were then kept for another 3 days in media containing either glu or gal alone or combined. SfS of cultures continued at glu 26.1 mM served as control (100%). Gal alone at any concentration (1.3-26.3 mM) was unable to replace glu, SfS remained severely depressed (1.5 to 2.9%). At high glu levels above 12.6 mM addition of gal did not influence SfS, thus excluding a toxic effect. At glu 7.5 mM which left cultures glu-deprived below 0.2 mM for at least 1 day, SfS fell to 35.9±10.6% (SD). Under this condition, SfS could be raised to 52.9±13.5% when gal 0.6 mM was added or even to 67.9±15.6% with gal 12.2 mM (p less than 0.05, resp. 0.001). Therefore, gal may not be necessary for SfS in glu-replenished states. Under glu-deprivation, however, gal could become essential for maintaining structural brain metabolism measured as SfS.

72 A. LUCAS*, T.E. ADRIAN*, S.R. BLOOM* and A. AYNSLEY-GREEN. University Dept. of Paediatrics, John Radcliffe Hosp., Oxford, and Hammersmith Hosp., London. GUT HORMONES IN THE NEONATE.

Gut hormones exert important effects on gut growth, secretion and motility and on intermediary metabolism, and may play a key role in the postnatal adaptations to enteral feeding. Using sensitive radioimmunoassays we have measured 10 entero-insular hormones in the plasmas of (a) 203 healthy term or preterm infants at birth, or during the first 24 days of life either before or at 30, 60 or 120min. after feeding and (b) 10 six-day old preterm neonates who had never been fed orally since birth on account of hyaline membrane disease. Each infant contributed, with ethical approval, only one plasma sample, removed at the time of a routine clinical blood test. Basal levels of gastric inhibitory polypeptide (GIP), pancreatic polypeptide (PP), enteroglucagon (EG), neurotensin (NT), motilin, and gastrin all rose steeply during the neonatal period, the latter four hormones reaching levels which exceeded significantly those seen in healthy fasting adults. In contrast plasma concentrations of GIP, EG, NT, motilin and gastrin did not show postnatal elevation in the unfed group of infants. In addition for 8 hormones; secretin, GIP, PP, NT, EG, motilin, gastrin and insulin, we observed a progressive postnatal increase in the endocrine response to a feed. Profound changes occur therefore in gut hormone physiology after birth and these changes may in part be due to enteral feeding itself. This data is of relevance to the design of optimal feeding regimes for high risk neonates.

73 N.C.R. RÄIHÄ, A.L. JÄRVENPÄÄ*, D. RASSIN*, and G. GAULL*, Depts. Pediatrics, and Obstetrics and Gynecology, University of Helsinki, Finland and Dept. Pediatric Research, N. Y. State Inst. Res. Ment. Retdn., Staten Island N. Y., U.S.A. Milk protein quality: Biochemical and growth effects in full-term infants.

Our previous studies have shown that both quantity and quality of ingested milk protein affects the metabolic homeostasis of low birth-weight infants. In this study, 37 well full-term infants were fed ad libitum for 12 weeks with either breast milk (BM) or with one of two formulas (F_1=1.5% prot., whey prots.: caseins, 60:40 or F_2=1.5% prot.; whey prots.: caseins, 18:82). No differences between feeding groups were found in weight gain, linear growth or head circumference during the study period. Significantly, greater negative base excess and higher BUN were found in the formula fed infants as compared to those on BM. Blood cholesterol at 12 weeks was much higher in the infants on BM when compared to those on F_1 and F_2 ($p<0.0001$). Plasma and urine taurine concentrations were higher in the infants on BM throughout the study and at 4, 8 and 12 weeks of age the urine taurine was 25 to 50 times higher in BM infants than in F_1 and F_2 infants. Plasma valine and isoleucine concentrations were significantly increased in the formula fed infants as was the valine/glycine ratio, suggesting the possibility of protein overloading in the formula fed infants.

