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INTRAVENTRICULAR HEMORRHAGE - A LIMITED PREDICTOR OF OUTCOME IN PREMATURE INFANTS. Yolande Smith, Anita M. Sostek, Kathy Katz, K.N. Siva Subramanian (Sponsored by P.L. Calcagno). Department of Pediatrics, Georgetown University Medical Center, Washington, D.C.

Intraventricular hemorrhage (IVH) was assessed serially by portable cranial sonography on 137 infants with birthweight (BW) ≤ 1750 and gestational age (GA) ≤ 34 weeks in 1980 & 1981 and classified according to Papile. 85 infants (62%) had evidence of IVH of whom 55 (65%) survived; 49 (94%) of the 52 infants with normal sonograms survived. 62 of the 137 infants studied were assessed quarterly by neurological evaluation and Bayley Scales of Motor & Mental Development, corrected for prematurity; scores ≥ 84 were assessed as normal. Mean age at last follow-up was 23.3 months. Mean BW & GA were similar in all groups. (3 infants were shunted for hydrocephalus.) Grade I IVH did not differ significantly from Grade II, and Grade III did not differ from IV; thus they were combined into Minor (I&II) and Major (III&IV).

IVH	Total	PDI ≥ 84	MDI ≥ 84	PDI < 84	MDI < 84	Abnormal Neuro
Normal	23	21	20	2	3	0
Minor	16	12	15	4	1	3
Major	23	14	18	9	5	11

33 (90%) of the 39 infants with IVH have normal mental evaluations at 2 yrs of age, similar to 20 of 23 infants with no hemorrhage; motor handicaps, however, are more common in IVH patients. IVH alone is therefore a poor predictor of outcome in premature infants. Other prenatal and neonatal factors are of major importance.

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INTRAVENTRICULAR HEMORRHAGE (IVH) & VITAMIN E (VE) IN VERY LOW BIRTH WEIGHT INFANTS: EFFICACY OF EARLY IM ADMINISTRATION. Michael E. Speer, Cindy Blifeld, Arnold J. Rudolph, Prabhajeet Chadda, Blair Holbein, Helen M. Hittner. (Spon. by Thomas N. Hansen) Baylor College of Medicine Texas Children's Hospital, Department of Pediatrics, Houston, Texas.

To determine whether early IM VE supplementation influences the incidence of IVH in infants < 1500 gms, data were analyzed prospectively from 181 inborn infants enrolled on protocols of 2 consecutive yrs. In the first study, (1981C), 47 patients received 100 mg/kg/day of oral VE (3000 mOsM) daily with the first dose administered within 8 hrs of birth. In the second study, 134 infants received 100 mg/kg/day of VE emulsion (150 mOsM) in the same manner; however, 64 patients received, in addition, IM VE on days 1, 2, 4 and 6 of life (1982T) while 70 patients received placebo injections (1982C) in a randomized double blind fashion. First wk VE levels were the same in the 1981C & 1982C patients but were significantly higher in the 1982T patients. In spite of this difference, no change in the incidence of sepsis or necrotizing enterocolitis was observed. Both the incidence and severity of IVH were reduced in the 1982T patients as compared to the 1982C patients ($p < 0.02$ & $p < 0.05$ respectively) and as compared to the 1981C patients ($p < 0.05$ & $p < 0.001$ respectively). The data suggests that VE, a natural antioxidant, may play an important role in protecting the CNS microcirculation from the effects of hypoxic/ischemic injury.

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BLOOD-BRAIN BARRIER PERMEABILITY (BBBP) FOLLOWING ASPHYXIA AND HYPOTENSION IN PIGLETS. B.S. Stonestreet, G.H. Burgess, and H.F. Cserr. Brown Univ., Women & Infants Hosp., Dep. Ped. & Physiol., Providence, RI.

