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INCREASED CEREBRAL METABOLIC RATE AND DECREASED ANOXIC SURVIVAL AFTER AMINOPHYLLINE IN YOUNG MICE. Jean Holowach Thurston, Richard E. Hauhart, and John A. Dirgo. Dept. Pediat., Wash. U. Med. School, St. Louis.

Last year we reported that in 17-21 d old mice, aminophylline (AP), 100 mg/kg i.p., increased brain levels of cyclic AMP 56% ($p = 0.01$), cyclic GMP 36% ($p = 0.01$), glucose 93% ($p < 0.001$), ADP 12% ($p = 0.04$), and AMP 70% ($p = 0.02$). ATP, P-creatine, glycogen and lactate were unchanged. Increased ADP and AMP levels are sensitive indicators of ATP (∿P) breakdown and suggest an increased cerebral metabolic rate (CMR). To test this hypothesis, the effect of AP (100 mg/kg i.p.) on CMR was determined in 48 weanling mice (Lowry et al, J. Biol. Chem. 239:18, 1964). AP increased CMR 3-fold - 34 mmol/kg/min ∿P (1.03 mmol/kg/min glucose) vs 12 mmol/kg/min ∿P (0.36 mmol/kg/min glucose) in controls. Increased CMR is accompanied by increased extraction of glucose from blood and could explain the brain glucose elevation. Since increased CMR also reflects increased neuronal function, this may be the mechanism by which AP restores normal breathing in premature babies with apnea. However, with a decreased glucose and/or O_2 supply to brain, increased CMR would be a distinct disadvantage. This suspicion was confirmed in 3-9 d old mice treated with a therapeutic dose of AP (7.5 mg/kg s.c.). Fifteen to 60 min after injection, one control and one AP-treated littermate were exposed to N_2 gas for variable intervals. Survival rate of 32 mice was 62% for controls vs 0% in AP-treated animals. The finding suggests caution in the use of AP in hypoglycemic and/or anoxic newborns.

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IONIZED Ca (iCa) IN RELATION TO GESTATIONAL AGE Reginald C. Tsang, Lori Abrams, Thomas H. Joyce, Charles Buncher and Jean J. Steichen, University of Cincinnati, College of Medicine.

Previous studies of serum Ca in relation to gestational age have not examined iCa, the physiologically active fraction of circulating Ca. Forty-three infants with birth weights appropriate for gestational age were studied from birth to 72 hrs.of age Ionized Ca was determined by the Orion 99-20 flow-thru electrode standardized with aqueous and serum standards. Normal serum iCa in 35 young adults ranged from 3.6 to 4.5mg/dl; in 34 well full term infants on day 3, iCa ranged from 3 to 4mg/dl. Fifteen of 43 (35%) of study infants were "hypocalcemic" (serum iCa ≤3mg/dl) on at least one occassion in the first 3 days of life. Serum iCa levels were correlated with total Ca levels (correlation $r=0.588, p<.001$). At birth, umbilical venous serum iCa was correlated with simultaneous maternal iCa ($r=0.658, p<0.01$), but significantly higher than maternal values (4.7±.11mg/dl, mean±SE, vs. 4.1±.07, respectively, paired t $p<.001$). A greater decrease of serum iCa from birth to 24-48 hrs. was related to a higher cord blood iCa ($r=0.611$, $p<.011$). Serum iCa at 24 hrs correlated with gestational age ($r=0.43, p<.05$) and the amount of bicarbonate received/kg body weight/first 24 hrs. ($r=.527$, $p<.01$) but not with birth weight ($r=.210$). Serum iCa at 24 hours was related to serum iCa at 48 and 72 hrs. ($r=.794$,.709). Thus, serum iCa at birth is correlated with, but higher than simultaneous maternal iCa; serum iCa at 24 hrs. of age is significantly correlated with gestational age.

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GLUCOSE INTOLERANCE IN VERY LOW BIRTHWEIGHT (VLBW) INFANTS. Yvonne E. Vaucher and Grant Morrow III, Dept. of Peds., Univ. of Ariz. Health Sciences Ctr., Tucson.

The frequency of glucose intolerance (blood glucose or Dextrostix® ≥130mg% for ≥12 hours accompanied by glucosuria ≥ tr) was determined in 30 consecutively born VLBW infants who weighed ≤1250g; lived for more than 48 hours; and received intravenous (IV) glucose (glu). The majority, 87% (26/30), survived.

Twenty episodes of glucose intolerance occurred in 14 (47%) of the infants. Day of onset varied widely ($\bar{x}$=8, range 0-25) as did duration ($\bar{x}$=4, range 0.5-9.0). Intolerant infants were smaller (0.98 vs 1.10kg $p<.01$); more premature (28.5 vs 30.2 weeks gestation, $p<.01$); more often had respiratory failure (90 vs 50%) and hyperglycemia (62 vs 33%) within the first 24 hours; and were fed orally later (da 13 vs da 5, $p<.001$) than infants who did not become intolerant.

Clinical events known to be associated with hyperglycemia preceded 1/3 of the episodes. The remainder were associated only with an increase ($\bar{x}$=0.2g/kg/h) in IV glu infusion rate. Only 3 episodes resolved without reducing the IV glu load. Eleven episodes (55%) required a decrease ($\bar{x}$=0.5g/kg/h) in glu infusion rates to less than that ($\bar{x}$=-0.3g/kg/h) tolerated prior to hyperglycemia and resulted in a 40% decrease in caloric intake.

