1684 RELATIONSHIP BETWEEN EARLY AUDITORY BRAINSTEM RESPONSES AND LATER DEVELOPMENT IN VERY LOW BIRTHWEIGHT INFANTS (VLBW), C.Cox, M.Hack, CSU & CMRU, Clevel. Oh.

The auditory brainstem response (ABR) is frequently used to assess auditory and neurologic function in the neonatal intensive care unit (NICU). Although longitudinal data on the relationship of ABR to later auditory function is available, there is no information on ABR and later development.

To assess the prognostic value of the ABR pertaining to later neurologic and cognitive development, 45 VLBW (<1.5kg) (X B.Wt. 1.2g, X GA 29wks) were tested in the NICU and followed for 3 yrs. Behavioral hearing test and acoustic immittance data were obtained in addition to neurologic outcome results, Bayley Developmental Scales at 2 yrs, and Stanford Binet data at 3 yrs. corrected age. The children were separated into two groups based on whether the initial NICU ABR data were normal or abnormal (absence of Wave V at 30 or 60 dB HL or unclassifiable waveform). 8 subjects (18%) had abnormal ABR's in the NICU.

NICU ABR	BAYLEY SCALES	STANFORD BINET	NEURO. ABR.	SENSORINEURAL HEARING LOSS
Normal (n=37)	Motor 88±13 Mental 95±16	93±15	3*	1
Abnormal (n=8)	82±10 84±13	85±15	0	1

*2C.P., 1 Hydrocephalus (this child later had an abnormal ABR) Although group means were different, a t-test analysis of differences between the mental and motor portions of the Bayley Scales and Stanford-Binet failed to reach significance (p<.05).

These results indicate that early ABR failures have little prognostic value with regard to subsequent Bayley and Stanford-Binet scores or neurologic abnormality.

1685 MATURATION OF BRAIN NEUROTRANSMITTER METABOLISM IN NEONATES. F.S. Silverstein, S. Donn and M.V. Johnston (spon. by G. Goldstein) Dept. of Pediatrics and Neurology, University of Michigan, Ann Arbor, MI.

Serotonin and catecholamine pathways originating in the brainstem regulate sleep, temperature, and feeding in infants. To assess maturation of these systems at birth we measured lumbar cerebrospinal fluid (CSF) 5-hydroxyindolacetic acid (5-HIAA) and homovanillic acid (HVA), stable acid metabolites of serotonin and dopamine, using high performance liquid chromatography with electrochemical detection. CSF was obtained for medical indications; samples were deproteinized with perchloric acid. 5-HIAA in preterm neonates 28-33/40 gestation (gstdn) was 4 times higher than in 6-10 yr olds (107±12 ng/ml, N=19, vs 27±1, N=43) and slightly higher than in term neonates 34-42/40 gstdn (96±10, N=29) and 1-6 month (mo) olds (91±8, N=13, p<.01 ANOVA). In contrast HVA peaked in the 1-6 mo olds group at 167±11 ng/ml; this level was 61% higher than in the 28-33/40 gstdn (104±12) and 22% above the 34-42/40 gstdn group (137±15, p<.01 ANOVA). In 6-10 yr olds HVA declined to 67±3. The HVA/5-HIAA ratio increased from 1.2±.2 in preterms to 1.94±.2 in 1-6 mo olds and 2.58±.1 (p<.01 ANOVA) in the older children. Lumbar CSF levels of HVA and 5-HIAA probably reflect turnover of transmitters emanating from brain since ventricular values in 2 infants were 2-3 fold higher than lumbar levels and obstructive hydrocephalus reduced HVA by 90% and HIAA by 67% in 1 patient. The results agree with experimental evidence that turnover of central biogenic amine transmitters is relatively high in perinatal mammals. Serotonin pathways may mature earlier than nearby dopamine neurons.

