1672 THE USE OF CAFFEINE (C) IN THE TREATMENT OF APNEA ASSOCIATED WITH THE ARNOLD-CHIARI MALFORMATION (ACM). J.M. Davis, T. Turmen, R. Zinman, J.V. Aranda, Dept Pediatrics, McGill University - Montreal Children's Hospital, Montreal, Quebec, Canada.

The occurrence of severe apnea, not associated with vocal cord paralysis, has been well documented in patients with ACM. The cause of this apnea appears to be brainstem compression and posterior fossa decompression is the only reported treatment. The methylxanthines (caffeine and theophylline) have been shown to be effective in the treatment of infantile apnea. We studied one infant with severe apnea and ACM before and after C. Ventilation (V_F) was measured by attaching the endotracheal tube to a pneumotachometer to measure flow and electronically integrated to give tidal volume (V_T), before and after C (10 mg/kg IV). Inspiratory times (T_I) and total cycle duration (T_{TOT}) were obtained directly from these recordings. In our patient, there was a significant decrease in apnea frequency (from 20 to 3 episodes/day), less variability in breathing patterns, and a shift to the left of the CO_2 response curve (V_F increased from 2.0 to 3.5 l/min, V_T from 36 to 46 ml). An increase in mean inspiratory flow was also noted (from 75 to 115 ml/sec), which is a mechanical transform of central inspiratory drive (V_T/T_I). Timing mechanisms were unchanged (T_I/T_{TOT}). Our findings in one infant suggest that C may be an effective adjunct in the treatment of apnea associated with ACM. Since the apnea is usually so severe and difficult to manage C may be useful in controlling apnea until further therapeutic modalities can be considered.

†1673 SAFETY OF A HIGHER LOADING DOSE OF PHENOBARBITAL IN THE TERM NEWBORN. SM Donn, TH Grasela, GW Goldstein. Depts. of Pediatrics, Neurology, Pharmacy, and College of Pharmacy, University of Michigan, Ann Arbor.

The conventional loading dose of phenobarbital (PB) for newborns with hypoxic-ischemic convulsions, 20 mg/kg, often fails to control seizure activity. To determine the safety of a higher loading dose, 10 severely asphyxiated term newborns at a mean age of 2.7 hours (range 0.6 - 11.5) were given 30 mg/kg of PB intravenously over 15 minutes. Three of the infants received PB after the onset of convulsions, while 7 infants were similarly treated to prevent seizures. None of the 10 infants displayed any evidence of respiratory depression, hypotension, or bradycardia during or after receiving PB. Mean serum PB concentration 2 hours after loading was 30.0 ± 3.2 µg/ml and the apparent volume of distribution was 0.97 ± 0.18 L/kg. Calculated mean serum half-life was 148 hrs and steady-state clearance was 0.08 ml/min/kg. One of the 3 seizing infants responded to this dose. Despite serum PB concentrations of 36 and 28.3 µg/ml, the other two seizing infants required additional therapy. None of the 7 infants treated prophylactically developed clinical or electroencephalographic evidence of seizures.

We conclude that the higher PB loading dose can be administered to term infants without short term adverse effects on cardiorespiratory function. The results of our observations suggest the need for a controlled trial to assess the efficacy of PB to prevent seizures in asphyxiated term newborns.

1674 INTRACRANIAL HEMORRHAGE IN BREAST FED INFANTS ASSOCIATED WITH VITAMIN K DEFICIENCY. W.T. Chaou and D.V. Eitzman, Changhua Christian Hospital (CCH), Changhua, Taiwan, and University of Florida, Department of Pediatrics, Gainesville, Florida.

During an 18 month period 30 infants, 1/2 to 6 months of age, who were previously well, were admitted to CCH with evidence of central nervous system involvement (seizure, conscious disturbance or bulging fontanel) and also with evidence of a bleeding disorder. They were studied with computerized axial tomography and ultrasound. All had intracranial hemorrhage although some only had subarachnoid hemorrhage. All were entirely or primarily breast fed, none had received vitamin K at birth and coagulation studies prior to treatment showed markedly prolonged PT and PTT which was corrected with vitamin K or fresh whole blood. All the evidence in this and other studies of similar babies indicates that this was a deficiency of vitamin K due in part to the omission of vitamin K at birth, but also due to the limited vitamin K intake. In only 2 studies has there been a suggestion of a coumarin compound in the mother's diet or administered to the infant. It should be possible to prevent this catastrophic event with either vitamin K at birth and/or a supplement of vitamin K in breast fed babies. Follow-up has demonstrated either neurologic problems or delayed head growth suggesting brain damage.

●1675 GLYCEROL INDUCED DECREASE CEREBROSPINAL FLUID FORMATION, Huda Y. El-Hibri, Sada Okumura, John P.