These data suggest that glucose intolerance, a common problem in the nutritional management of VLBW infants, is usually due to an increase in IV glu load alone; that early oral feeding may reduce the risk of occurrence; and that glu tolerance frequently deteriorates following persistent hyperglycemia and glucosuria.

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SKIN OXYGEN PERMEABILITY IN PREMATURE INFANTS. Hans T. Versmold, Mathaeus Holzmann, Otwin Linderkamp, Klaus P. Riegel (spon. William H. Tooley) Division of Neonatology, Dept. of Pediatrics, Univ. Munich, W. Germany.

Human skin is permeable to O_2 but the Po_2 on the unheated intact skin is below 3.5 torr in adults and below 7 torr in term infants, both during air and O_2 breathing. In small premature infants, however, we found skin Po_2 to be much higher.

We measured the Po_2 on the nonheated skin surface with an unheated HUCH $tcPO_2$ electrode in 24 newborn infants (gesta. 24-41 wks) at various F_iO_2 levels. The infants were studied in a thermoneutral environment at age 2-48 hrs. When the arterial O_2 tension (PaO_2) was 50-100 torr the mean surface Po_2 of unheated skin was 27.2 (range 19-38) torr in infants <1500g, 14.3 (4-23) torr and those of 1500-2500g and 2.9 (2.5-5.0) torr in infants >2500g. Skin temperatures were not different between these groups. In contrast to adults and term infants, in infants <1500g the skin surface Po_2 correlated with the PaO_2 up to 100 torr ("unheated" skin $Po_2=0.33\ PaO_2+5.42$; $r=0.76$). Crying, blood transfusion and phototherapy markedly increase the skin Po_2 suggesting that a higher skin blood flow contributes more than differences in skin diffusion resistance or metabolism to the higher skin surface Po_2 in resting premature babies.

The concept of the unheated skin as a virtually oxygen tight system obviously has to be revised for premature infants. Practical implications however, must remain a matter of speculation since oxygen fluxes across the unheated skin have not been measured in small premature infants. Supported by Deutsche Forschungsgemeinschaft (SFB 147 and Ve 32/3).

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A NEW DEVICE FOR DIAGNOSIS AND EVACUATION OF NEONATAL PNEUMOTHORACES. Marcia J. Wagaman, John G. Shutack, Ara S. Moomjian, Ronald D. Eavey, Thomas H. Shaffer, William W. Fox. (Spon. by Jean A. Cortner), Univ. of Pa. Sch. of Med., Dept. of Peds., The Children's Hospital of Philadelphia, and Temple University, Dept. of Physiology, Philadelphia, PA.

A closed system (CS) device with teflon needle, sideholes, and attached stopcock was compared to a Medicut needle to determine incidence of unintentional introduction of air during diagnosis, and efficiency of evacuation of neonatal pneumothoraces (PTX). Thoracentesis was evaluated in 10 white rabbits (1.3-1.6 kg) with the CS needle in R chest and Medicut in L chest. Evacuation of free intrapleural air following thoracentesis and evacuation of intentionally injected air (20 cc) was performed on both sides of the chest. Intrapleural pressure measurements, x-rays,and number ml. air evacuated were used to quantitate each step. The CS needle produced no air entry on x-ray and no changes ($P>0.05$) in (mean ± SEM) inspiratory pleural pressure (IPP) (-5.2 ± 0.62 cm H_2O) or expiratory pleural pressure (EPP) (-0.94 ± 0.55). Medicut taps (4.5 sec. to position stopcock) resulted in PTX on x-ray in 70% of trials and significant increase ($P<0.05$) of 1.28 ± 0.28 cm H_2O in IPP and 1.58 ± 0.36 cm H_2O EPP from baseline values. 23.7 cc (mean) air was evacuated from Medicut side. After 20 cc injection of air on CS needle side, a mean of 25.0 cc air was removed. Complete air evacuation occurred in 90% of CS needle trials vs. 60% with Medicut. The CS needle was safer, and more efficient than Medicut in evacuating air. In addition, since it is an airtight system, the CS needle can be used for diagnosis of PTX without the risk of introducing air.

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FACTORS DETERMINING THE CELLULAR UPTAKE OF BILIRUBIN. Richard Wennberg and L. Fraser Rasmussen. University of California, Davis - Sacramento Medical Center, Sacramento, California.

The toxicity of bilirubin is a function of the amount of bilirubin bound to cellular elements and the sensitivity of the cell to a given bilirubin load. We have examined the stoichiometry of cell binding of bilirubin by incubating red blood cells with various concentrations of bilirubin and serum in vitro, measuring the serum unbound bilirubin concentration (UBC) with the peroxidase assay, and extracting the RBC bilirubin with a human serum albumin solution.

Results: (1) The partitioning of the total bilirubin pool between serum and cells reached equilibrium within 10 minutes. (2) At equilibrium, the cellular content of bilirubin was a function of the UBC and not the total bilirubin concentration or bilirubin/albumin molar ratio.
(3) Albumin binding of bilirubin was not affected by pH.
(4) Cellular uptake of bilirubin was greatly influenced by pH. At physiological pH, bilirubin exists predominantly as an anion with only a small fraction present as the bilirubin acid. The increased bilirubin uptake at pH 7.0 vs. pH 7.4 corresponded to the calculated increase in the less soluble protonated bilirubin.

Conclusions: Cellular uptake of bilirubin is a function of the concentration of free bilirubin acid. It is probable that the risk for kernicterus (with respect to blood chemistries) can be estimated by measuring the serum UBC and blood pH.