74 A.L. JÄRVENPÄÄ*, N.C.R. RÄIHÄ, P. KUITUNEUN*, D. RASSIN* and G. GAULL*, Depts. Pediatrics and Obstetrics and Gynecology, University of Helsinki, Finland and Dept. Pediatric Res., N. Y. State Inst. Res. Ment. Retdn., Staten Island, N.Y. U.S.A. Effect of taurine supplementation to the diet on bile acid conjugation in low birth-weight infants (LBWI).

Previous results have shown that plasma and urine taurine concentrations decrease when LBWI are fed with taurine deficient formulas. In this study, 63 well LBWI with gestational ages of 31 to 36 weeks were randomly assigned to either breast milk (BM) or formula (1.5%, prot. 60:40 whey: caseins) without (F1) or with addition of taurine (30 µmol%, F_2). Duodenal fluid bile acids and glycine-taurine ratio (G:T) were determined with high-performance liquid chromatography. The plasma taurine levels and urine taurine excretion fell significantly in the infants fed with the taurine deficient F_1 formula. At the age of 7 days the G:T ratios were 0.64 (BM), 0.44 (F_1) and 0.47 (F_2). In the infants on BM and F_2 the G:T ratio remained on the same level throughout the study and at the age of 36 to 40 days it was 0.58 and 0.69 respectively on the two diets. In the infants fed with formula F_1, the G:T ratio increased significantly after the age of 21 days being 1.32 at a mean age of 39 days ($p<0.001$). Our results indicate that dietary taurine intake affects duodenal bile acid conjugation.

75 T. TIKANOJA* and O. SIMELL* (Intr. by J. Perheentupa). Children's Hospital, University of Helsinki, Helsinki, Finland. Plasma amino acids in healthy newborns after a feed of breast milk or formula.

Postprandial concentrations of plasma amino acids were followed in 20 full-term healthy infants, aged 4.5-8 days, to quantitate differences in response to a physiologic feed of breast milk or formula. The study had been approved by the ethical council of the hospital; the parents of each infant had given their informed consent. After a 4 hr fast, 10 infants received from bottle a normal feed (1/36 of body wt) of pooled breast milk; 10 infants received milk formula. The true protein contents of the milks were 0.8% and 1.5%, respectively. Venous blood samples were drawn just prior and 30, 60, 120 and 210 min after the beginning of the feed. Peak plasma concentrations were reached with both milks in 30-60 min and starting values in 210 min. Valine, leucine, tyrosine, lysine and arginine showed highest molar increased amounting 50-100% above their fasting concentrations. The rises in plasma amino acids were approximately equal after both meals despite differences in the proteins of the milks. Thus, (1), the absorption of amino acids is significantly more efficient from breast milk than from formula, or (2), the postprandial amino acid curves are strictly regulated by the metabolic clearances and poorly reflect absorption in the newborns.

76 J. RAJANTIE*, O. SIMELL* and J. PERHEENTUPA Children's Hospital, University of Helsinki, Helsinki, Finland.

Orotic aciduria, an indicator of adequacy of treatment in lysinuric protein intolerance (LPI).

The basic defect in LPI is in the transport of the diamino acids in kidney tubuli, jejunum and liver cells. This leads to a deficiency in the liver of the urea cycle intermediates arginine and ornithine, a malfunction of the cycle and an accumulation of ammonia. Like in the other conditions in which hyperammonemia is associated with accumulation of carbamyl phosphate, urinary excretion of orotic acid is excessive. Orotic acid is an intermediate of the synthesis of the pyrimidines from carbamyl phosphate. We measured orotic acid excretion in controls and patients with LPI. The controls in all situations excreted less than 20 µg/kg/hr. The patients excreted normal amounts during fasting (4.6, 2-8, 5 for mean, range, number of subjects). Their excretion was increased in 24-hr urines during a self-chosen low-protein diet (125, 3-366, 7), in 4 to 6 hr urines after a milk load with 0.5 g of protein/kg (488, 251-1747, 3), in 2-hr urines after oral ammonium lactate, 2.5 mmoles/kg (212, 15-1126, 10), and in 6-hr urines after iv alanine, 6.6 mmoles/kg in 90 min (790, 47-1831, 11). If the loads were given with an iv infusion of arginine, ornithine or citrulline, the orotic aciduria did not appear. Given orally, citrulline was the most efficient of the three in preventing orotic aciduria. Orotic aciduria thus is a reliable indicator of the function of the urea cycle in LPI and enables us to monitor the home treatment.

