f, Ti, Te, V_T/Ti and Ti/T_{tot}. D_S and D_E were analyzed for integrated electrical activity (EMG_i), total (TPA) and expiratory (EPA) phasic activity, EPA/TPA, and presence of "tonic" activity. In non-REM sleep, 3% CO_2, $\dot{V}_E$ increased (.392 to .616 L/min, p<.001), due to a primary change in V_T (15 to 19, p<.006), V_T/Ti increased (28 to 34, p<.02) with no change in Ti/T_{tot}. Similar changes were observed in REM sleep. In both non-REM and REM sleep EMG_i increased (11.7 vs 28.2 uV, p<.01, 10.3 vs 15.7 uV, p<.02, respectively), but TPA, EPA, EPA/TPA and "tonic" activity did not change. Abdominal loading (sand bags) did not alter $\dot{V}_E$ or the "structure" of V_T, but it did increase TPA (0.68 to 0.78, p<.03), EPA (0.21 to 0.32, p<.01), EPA/TPA (0.28 to 0.39, p<.03) and tonus (4 to 25%, p<.04) of D_S, particularly in REM sleep. D_E behave similarly. We suggest: 1) In healthy preterm infants, inhaled CO_2 alters the "structure" of V_T and diaphragmatic EMG in exactly the same manner; peak activity increases, timing and tonus are not changed; 2) Abdominal load does not alter the "structure" of V_T but does change the "structure" of D_S and D_E significantly with increase in Te and tonus. (Supported by Medical Research Council of Canada, MA 4980).

1690 EFFECTS OF LUNG VOLUME ON LUNG MECHANICS IN NORMAL AND EDEMATOUS LUNGS. Peter Richardson, (Spon. by Lowell Glasgow). University of Utah College of Medicine. Department of Pediatrics, Salt Lake City, Utah.

We measured the functional residual capacity (FRC), lung compliance (C) and pulmonary resistance (R) in 20 cats on PEEP at levels ranging from -8 to +10 cm H_2O. Negative PEEP was used to induce atelectasis in healthy lungs. We induced hemorrhagic pulmonary edema (alloxan, 75 mg/kg) then repeated measurements at PEEPs from 0 to 10 cm H_2O. Computerized N_2 washout was used to measure FRC; a syringe pump supplied smooth sinusoidal pressure waves (0.5 H_z) for lung mechanics measurements. At 9 cm H_2O (ZEEP) edema caused a 38% decrease in FRC, 66% decrease in C and 175% increase in R, all differences were statistically significant (p<.001). Increases in PEEP caused significant increases in FRC (p<.001) at all PEEP levels in both control and edema groups. At 4 cm H_2O PEEP, FRC (edema) reached 24.6 ± 1.8 ml/kg (mean ± SE) which was near control levels of 24.2 ± 1.4 ml/kg measured at ZEEP. C (control) was a maximum at ZEEP (8.7 ± 1.4 ml/cm H_2O and decreased significantly as PEEP was raised or lowered. C (edema) was a maximum 3.7 ± 0.4 ml/cm H_2O at a PEEP of 4 cm H_2O. Major changes in R occurred as FRC decreased in both groups. PEEP caused R (edema) to decrease from 81.1 ± 19.7 (ZEEP) to 44.2 ± 6.5 cm H_2O/ℓ/sec (4 cm H_2O). These results show that 1) decreases in the FRC of a) healthy and b) edematous lungs adversely affects both C and R and 2) in edema PEEP may be used to improve C and R as well as to counter atelectasis and 3) optimal lung mechanics exist when FRC is near normal values in healthy and edematous lungs.

1691 DOES SEQUENTIAL TECHNIQUE AFFECT BRONCHODILATOR RESPONSE TO A B_2 AGONIST? J. Rivlin and H. Levison The Hospital for Sick Children, Department of Pediatrics, Toronto, Ontario, Canada.

There is no uniformly accepted technique for the use of pressurized bronchodilator aerosol administration. Product instruction leaflets give varying advice regarding time of aerosol release in relation to inspiration, rate of inhalation and duration of breath-holding. If these technical details are important then small children may be unable to comply with the instructions, thus raising doubts about the adequacy of these products for younger age groups. The effectiveness of aerosol administration in 27 children aged 5-20 years with bronchial asthma was studied. Baseline FEV_1 was measured. The patient was then asked to open his mouth and the aerosol was administered into the open mouth. No further instructions were given to the patient. FEV_1 was measured at 10 and 30 minutes after the aerosol. Group 1 patients (n = 19) who received 200 ug fenoterol were divided into two subgroups on the basis of baseline FEV_1. Group Ia (n=10) aged 5 - 11 years with baseline FEV_1 = 33.9% predicted had a mean increase in FEV_1 of 19.9%. Group Ib (n=9) aged 10-20 years with baseline FEV_1 = 64.4% predicted had a mean increase of 19.4%. Group II patients (n=8) who received 400 ug fenoterol with baseline FEV_1 = 65% predicted had a mean increase in FEV_1 = 19.3%. There was no difference in response between 200 ug and 400 ug fenoterol doses. We conclude that pressurized aerosols may, therefore, be useful in small children who cannot comply with the manufacturers instructions.