1686 REGIONAL CEREBRAL BLOOD FLOW (CBF) IN A RAT MODEL PARALLELS CHANGES IN HUMAN PERINATAL HYPOXIC-ISCHEMIC ENCEPHALOPATHY (HIE). F. Silverstein, K. Hassett, and M. Johnston. (Sponsored by Gary Goldstein) University of Michigan, Dept. of Pediatric Neurology, Ann Arbor.

Exposure of immature rats to 8% O₂ after unilateral carotid artery ligation (UCL) is used as a model of perinatal HIE. The procedure causes reproducible metabolic, neurochemical and histopathological changes lateralized to forebrain on the side of ligation. Tissue effects are attributed to a combination of hypoxemia and relative ischemia, but CBF has not been measured. To study regional CBF in 7 day old pups, we did intracardiac injections of ¹⁴C-iodoantipyrine (IAP) and measured tracer accumulation in brainstem, striatum and frontolateral cortex. In controls, brainstem values (dpm/mg tissue) were 220±9% higher than those in striatum and cortex and side to side variation was negligible. Hypercarbia (pCO₂60) doubled accumulation of tracer but 8% O₂ (pAO₂30) had no effect. Relative CBF to each hemisphere was expressed as striatum/brainstem (S/B) ratio since brainstem is not supplied by the carotid arteries (S/B=.49±.03 in controls). UCL reduced IAP in the ipsilateral hemisphere by 20% (S/B=.46±.01 contralateral vs .37±.02 ipsilateral, P<.05, N=8). 8% O₂ superimposed on UCL progressively reduced ipsilateral hemisphere flow to 30% of the contralateral hemisphere value at 2 hrs (S/B=.48±.02 vs .14±.01, p<.001, N=10). IAP autoradiography and India ink perfusions confirmed that the ipsilateral hemisphere became ischemic and remained so for up to 4 hrs after hypoxia ended. The decrease in CBF in this rat model parallels changes which probably lead to brain injury in human perinatal HIE.

1687 EFFECT OF HEMATOCRIT ON CEREBRAL BLOOD FLOW (CBF) IN LAMBS. M.L. Hudak, R.C. Koehler, A.A. Rosenberg, R.J. Traystman and M.D. Jones, Jr. The Johns Hopkins Hospital, Baltimore, Maryland 21205

In anemia and polycythemia the relative contributions of changes in arterial O₂ content (CaO₂) and blood viscosity are unclear. We studied this question in 9 unanesthetized lambs (<7 days of age). After initial measurements of arterial and sagittal sinus PO₂, PCO₂, CaO₂, CBF (microsphere technique), cerebral O₂ consumption (CMRO₂), cerebral fractional oxygen extraction (E=CMRO₂/CBFxCaO₂) and the position of the oxyhemoglobin dissociation curve (P₅₀) were made (State 1), we performed an exchange transfusion with methemoglobin-containing adult sheep red cells. This changed hematocrit without changing CaO₂. After exchange, the hematocrit increased from 20 to 40% while CaO₂ changed from 8.8±0.2 (X±SEM) to 10.1±0.2 ml/100 ml. Repeat measurements were made in 1 hour (State 2). PCO₂ and P₅₀ did not change (paired t test). CBF fell (138.8±14.1 vs 102.4±5.4 ml/100g/min, p<.02), and E rose in each experiment (0.51±0.01 vs 0.60±0.01, p<.001). CMRO₂ was constant (6.2±0.5 vs 6.2±0.4 ml/100g/min). Viscosity rose from 1.7 to 3.7 centipoise (measured at a shear rate of 230/sec.). Four of these animals were given methylene blue to reduce methemoglobin and CaO₂ rose to the value appropriate for the hematocrit. Measurements were repeated (State 3). The ratio (CBF₁-CBF₂)/(CBF₂-CBF₃) represents the proportion of the change in flow resulting from a change in viscosity. This ratio is 0.45. Thus changes in viscosity account for about half of the changes in CBF. (NIH Grant HD 13830)

1688 FLUID BALANCE IN LOW BIRTH WEIGHT (LBW) INFANTS: RELATIONSHIP TO INTRACRANIAL HEMORRHAGE (ICH). Robert Kahle, Jo Anne Nakagawa, W. Donald Shields, Michael Sherman (Spon. by Dale L. Phelps). UCLA School of Medicine, Center for the Health Sciences, Dept. of Pediatrics, Los Angeles.