77 M. DURAN, F.A. BEEMER, S.K. WADMAN, J.L. JOHNSON, W.R. WAUD, K.V. RAJAGOPALAN, University Children's Hospital Het Wilhelmina Kinderziekenhuis, Utrecht, The Netherlands and Duke University Medical Center, Dept. Biochemistry, Durham NC, USA.
Combined deficiency of sulfite oxidase and xanthine oxidase as a result of defective synthesis of molybdenum-cofactor.

A girl is presented with congenital abnormalities including asymmetry of the skull and slight mediofacial dysplasia. The eye lenses were dislocated. Severe neurological abnormalities and deep mental retardation were observed. On routine screening a low serum urate (0.01-0.07 mmol/l) was observed. Chromatography of urinary purines revealed xanthinuria. In addition the sulfite test in the urine was repeatedly positive. Sulfite oxidase deficiency was suggested by high excretions of S-sulfocysteine, taurine and thiosulfate and low levels of urinary sulfate. Deficiencies of both xanthine oxidase and sulfite oxidase were demonstrated in a liver biopsy specimen. Because sulfite oxidase and xanthine oxidase are known to require an activated form of molybdenum (Mo-cofactor), investigations of Mo metabolism were carried out. A complete absence of hepatic Mo-cofactor activity was demonstrated and analysis by atomic absorption revealed a severe depletion of hepatic Mo as well. A near normal amount of inactive xanthine oxidase protein was present, but several immunological techniques failed to detect any sulfite oxidase apo-enzyme. It is suggested that a defective synthesis of Mo-cofactor causes the biochemical abnormalities. Treatment with oral supplements of molybdenum did not result in biochemical or clinical improvement.

78 K.O. RAIVIO, H. KRUMHOLZ, C. LAZAR and M.A. BECKER Children's Hospital, University of Helsinki, Finland, and V.A. Hospital, San Diego, CA.
5-phosphoribosyl-1-pyrophosphate (PRPP) synthesis in glucose-6-phosphate dehydrogenase (G6PD) deficiency.

The supply of ribose for nucleotide synthesis is considered a major function of the oxidative pentose shunt (PS). We have evaluated this function on the basis of ribose-5-phosphate (R5P) and PRPP concentration and generation in normal and G6PD-deficient fibroblasts. PS in normal cells accounts for 0.8% of glucose utilization. It can be stimulated over 10-fold by methylene blue (MB) and inhibited 85% by 6-aminonicotinamide (AN) without affecting PRPP levels or generation. PS in mutant cells is 30% lower than normal and barely affected by MB or AN. Basal R5P,

PRPP, and inorganic phosphate (P_i) levels are somewhat higher in mutant cells, and MB elevates PRPP. Addition of AN plus MB depletes P_i, PRPP and adenine nucleotides in normal cells, but in the mutant R5P and PRPP rise and nucleotides remain unaltered. We conclude that oxidative PS is not essential for R5P generation: hence G6PD-deficient cells have no defect in PRPP or nucleotide synthesis. They are also protected from the combined effect of AN and MB, which is based on P_i depletion in normal fibroblasts. P_i is the prime modulator of PRPP synthetase in vivo.

Supported by the Academy of Finland, NIH (18197), the Kroc Foundation, and V.A. Medical Research Service.

79 G.KOSZTOLÁNYI*, K.JOBST*, M.KELLERMAYER* and A.LUDÁNY*/Intr.by J.MESTYÁN/. Departments of Paediatrics and Clinical Chemistry, University Medical School,Pécs,Hungary. Comparison of surface charge and ADP induced electrokinetic behaviour of fetal and adult platelets.

The electrophoretic mobility of washed platelets as well as of platelets suspended in diluted plasma obtained from adults and newborns was practically the same. No significant difference could be observed in the pH-mobility relationship of the two types of platelets. These comparative studies indicate that the actual charge density, i.e. the number and sign of the charges groups at the fetal and adult platelet surface are essentially identical.