1692 A CLINICAL TEST OF PHARYNGEAL AIRWAY (PAW) STABILITY. John L. Roberts, Oommen P. Mathew, William R. Reed, and Bradley T. Thach. Washington Univ. School of Medicine, Dept. of Pediatrics, St. Louis, Missouri 63110.

The PAW is prone to collapse when exposed to the negative pressure associated with inspiration. In certain patients with obstructive sleep apnea, PAW instability leads to episodes of PAW closure. No clinical test of PAW stability is available. We have adapted the closing pressure (CP) determination of PAW stability, previously used in animal studies, for use in infants; the CP is the negative pressure required to close the PAW. In 4 infants with the Pierre Robin Syndrome and obstructive apnea, we recorded pressure in the nares, pharynx and esophagus. We intermittently occluded a nasal prong airway at end expiration. As the PAW pressure fell during subsequent inspiratory efforts, the PAW closed as indicated by the failure of the pressure in the pharynx and esophagus to be transmitted to the nares; the nares pressure at PAW closure is the CP. Multiple CP determinations in a given infant had low variability (mean coefficient of variation = 34%). Values for the infant with the least stable PAW differed significantly from those of the infant with the most stable PAW (CP = -6.1±1.1 vs. -9.3±.8cm H_2O; P<0.001). In one infant nasal occlusion extending over several breaths showed progressive improvement in PAW stability (i.e. more negative CP with subsequent breaths). This suggests mechanoreceptor or chemoreceptor mediated recruitment of PAW dilating muscles. We conclude that the CP is a measure of the stability of the PAW which could have clinical applications in determining risk for obstructive apnea.
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1693 DIFFERENCE IN RESPIRATORY RESPONSE OF HEART AND BRAIN MITOCHONDRIAL ACTIVITY FOLLOWING CARBON MONOXIDE (CO) INHALATION IN GUINEA PIGS. Linda M. Sacks, David W. Herbert, Ann Godart-Wlodaver and Maria Delivoria-Papadopoulos. Univ. of PA., Depts. of Physiology and Pediatrics, Phila., PA.

Tissue mitochondria exposed in-vivo to hypoxic stress adapt by increasing state 3 respiratory activity. The present study investigates the adaptive response of cardiac and brain mitochondria to increased but similar levels of blood carboxyhemoglobin (COHb). Brain and subsarcolemmal cardiac mitochondria were isolated from 29 guinea pigs after 1 hr of inhalation of varying levels of CO. State 3 respiratory rate (RR), state 4 RR (nmol O_2 min^{-1} $nmol^{-1}$ cytochrome oxidase ± SEM), respiratory control ratio (RCR) and rate of Ca^{2+} uptake were assayed. In heart mitochondria, state 3 increased linearly (r=.85, p<.005) from 340 at 0.5% [COHb] to 630 nmol O_2 at 40% [COHb]. There was an inverse correlation of state 3 RR and O_2 content. Ca^{2+} uptake correlated linearly with increasing [COHb] (r=.67, p<.05). In the brain, correlation of state 3 RR to [COHb] was hyperbolic (r=.7, p<.002) as brain mitochondria achieved markedly increased state 3 RR at relatively low [COHb], sustaining it through 80% [COHb]. Brain mitochondria from animals exposed to CO had higher state 3 RR than controls (506±36 vs. 258±33 nmol O_2, p<.005) and higher RCR (8.1±.3 vs. 6.3±.1, p<.05). There was no difference in brain state 3 RR between animals with 12-40% [COHb] and those with 41-80% [COHb]. These data indicate that differences in heart and brain cellular respiration, as shown by the variability of mitochondrial adaptive response, may be intrinsic to tissue-specific mitochondria or may reflect inherent characteristics of microcirculatory adjustments to O_2 requirements.

1694 HYPOXANTHINE (Hx) AND O_2 INDUCED LUNG DAMAGE. A BASIC MECHANISM MEDIATED BY FREE RADICALS? Ola D. Saugstad, Mikko Hallman, Jerrold L. Abraham, Charles Cochrane, Louis Gluck. Univ. California, San Diego, UCSD Med. Ctr., Dept. Ped.&Path., & Scripps Clinic & Research Foundation, La Jolla, CA.