Alterations in cerebral transvascular pressure, associated with dehydration or hyperosmolality, have been implicated as contributing factors in ICH of LBW infants. If correct, fluid restriction of LBW infants (<1500 gms) with respiratory distress or patent ductus arteriosus should be curtailed. We reviewed the fluid balance of 80 LBW infants who had serial cranial ultrasound exams between birth and 5 days of age. The frequency of ICH was 55% (44/80), and ICH occurred in 40/44 infants by 2 days of age. Over this period, weight loss, fluid intake and serum Na⁺ did not differ in the infants with and without ICH (x±SD).

Weight Loss (% of Birth Weight)		Fluid Intake (cc/Kg/day)		Serum Na ⁺ (meq/L.)	
(-) ICH	(+) ICH	(-) ICH	(+) ICH	(-) ICH	(+) ICH
6.4±5.0	5.2±6.7	91±26	95±36	140±5	143±9

These parameters remained similar in the two groups between 3 and 5 days of age. Birthweight (BW) and gestational age (GA) were significantly lower in the ICH group (1050±196 gm and 28.4±2.1 wks vs 1186±201 gms and 30.0±1.9 wks; x±SD, p < 0.005). When narrower BW and GA ranges were analyzed, weight loss, fluid intake and serum Na⁺ remained the same in the two groups, but BW and GA remained lower in the ICH group. We conclude that it is unlikely fluid restriction contributes to the pathogenesis of ICH, although its contribution to the extension of ICH cannot be excluded.

1689 SYSTEMIC HYPERTENSION ASSOCIATED WITH POOR OUTCOME AFTER ACUTE BRAIN INJURY. Robert K. Kanter, James B. Carroll, Ernest M. Post, (spon. by Roger E. Spitzer), SUNY, Upstate Medical Center, Dept. of Peds., Syracuse, N.Y.

We studied intensive care unit (ICU) records of 42 children with Glasgow Coma Score ≤ 7 to better define the relation between high blood pressure (BP) and poor neurologic outcome following acute brain injury. Diagnoses included Reyes Syndrome (10), head trauma (16), anoxia (13) and CNS infection (3) and excluded those dying of circulatory failure. Corrected peak BP (in mmHg): BPC= (peak systolic BP)-(systolic BP 95%ile for age), was recorded in each 6 hour interval. Persistence of high BP was defined as BP >95%ile in 2 successive 6 hour intervals. Outcome was classified as good (mild or no deficit) or poor (death or severe neurologic deficit making patient dependent on special care). All patients' highest BP exceeded 95%ile. Highest BPC was: 1-20 in 8/42 (19%), 21-40 in 19/42 (45%), and >40 in 15/42 (36%). In those with highest BPC >20, poor outcome occurred in 19/34 (56%) while in those with highest BPC ≤ 20, poor outcome occurred in only 1/8 (13%) (p=.0316). Of those with high BP persisting until ICU discharge, 14/19 (74%) had poor outcome, while those with BP normalizing prior to ICU discharge had poor outcome in only 6/23 (26%) (p=.0026). Mean BPC in those with poor outcome tended to exceed mean BPC in patients with good outcome in each time interval from day 4 onward, with the difference reaching p<.05 on days 7, 9 and 10. Severity as well as persistence of high BP identify patients with poor outcome after acute brain injury. This finding justifies further attempts to test the benefit of controlling high BP in the brain injured patient.