Significant difference between the two platelet population was found, however, in the mobility changes induced by ADP. On the basis of "cross over" experiments between the platelets and plasma of adults and newborns it seems likely that the different behaviour of fetal platelets arises from a dissimilarity between adult and fetal plasma. The adult plasma might have a factor which is not present in the fetal plasma. Preliminary results indicate that this factor is a plasma component with mol.wt. about 1o ooo.

80 M.OBLADEN*and I. KLATT*(Intr.by H. BICKEL) Universitäts-Kinderklinik,69 Heidelberg,FRG. A Synthetic Surfactant Substitute.

A crystalline mixture of 90 % Dipalmitoylphosphatidylcholine (DPPC) and 10% Dipalmitoylphosphatidylglycerol (DPPG) was analyzed for its suitability as a surfactant replacement using a specifically designed modified Wilhelmy balance.A suspension prepared by vigorous shaking in 0.9% NaCl at 20° and 37° did not adsorb to the air-water interface (γmax 72.6 dyn/cm, γmin 69.8 dyn/cm,S.I. 0.04). When prepared in multilayered liposomes after drying,the material was adsorbed to the surface, spread rapidly to a film,and was highly surface-active (γmax 70.4 dyn/cm, γmin 3.7 dyn/cm,S.I. 1.83). After solubilization with ultrasound,a clear solution resulted which was not surface-active (γmax 72.2 dyn/cm, γmin 56.1 dyn/cm,S.I. 0.39) due to the formation of stable vesicles unable to form a film at the surface. Compared to DPPC alone which adsorbs to the surface in more than 90 minutes at 37°C,the material investigated adsorbed to a surface-active film in less than 10 minutes. The minimal film concentration of DPPC-DPPG displaying maximal surface-tension lowering ability was 2.55 $\mu g/cm^2$ in the liposomal preparation.
No local or general toxicity was found in rabbits after tracheal instillation of the surfactant substitute during mechanical ventilation. Autohistoradiography showed the 3-H-labeled material at the alveolar wall 30 minutes after instillation into the tracheal tube.

81 **J.J.PIETRZYK.Clinical Genetics Department, Institute of Pediatrics,Kraków,Poland.**

Genetic analysis of HLA and spina bifida association.

The HLA typing and routine segregation analysis of HLA haplotypes were performed in the group of 68 families with single and multiple cases of spina bifida /SB/.A significant associations of SB with HLA-B27 allele /Chi2=78.073 p<0.0145/ and HLA-A3,B27 haplotype /Chi2=7.371 p<0.01/ were found.The observed distribution of B27 among the affected children fits the distribution expected on the assumption that this antigen makes the zygote more susceptible to the abnormal neural tube development /Chi2=0.161 p>0.5/.The significant relative risk of SB development given B27 allele and HLA-A3,B27 haplotype was 3.4/p<0.0005/ and 4.6 /p<0.005/,respectively.The analysis of parental HLA phenotypes revealed significantly higher frequency of common HLA antigens shared by both members of the couples as compared to the expected values /Chi2=314.040 p<0.0005/.The couples which shared two or three HLA antigens yield the highest realitive risk of SB for their children /RR=17.8 p<0.0005/.The results raise the possibility that HLA antigens may interact with other developmental factors during the ontogenesis. Non-random association of HLA antigen and HLA haplotype with SB,as well as the very high frequency of common HLA antigens among the parents of the affected children might be used in identification of risk families.

82 J.C. ROUGE*, L. TISSOT* and G.C. LACOURT* (Intr. by P.C. Sizonenko). Dpt of Anesthesia, Pediatrics and Genetics, University of Geneva, Geneva, Switzerland. Effects of continuous positive airway pressure breathing (CPAP) after pediatric open heart surgery.

CPAP is an advance in the treatment of pulmonary dysfunction after cardiac surgery. The effects of different levels of CPAP on lung functions were determined immediately after weaning from the respirator in 14 children. The following parameters were measured: - tidal volume (V_T), compliance (C_L), resistance (R_{TL}) and blood gases ; the work of breathing (W_T) was calculated.