Metabolism of Hx may generate O_2 radicals, which, if elevated, may be a major factor in lung damage during hyperoxia. Study rats were treated with 100% O_2 and continuous i.v. Hx for 48 h (Group 1). Controls: Untreated (Group 2): Hx + room air (Group 3): O_2 + glucose i.v. (Group 4). Group 1 showed significantly more lung hemorrhage and alveolar edema (p<01) than the others and had elevated levels of α_1-antitrypsin (α_1-PI) in lung lavage, suggesting acute inflammation. No elastase was found.

	group 1	group 2	group 3	group 4
α_1-PI (µg/mg)	16.0±8.5	3.3±2.0	7.6±5.6	4.8±5.4
p (vs group 1)		<0.005	<0.005	<0.01

The distribution of phospholipids in lung lavage from group 1 did not differ from the controls. However, the surface activity in lavage from group 1 was inhibited, as evidenced by a higher minimum surface tension and a faster surface collapse rate than in the other groups. The protein-rich fraction of lavage from groups 1 and 4, increased minimum surface tension of lung surfactant. Conclusion: Hx and O_2 in combination are destructive to lung tissue, possibly due to increased free radicals. Hx accumulates in neonatal hypoxia, and free radicals can be produced during resuscitation with O_2. The present study contributes to the understanding of the pathophysiological mechanism of hypoxic-hyperoxic insult.
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1695 VENTILATION AND GAS EXCHANGE OF INFANTS ON ASSISTED VENTILATION. Karl Schulze, Andrew Schenkman, Michael Graff, Mark Stefanski, Julia Masterson and L. Stanley James. Columbia U., Coll.of P&S, Div. Perin. Med., Dept.Ped., NY.

The physiology of the infant on assisted ventilation has not been well studied. The purpose of this study was to determine the absolute level, spontaneous variability and inter-relationships of oxygen consumption ($\dot{V}O_2$), carbon dioxide production ($\dot{V}CO_2$), minute ventilation ($\dot{V}_I$) and heart rate (HR) in LBW infants on assisted ventilation. 7 infants, ranging in weight from 780 to 1600 grams and in age from 1 to 32 days were studied on the Sechrist IV100 ventilator at FiO_2 ranging from .21 to .40, rate 8 to 26, PEEP from +2 to +7. Continuous measurements of $\dot{V}O_2$ and $\dot{V}CO_2$ (open circuit indirect calorimetry) $\dot{V}_I$ (body plethysmography) HR, $TcpO_2$ and activity state were made for 2 hours under thermoneutral conditions. PEEP was varied during the study of 5 infants.

Mean $\dot{V}_I$ was 218 ml/kg.min.(range 176-313), mean $\dot{V}O_2$ was 5.7 ml/kg.min.(range 3.5-7.8), mean $\dot{V}CO_2$ was 4.7 ml/kg.min.(range 3.4-5.4), mean HR was 151(range 131-170). Within infants the mean coefficient of variation for $\dot{V}O_2$ was 12.6%, $\dot{V}CO_2$ 30.2%, $\dot{V}_I$ 25.3% and HR 4.1%. Following time series corrections for lags, successive 3 min. average measurements of $\dot{V}O_2$ were cross correlated with $\dot{V}_I$ and HR. Strong correlations were noted between $\dot{V}O_2$ and $\dot{V}_I$ (r = .69, n = 40) and $\dot{V}O_2$ vs HR (r = .72, n = 40). When PEEP was lowered $\dot{V}_I/\dot{V}O_2$ increased suggesting less efficient ventilation.

We conclude (1) that $\dot{V}O_2$ and $\dot{V}CO_2$ of ventilated infants are not strikingly different from normal infants, (2) considerable synchronous variability in $\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}_I$ and HR is present in these infants and (3) the $\dot{V}_I/\dot{V}O_2$ relationship appears to change favorably with PEEP.

● **1696** LIQUID VENTILATION (LV): IMPROVED OXYGENATION IN MECONIUM STAINED LAMBS WITH PERSISTENT FETAL CIRCULATION. T.H. Shaffer, P.R. Douglas, E.M. Sivieri, C.A. Lowe, S.M. Snyder & V.K. Bhutani (Spon. A.M. Bongiovanni), Temple University Sch. of Med., Dept. of Physiology, Phila., Pa.