Laurent, Marvin A. Fishman, Baylor College of Medicine, Texas Children's Hospital, Dept. Pediatrics & Neurology, Houston, TX

Glycerol is used in the treatment of increased intracranial pressure, cerebral edema, and hydrocephalus in infants. The effects of glycerol on cerebrospinal fluid (CSF) dynamics have not been studied. Accordingly, we studied the acute effect of glycerol administration on CSF production in nine anesthetized mongrel dogs. CSF formation rates were measured by ventriculo-cisternal perfusion utilizing artificial spinal fluid and albumin - 1^{131} . Serial measurements of CSF formation rates and serum osmolalities were obtained during an eight hour period, four hours preceding and following the nasogastric administration of 3gm/kg of glycerol.

The mean rate of CSF formation during the control period was 0.04 ± 0.02 ml/min decreasing to a trough of 0.01 ± 0.01 ml/min at both 90 and 120 minutes post glycerol administration $P < 0.025$. When analyzing the decrease in CSF production using each dog as its own control, the change was significant at $P < 0.001$ level. Mean serum osmolality increased from 296 ± 4 mOsm/kg water to a maximum of 308 ± 7 mOsm/kg water at 90 minutes after glycerol administration. CSF production and serum osmolality were inversely related with an r value of -0.85 .

In summary, acute glycerol administration decreases CSF production in dogs. The rate of CSF production is inversely related to the increase in serum osmolality after glycerol administration.

1676 CEREBRAL BLOOD FLOW IN THE NEWBORN: VARIABLES WHICH EXPLAIN THE RELATIONSHIP BETWEEN DOPPLER ULTRASOUND AND 133 -XENON CLEARANCE

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We have previously reported correlations between 133 -Xenon cerebral blood flow measures and two forms of Doppler ultrasound measure — continuous wave and range-gated — in studies of neonatal cerebral blood flow (Greisen, Johansen, Ellison et al.). In the present study, the contributions of pCO_2 , heart rate (HR), gestational age (GA) and blood pressure (BP) to these correlations were analyzed. Using jackknife techniques (Mosteller and Tukey), we also examined the stability of prediction of 133 -Xenon flow from the ultrasound measures.

GA was a major contributor to the covariance between 133 -Xenon and the 12 ultrasound measures (two methods, three measures — pulsatility index (PI), mean flow velocity (MFV) and end diastolic flow velocity (EDFV), at two sites — anterior cerebral artery (ACA) and internal carotid artery (ICA)). The contributions of pCO_2 , HR and BP were small, both singly and in combination, after the removal of that portion of the covariance accounted for by GA. We suggest that investigators should control for GA in studies of neonatal CBF.

Four ultrasound measures accounted for a notable portion of the 133 -Xenon CBF variance and were significantly stable predictors according to the jackknife analysis: EDFV of the ICA by continuous wave Doppler, and three measures by range-gated Doppler — MFV of the ACA, MFV of the ICA and EDFV of the ICA. None of the PI measures at either site by either Doppler technique had stable and noteworthy relations to 133 -Xenon CBF measures.

The results, the methods of data analyses and their implications will be discussed.

1677 CSF LACTATE DEHYDROGENASE PREDICTS SEVERE NEONATAL INTRAVENTRICULAR HEMORRHAGE. Stephen Engelke, John

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CSF LDH is elevated in neonatal IVH and may arise from cerebral injury (Engelke, 1983). To test the value of CSF LDH in detecting cerebral injury, a prospective study was carried out in 57 neonates ≤ 32 weeks gestation. Total CSF LDH and its isoenzymes were measured on admission and cranial ultrasound (US) was performed on day 1 and 3. Ultrasounds were graded normal, small-moderate IVH, moderate-large IVH with ventricular dilation or parenchymal extension. There was a significant correlation of CSF LDH with severity of US hemorrhage ($p < 0.02$), although CSF red and white cell counts and glucose did not correlate with IVH. Comparing patients with large IVH and ventricular dilation or parenchymal extension vs patients with normal US or small IVH, mean CSF LDH was 169 v. 49 U/L. LDH isoenzyme 2 also correlated with severity of IVH ($p < 0.01$).

Elevated CSF LDH was also significantly related to mortality ($p < 0.04$). Mean LDH in patients who died compared to survivors was 174 v. 48 U/L. In addition, elevated LDH isoenzyme 1 correlated with mortality ($p < 0.02$).

In conclusion, our results show an increase in CSF LDH in patients with IVH and ventricular dilation or parenchymal hemorrhage, which may reflect cerebral infarction. Elevated CSF LDH also correlated with risk of death. Follow-up testing will assess its predictive value for long term neurodevelopmental handicap.