CPAP (cmH_2O)	0	5	10	15	0
	Mean initial value (±SEM)	Change from mean initial value (in percent)			
C_L (ml/cmH_2O)	21 ± 4,9	+ 47	+ 57,6*	+ 86,2*	+ 84,3
V_T (ml)	122 ± 20	+ 15*	+ 8,6	+ 25,8*	+ 7,9
PaO_2 (kPa)	12,6 ± 1	+ 19	+ 23*	+ 32,5*	+ 30,9
$PaCO_2$ (kPa)	4,4 ± 0,2	+ 1,8	- 7*	- 6,1*	- 12,3*

* Significant at the 5 % level.

Simultaneous beneficial effects on C_L, R_{TL}, W_T and PaO_2 were obtained with increasing values of CPAP up to 15 cmH_2O, the prefixed maximum value in this study. No deleterious effects on hemodynamics were found.

83 P. SCHWARTZE* (intr. by L. Corbeel). Department of Pathophysiology, School of Medicine, Karl-Marx-University, Leipzig GDR.
Does rotatory stimulation or handling influence the development of vestibular system?

Rabbits were used to test whether repeated vestibular stimulation or handling during the first 1o postnatal days accelerates the development of vestibulo-oculomotor reactions. The animal material was devided into two experimental groups, and each of these into three subgroups: stimulated rabbits, handled rabbits and controls. Meanwhile the handling procedure was the same, two different rotatory stimulation programs were used in the respective subgroups from the 1st to 12th postnatal day. At this day chronic electro-oculographic electrodes were implanted to all of the stimulated and handled animals and the controls. Nystagmic eye movements (NEM) were recorded daily during a standard rotation stimulus between the 12th and 2oth day. No systematic differences were observed between number and latency of NEMs of stimulated, handled and control animals. Further, no correlation was found between the speed of body weight increase and of nystagmic parameters in the subgroups.

84 M. GARCIA-FUENTES*, A. RUBIO*, J.L. ARCE*, E. BUREO*, V. MADRIGAL* and M. LOPEZ-COLLADO* (Intr. by J. Rodríguez-Soriano). Dept. of Pediatrics, National Med. Center "M. de Valdecilla", School of Medicine. Santander, Spain. Alterations of the complement and coagulation systems in meningococcal infections.

Serum levels of complement components (C1q, C4, C3, C5, C9, C3PA and C1I), platelets, prothrombin time (PT), fibrinogen concentration and fibrin degradation products were measured at admission in 93 children (mean age 3.1±2.0 y)with meningococcal infections, 86% type B. Results were compared with an age matched normal group. Patients were classified in three groups: 21 with meningitis without systemic manifestations; 39 with uncomplicated septicemia and 33 with septicemia and shock.
C1q was decreased ($p<.001$) in the three groups; C3 was also low but only in the last two groups was significantly diminished ($p<.005$). Forty-seven patients, regardless of the groups, showed a prolonged PT and 7 out of these 47 showed a disseminated intravascular coagulation. These 47 patients had lower levels of C1q ($p<.02$), C3 ($p<.05$), C5 ($p<.05$), C3PA ($p<.005$) when compared with the remaining patients with normal PT. Values of PT in all patients correlated well with the levels of C1q ($p<.05$), C4 ($p<.01$), C3 ($p<.001$), C5 ($p<.001$), C9 ($p<.001$) and C1I ($p<.05$). These results suggest that activation of the classical pathway of complement occurs in all patients with meningococcal infections, even in benign cases, and that such activation may be related to the alteration of the coagulation system.

85 F.LAURENTI^,R.BALDUCCI^,P.CRISPINO^, F.MALAGNINO^, and D.PALERMO^(Intr. by Bucci). Depts of Pediatrics and Hematology, CNR Centre for Respiratory Viruses, Univ. of Rome, Italy. Functional activity of packed polymorphonuclear leukocytes (PMN) obtained by leukafiltration.

We recently obtained a striking increase of the survival rate in very small pre-term infants with sepsis through daily transfusions of packed PMN (2Oml/Kg equal to 0.5 x 10^{10} cells). In order to increase the availability of PMN concentrates and to reduce the risk of sentization, it would be useful to transfuse repeatedly, in the same patient, PMN collected from the same donor. We, therefore, evaluated the rate of functional decay of packed PMN obtained by leukafiltration and