Seven lambs (0.93 term gestation) were delivered by Cesarean section (epidural anesthesia) with evidence of meconium in the amniotic fluid, meconium staining, cyanosis and respiratory distress. Initial status indicated severe hypoxemia (mean PaO_2 = 58±9.8 Torr) and right to left shunt: mean alveolar-arterial O_2 gradient ($A\text{-}aDO_2$) = 590±10 SE Torr at PIO_2 713 Torr. The mean $PaCO_2$ was 64.6 Torr and mean pH was 7.16. The effect of LV was determined on arterial blood gas tensions, acid base, and cardiovascular parameters (heart rate, EKG, central venous and arterial pressures) and compared to control (CV) and recovery(RV) gas ventilation. CV was instituted and adjusted to achieve optimum gas exchange and ventilation ($\dot{V}$). Mean ± SEM values of $A\text{-}aDO_2$ = 579± 37 Torr (PIO_2 713 Torr); PaO_2 = 96.8±33 Torr; $PaCO_2$ = 37.4±1.8; pH = 7.39±0.03 and tracheal pressure Ptr= 39.4±2.9 cmH_2O. 3 lambs developed pneumothoraces during CV. LV was commenced at 55-150 mins of age for approx. 60 mins. with warm (39°C), oxygenated (PIO_2 = 550 Torr) fluorocarbon.$A\text{-}aDO_2$ decreased significantly by 38% (p<0.004) and PO_2 increased 59% (p<0.01) with no change in $PaCO_2$ or pH. There were no significant changes in the cardiovascular parameters. During RV, decreases in $A\text{-}aDO_2$ (21%; (p<0.02), $PaCO_2$ (25%, p<0.02) and Ptr (20.3%, p<0.02) were seen, PaO_2 rose 74% (p<0.005) when compared to CV.Improved oxygenation and $\dot{V}$ were demonstrated and may be attributed to uniform $\dot{V}$ improved perfusion ($\dot{Q}$) or better $\dot{V}$-$\dot{Q}$ matching during and after LV.(Supp.HL22843)

1697 FETAL MORPHINE TREATMENT RESULTS IN "NEONATAL TYPE" FETAL BREATHING IN THE LAMB. Roger E. Sheldon and Paul L. Toubas (Spon. by Owen M. Rennert) University of Oklahoma College of Medicine, Department of Pediatrics, Oklahoma City.

In studies on the control of fetal breathing movements and the onset of breathing at birth, we equipped seven fetal lambs with intratracheal, intravascular and amniotic sac catheters under pentobarbital sedation and tetracaine spinal anesthesia. After 48-72 hours recovery at gestational ages of 130-146 days, continuous polygraphic recording of tracheal and amniotic pressures was begun. The presence of "neonatal type" of deep, sustained, and regular fetal breathing was noted to the nearest minute. Specifically this breathing was defined as tracheal pressure excursions of at least -10 mmHg (not seen in the amniotic sac) at a regular rate exceeding 40 min^{-1} and persisting for at least 30 sec.

Intravenous injection of 1-4 mg of morphine sulfate resulted, after a delay of 42±11 min (mean ± SEM), in deep (-36±3 mmHg), rapid (77±15 min^{-1}), sustained (84±17 min) fetal breathing which persisted intermittently for 300±36 min. The percentage of time spent in this neonatal type breathing rose from a control of 1% to 48% in the first 100 minutes after medication and to 56% in the second 100 minutes. (p=<0.05). The time spent in the "fetal type" of breathing (<10 mmHg and irregular) is not increased or decreased by morphine. Fetal blood gases did not change.

We conclude that in fetal lambs, vigorous breathing activity follows morphine treatment. This stimulation (or disinhibition) appears to involve an indirect mechanism with a delay of 42 min. Preliminary data suggests that naloxone eliminates the response.

1698 ISOLATION OF GOBLET CELLS FROM CAT TRACHEA: James M. Sherman, Bernard Tandler, Thomas F. Boat; U. of So. Fla. College of Medicine, Dept. of Peds., Tampa, FL; and Case Western Reserve School of Medicine, Rainbow Babies and Children's Hospital, Dept. of Anat. and Peds., Cleveland, OH.

Surface epithelial goblet cells, and submucosal mucous glands are mucus secreting elements of the respiratory tract. Studies with epithelial sheets and subepithelial tissue separated by EDTA have shown these tissues to secrete mucous glycoproteins (MGP) of differing biochemical properties. Investigation into the subcellular mechanisms of goblet cell MGP production requires isolation of these cells. 3x5 mm explants of cat trachea are incubated in Ca, Mg, free Earles Balanced Salt Solution (EBSS) containing 20 mM Na_2 EDTA for 1½ hrs. on a rocking platform (3 cycles/min) at 35°C, 100% humidity, 95% O_2, and 5% CO_2. The epithelium is removed with a fine dissecting needle, transferred by pipette to a culture dish containing Ca, Mg free EBSS and 40 units/ml crystalline elastase (Calbiochem). After 15 min. on the rocker at the previously described conditions, the tissue is gently pipetted and layered at the top of a gradient preformed by centrifuging 30% Percoll in EBSS for 1 hr. at 20,000 g. Cells are recovered from near the bottom of this gradient after centrifuging for 30 min. at 1000 g and 20°C. All cells exclude trypan blue. The cells are washed and fixed in ½ strength Karnovsky's fixative and examined by light and transmission electron microscopy. The recovered cells are a virtually pure population of goblet cells. By TEM, the goblet cells show excellent retention of morphological integrity. This technique allows recovery of goblet cells for culture and biochemical analysis.

1699 EFFECTS OF RAPID RATE VENTILATION ON LUNG COMPLIANCE. Melinda R. Slack, Nirmala S. Desai, Deborah J. Boyer, M. Douglas Cunningham, Department of Pediatrics, College of Medicine, University of Kentucky, Lexington.

The increased mean airway pressure required to maintain tidal volume when rapid ventilatory rates are employed in neonates implies alterations of lung mechanics. Serial measurements of dynamic lung compliance (C_L) and lung resistance (R_L) were made concomitant with increasing ventilatory rates in 5 adult cats. Animals were sedated with α-chloralose and pentobarbital, and ventilated with a volume controlled respirator at slow rates of 10-40 (SR), and at rapid rates of 80-120 (RR). Tidal volume with spontaneous breathing was determined and held constant throughout the experiment. Using a multichannel recorder, transpulmonary pressure (P_{tp}), airflow, and tidal volume (an integral of flow) were measured and C_L and R_L calculated. $PaCO_2$ decreased from 38.8±3.5 torr to 11.2±1.5 torr with increasing rates (r= -0.93; p=0.05). No significant increase in P_{tp} was seen with SR (3.27±0.40 to 3.23±0.38 cmH_2O), however, a 38% increase in P_{tp} (4.46±0.71 to 7.17±1.92 cmH_2O) occurred with RR. Compliance decreased from 10.03±3.58 cc/cmH_2O with SR to 5.10±0.82 cc/cmH_2O with RR (r= -0.98; p=0.01). The percent change of compliance with SR was negligible (2%) vs a 31% decrease with RR. No significant change in R_L was observed with increased rates. We conclude that a significant loss of lung compliance occurs with constant volume rapid rate ventilation. This effect may result from a maldistribution of ventilation as it relates to distention of proximal airways and increased resistance of peripheral airways.

1700 SYNERGISTIC EFFECTS OF GLUCOCORTICOIDS AND THYROID HORMONES ON LUNG MATURATION: ROLE OF FIBROBLAST-PNEUMONOCYTE FACTOR(FPF). Barry T.Smith, Karim Sabry, Harvard Medical School, Department of Pediatrics, Boston, MA.

Both glucocorticoids and thyroid hormones regulate lung maturation. With mixed fetal rat (d.20) lung cell cultures, we observed that cortisol (F, 10^{-6}M) increased ^{3}H-choline incorporation into saturated phosphatidylcholine(SPC)(13516 ± 1700 cpm/10^6 cells; control - 6658 ± 1861; t = 6.66, p<.0001) while triiodothyronine (T3, 10^{-8}M) had no effect. In contrast, incubation of both F and T3 further increased this process (19611 ±2673; t = 4.71, p<.0001 as compared to F alone).

With enriched alveolar Type II cell cultures, pre-incubation of the cells with T3 significantly enhanced the slope of the dose-responsive increase of ^{3}H-choline incorporation into SPC when the cells were incubated with FPF (1 - 1000 ng/ml)(t = 5.95, p<.001). FPF (1000 ng/ml) increased intracellular 3'5'-cyclic AMP content (.18 ± .05 picomoles/culture vs. .11 ± .04) and this increase was further enhanced in T3 pretreated cells (.31 ± .12; t = 2.50, p = .03 vs. FPF alone).

We conclude that T3 potentiates FPF action on the alveolar epithelial cell, perhaps via a cell surface receptor mechanism.

Supported by NIH grant #HL 25907 and HL 27327.

1701 BACTERIAL TRACHEITIS - A DISORDER WHICH MIMICS CROUP OR EPIGLOTTITIS. Shaul Sofer, Peter G. Duncan, Victor Chernick. University of Manitoba, Departments of Pediatrics and Anesthesia, Winnipeg.

We have seen 7 patients from Aug.1978 to Sept.1981 who have presented with signs and symptoms of croup or epiglottitis but in whom severe airway obstruction was related to the accumulation in the trachea of thick purulent secretions (table). The average age was 24.4 months (range 8 to 78 months).

Number of Patients Admitted to:	Hospital	I.C.U.
Croup	297(89.5%)	16(31.4%)
Epiglottitis	28(8.4%)	28(54.9%)
Bacterial Tracheitis	7(2.1%)	7(13.7%)

In addition to inspiratory stridor all had high fever and toxicity. 5 of 7 grew Staph.aureus and 2 of 7 had H.influenza in tracheal secretions. Blood cultures were negative as were extensive viral studies. 6 of 7 were intubated (1 tracheostomy); in two cases intubation was done at the time of cardiorespiratory arrest which was promptly relieved by the aspiration of thick purulent mucus. All patients were treated with antibiotics and survived the acute phase. Our experience and recent reports (Jones et al, JAMA 242,721,1979; Han et al, AJR 133:53,1979) indicate that bacterial tracheitis is not a rare disease and must be included in the differential diagnosis of acute upper airway disease in children. The disorder is caused by a primary bacterial infection of the upper airway since we did not find evidence of a preceding viral infection. Since the obstruction may be severe all patients must be treated in an ICU. Most require an artificial airway and all need frequent suctioning and antibiotics.

● **1702** IMMUNOREACTIVE (IR) BOMBESIN AND CALCITONIN PARACRINE CELLS OF HUMAN FETAL AND NEWBORN AIRWAYS. Mildred T. Stahlman, Mary E. Gray, A.G. Kasselberg, and David N. Orth. Vanderbilt University Medical School, Departments of Pediatrics, Pathology and Medicine, Nashville, Tennessee.

IR-bombesin and calcitonin, peptide hormones common to brain and gut, have been reported in cells of human fetal airways. Electron microscopically, we have identified paracrine cells in the lungs of 45 human fetuses and newborn infants (8-41 weeks) and in tracheas of 13. Kultschitsky-like cells were seen in the distal conducting airways from bronchioles through alveolar ducts in all 45 subjects, never in alveolar walls, rarely in bronchi. These cells were in contact with the basement membrane, their luminal surface always covered by other cells. Long dendritic processes containing many dense core granules (DCG) extended along the basement membrane, interdigitating with distant cells. In addition, in bronchi and trachea, a different type of cell containing DCG was seen. These were tall, thin and without dendrites, reaching from lumen to basement membrane, where footlets covered with basement membrane extended into the interstitium. Their granules varied in size, shape and density. Stubby microvilli covered their luminal surface. Immunocytochemically, IR-bombesin cells were found in distal conducting airways in 24/29 of the subjects, rarely before 12 weeks, but readily thereafter. IR-calcitonin cells were present in 5/10 tracheas. Since bombesin has been shown to increase airway resistance in lambs and guinea pigs, we suggest that IR-bombesin-containing cells may regulate distal airway size, possibly as mechanoreceptors. The functional significance of IR-calcitonin cells in the trachea is, at present, unknown. We suggest that, because of their orientation, they may act as chemoreceptors. (Sponsored by HL 14214)

1703 A COMPARISON BETWEEN HIGH FREQUENCY AND CONVENTIONAL VENTILATION IN DOGS WITH OLEIC ACID LUNG INJURY. R Stoddard, L Minnick, N Ackerman, D Null, R deLemos (Spon. by J Robatham), Wiltord Hall USAF Medical Center, Department of Pediatrics, San Antonio, Texas

Eight paralyzed mongrel dogs with oleic acid lung injury were ventilated either with HFOV or standard ventilation for a five hour period using a newly designed pneumatic ventilator capable of function in either mode. During HFOV the animals were maintained at 5 Hz with variation of the oscillatory amplitude and distending pressure used to optimize PaO_2 and $PaCO_2$. V_T, frequency and PEEP were regulated in the control group. Post resuscitative blood gases were similar with either technique.

There were no significant differences in pH, PCO_2, pO_2 or $A\text{-}aO_2$ gradient at any point in the study period. The MAP required to maintain oxygenation in the HFOV animals was higher and cardiac output, cardiac index and stroke volume were significantly lower throughout the study period. A progressive rise in both pulmonary artery pressure and pulmonary vascular resistance was seen in the HFOV group.

Fx BASELINE VALUE (4 HRS.)	C.O.	H.R.	PAP	PVR
HFOV	0.70	1.48	2.7	2.0
IPPV	1.35	1.1	1.8	1.4

Although this study clearly demonstrated our ability to maintain comparable blood gases with HFOV in this experimental model, it also showed that HFOV can have significant adverse cardiovascular effects. While these were apparently well tolerated during the experiment, the long term cardiovascular consequences of high frequency ventilation require detailed evaluation.

1704 EFFECT OF CORTICOSTEROIDS ON POSTNATAL LUNG FUNCTION
Dennis Stokes and Wayne Mitzner (spon. Jerry Winkelstein), The Johns Hopkins Medical Inst, Dept Ped, Environ Health Sci, Balto, MD

Prenatal administration of corticosteroids increases lung volume/lung weight and deflation stability. Studies in older animals are complicated by immunosuppression & frequency of respiratory pathogens in lab animals. To determine the effect of steroids on postnatal lung function, germ-free SD rats (Harlan), 70-80gms, received dexamethasone (1mg/L. drinking water) and were maintained in sterile conditions in an isolator. Pulmonary function studies were done in a group prior to treatment & after 6 weeks in steroid & control animals. Forced expiratory maneuvers were done in a pressure plethysmograph & lung pressure-volume (P-V) curves in excised lungs. After fixation, histological sections were examined for morphology and to exclude P. carinii infection.

TIME	GROUP	LUNG WT(LW)	LWx10³/BW	FVC	FVC/LW	$FEV_{.05}$	FEV_1
0	Control	.111	1.08	2.92	26.5	53.8	80.8
	n=5	(±.009)	(.13)	(±.15)	(±2.5)	(±21.9)	(±16.8)
6wks	Control	.219	1.43	8.09	37.1	49.8	80.4
	n=5	(±.028)	(.14)	(±.56)	(±3.4)	(±2.7)	(±2.6)
	Steroid	.132*+	2.30*+	3.78*+	28.8+	68.3+	88.8
	n=5	(±.017)	(.25)	(±.65)	(±3.9)	(±14.2)	(±11.6)

* $p < .05$ vs 0 wk C, + $p < .05$ wk C; all m (± S.D.)

Postnatal steroid treatment thus reduced lung volumes/lung wt cpd to age-matched controls. These lungs emptied faster during forced expiration and lung P-V curves suggest this is due to increased elastic recoil in the steroid-treated group. The observed effects of steroids in this dosage and age animal--reduced volumes and stability--are opposite those seen with prenatal treatment.

● **1705** HYPOXIC AND HYPERCAPNEIC AROUSAL RESPONSES IN INFANTS SURVIVING NEAR-MISS SUDDEN INFANT DEATH SYNDROME.
AL van der Hal, CW Sargent, ACG Platzker, and TG Keens, (Spon. by GN Donnell). University of Southern California School of Medicine, Childrens Hospital of Los Angeles, Neonatal-Respiratory Disease Division, Los Angeles.

We tested hypoxic and hypercapneic arousal responses in 6 normal infants (aged 10.9±4.5 (SE) months) and 15 infants who survived a near-miss sudden infant death syndrome (NMSIDS) episode (cyanosis, limpness, and apnea requiring vigorous stimulation or resuscitation, in whom no treatable etiology could be found). The age at initial NMSIDS episode was 2.7±0.6 months, and all infants were tested while still having recurrent apnea (age 4.1±0.7 months). For hypoxic arousals, the PIO2 was rapidly decreased during quiet sleep to 74±1 mmHg unless arousal occurred (restlessness, agitation, eye opening). All normals aroused to hypoxia (PIO2 76±1 mmHg). 9 of 15 NMSIDS (60%) failed to arouse to hypoxia (PIO2 74±1 mmHg). The normals had more hyperpnea in response to hypoxia ($\Delta PACO2$ 5.5±0.6 mmHg) than NMSIDS ($\Delta PCO2$ 3.8±0.4 mmHg; $P < 0.025$), suggesting abnormal hypoxic ventilatory response in NMSIDS. For hypercapneic arousals, PICO2 was rapidly increased during quiet sleep to 60 mmHg unless arousal occurred. All normals and NMSIDS infants aroused, but PICO2 was greater at arousal in NMSIDS (44±1 mmHg) than in normals (38±2 mmHg; $P < 0.025$), suggesting an abnormal hypercapneic response in NMSIDS. We conclude that NMSIDS infants have decreased responses to hypoxia and hypercapnea.

1706 CALORIC INSUFFICIENCY WITH DELAYED GROWTH IN INFANTS WITH CHRONIC NEONATAL LUNG DISEASE.
Feizal Waffarn, Dale R. Gerstmann, Melody D. Jacobson, Dorothy A. Cuneo, and David A. Hicks (Spon. by Beverly C. Morgan). Coll. of Med. Univ. of California, Irvine, Dept. of Peds., Irvine, CA

Neonates with chronic lung disease (CLD) lack catch-up growth (Markestad, J Pediatr, 1981). To explore the causes for this lack we compared the nutrition and growth in the first 2 yrs of 19 infants with CLD to a control group (grp) of 15 infants matched for birthweight, gestational age and acute lung disease. CLD was documented by oxygen dependency for >21 days and chest x-ray. Growth was measured at 6 mo intervals as changes in the percentiles for weight (Wt), height (Ht) and head circumference (HC), from birth through 2 yrs corrected age. At each visit, nutritional intake was calculated from a 5 day food diary. The mean birth Wt and gestational age for the CLD grp was 1066±280 gm and 28.7±2.2 wks and control grp was 1263±257 gm and 29.5±1.7 wks. At birth the CLD grp was relatively growth-retarded as their mean Wt, Ht, and HC were at the 22, 25, and 28th percentile. At 40 wks gestation both grps were at significantly lower Wt percentiles as compared to their birth percentiles($p<.005$) with the CLD grp being 50% lighter. While the controls regained their birth percentiles for Wt and Ht by 6 mos the CLD grp recovered Ht by 6 mos and Wt by 12 mos. Head growth was unaltered in either grp. The CLD grp had a significantly lower caloric intake than controls for the first yr, 101±5 vs 116±7($p<.05$) and second yr 100±9 vs 137±8($p<.005$) kcal/kg/day. The protein intakes were similar. We conclude that neonates with CLD show effects of prenatal undernutrition and compared to a control grp also show delayed postnatal growth partly related to a lower caloric intake.

1707 PERSISTANT PULMONARY HYPERTENSION IN THE NEWBORN (PPHN) ASSOCIATED WITH ABNORMAL PULMONARY CAPILLARY DEVELOPMENT.
Kenneth M. Weesner, Robert Jensen, Robert J. Roberts, Depts. Pediatrics, Pathology, Pharmacology, Univ.of Iowa, College of Medicine, Iowa City, Iowa 52242.

Recently the condition alveolar capillary dysplasia was reported as an unusual cause of PPHN. We have seen an infant who had similar microscopic findings, in whom we were able to analyse the pulmonary vascular bed by use of a methylmethacrylate corrosion cast. Conventional microscopic sections, using standard staining techniques were performed on the inflated lung. These studies revealed thickened lung parenchyma without fibrosis, an underdevelopment of alveoli with an increased number of respiratory bronchioles and alveolar ducts, and a decreased number of capillaries with a reduction also in the number which made contact with the alveolar epithelium. These changes were uniform throughout the lung. A corrosion cast of the right lower lobe was studied using scanning electron microscopy (SEM). SEM photographs showed a reduced number of capillaries. The capillary network which was present was disorganized compared to the usual uniform meshwork pattern. The capillaries had areas with irregular lumen dimension and there appeared to be a number of abnormal vascular connections, possibly venules. We conclude that SEM casting is a useful technique for the study of normal vascular development and structural abnormalities in pathologic specimens. Supported by NIH Grants #GM12675 and #HL07413.

1708 EVALUATION OF EFFECT OF BREATHING EXERCISES ON EXERCISE INDUCED ASTHMA.
A.E. Zuckerman, M. Osterweis, R.M. Sly, T.M. Murphy, W.H. Pillsbury, N.Rohatgi, V.S. Taggart, J.A. Bellanti. Georgetown University Medical School, National Children's Hospital Medical Center, Center for Immunologic Disease at Georgetown University, Washington, D.C.

Breathing exercises (BE) are popular techniques for managing acute asthma, but their impact on lung function and subjective perception of benefits have been inadequately evaluated. BE's efficacy in minimizing the bronchoconstrictive effect of exercise was evaluated using the cumulative percent deficit from pre-exercise baseline FEV1, PEFR, and MMEF, measured as they are under the curve of function tests against time during the first hour after exercise. Thirteen asthmatic children age 7-13 years were treadmill challenged; PFT measures were made on a baseline observation and subsequent challenges using BE. Differences between experimental and control subjects were in the predicted direction but not statistically significant. Comparison of 12 subjects as their own controls showed significant improvement using BE in FEV1 (42%, p .05) and MMEF (34%, p .05) but not in PEFR. The mean improvement for the 10 who improved was 70%. Each child's opinion of BE's value correlated with function testing. Linear regression analysis of all observations confirmed individual variation, improvement in FEV1 and MMEF using BE, and no difference in repeated observations on the same subject. The study reflects the utility of using cumulative measures of PF change to assess BE, indicates that BE are probably helpful in most children who use them properly, and suggests a role for children's self-assessment of BE in management of asthma.