Asphyxia (A) and hypotension (H) may alter BBBP and cause cytotoxic edema in piglets (P). 2-4 day old spontaneously breathing P underwent A for 1 hour by exposure to 15% CO₂, 12% O₂, and balanced nitrogen resulting in pH=6.6 $\pm$ 0.2, PaO₂=34 $\pm$ 3 mmHg and PaCO₂=70 $\pm$ 6 mmHg, M $\pm$ SD. During the last 20 min of A, superimposed hemorrhagic H by phlebotomy (blood removed=30 $\pm$ 9 ml/kg), resulted in a fall in mean arterial blood pressure to 29 $\pm$ 10 mmHg. BBBP to ²⁴Na and ¹⁴C-mannitol was measured as the permeability X surface area product (PS). BBBP, brain water and brain electrolytes were determined 10 min (acute A&H) or 24 hours (post A&H) after A&H. Compared to age matched controls, A&H resulted in the following changes:

Groups	N	2 ⁴ PS(ml/min/g brain x 10 ⁴) Na	1 ⁴ C-Mannitol(M)	Ratio Na/M
Acute A&H	6	8.5 $\pm$ 1.9*	3.3 $\pm$ 0.9*	2.6 $\pm$ 0.4
Control(C)	12	15.9 $\pm$ 2.4	5.2 $\pm$ 1.6	3.3 $\pm$ 1.2
Post A&H	6	14.5 $\pm$ 2.7	ND	ND
Control(C)	7	15.8 $\pm$ 1.3	ND	ND

M $\pm$ SD, * $p < 0.05$ compared to age matched C, ND: not determined. Brain water & electrolytes were similar in all groups. PS for ²⁴Na and M was decreased following acute A&H. Na/M values were similar in acute A & H vs C indicating a lack of change in the endothelial "pore" size. The decrease in PS may indicate a reduction in Na and M transport and/or more likely a reduction in brain endothelial capillary surface area.

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SINGLE DOSES OF VALPROATE (VAL) REDUCE KETONEMIA IN INFANT MICE: REVERSAL BY L-CARNITINE. J.H. Thurston, R.E. Hauhart, J.E. Carroll, J.A. Schiro. Washington University, Dept. of Pediat., St. Louis, MO.

We have reported that chronic VAL administration reduced plasma β -hydroxybutyrate (β -OHB) levels in suckling mice and fasting epileptic children. This is a study of the effect of single doses of VAL in mice, and possible therapeutic measures. Plasma β -OHB levels (mean $\pm$ SE) in 2 to 10-d-old mice (number in parentheses) 30 min after s.c. VAL injection are given below.

Control (0.9%NaCl)	mg/kg	VAL	Change	P value
1.06 $\pm$ 0.13 (4)	50	0.271 $\pm$ 0.043 (4)	-74%	< 0.001
0.965 $\pm$ 0.082 (4)	10	0.416 $\pm$ 0.013 (4)	-46%	< 0.001

In other mice, 15 mg/kg of VAL reduced liver free carnitine (CARN) levels 47% in 30 min (74.5 $\pm$ 9.2 μ mol/kg (4) vs 140 $\pm$ 14 in controls (4), $P < 0.001$). Since CARN is essential for long-chain fatty acid oxidation (hence ketogenesis), we examined the effect of concomitant administration of 2.5 mmol/kg L-CARN with 10 mg/kg of VAL (0.06 mmol/kg). The addition of L-CARN increased plasma β -OHB levels from 0.416 $\pm$ 0.013 mm (4) (VAL alone) to 0.606 $\pm$ 0.028 mm (4) ($P < 0.001$) (still 37% less than in controls, 1.06 $\pm$ 0.03 mm (4), $P < 0.001$). Injection of 2.5 mmol/kg of L-CARN with a smaller dose of VAL, 5 mg/kg, increased plasma β -OHB levels from 0.586 $\pm$ 0.039 mm (4) (VAL alone) to 0.843 $\pm$ 0.037 mm (4) ($P = 0.003$) (not different from the control value, 0.979 $\pm$ 0.059 mm (4)). Decreased liver CARN levels suggest one explanation for VAL-induced hypoketolemia in mice and possible stratagems for prophylaxis and/or treatment of VAL-associated hepatotoxicity in infants and children.

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DICARBOXYLIC ACIDS AS UNCOUPLERS IN REYE'S SYNDROME. James H. Tongard, Godfrey S. Getz (Spon. by Peter R. Huttenlocher). Pritzker School of Medicine, Univ. of Chicago. Depts. of Pediatrics, Neurology, and Pathology.

A general impairment of liver mitochondrial enzymes is central to Reye's Syndrome (RS). The effect of RS serum from 8 patients in profound coma on respiration of isolated liver mitochondria was measured with 2.5 mg of mitochondrial protein, 3 mM substrates, and 5x concentrated serum. RS serum stimulates respiration (1.05 $\pm$.14 nmol O₂/min/mg protein, control .30 $\pm$.08). This effect is due to: 1.) oxidation of uric acid by microsomes contaminating the preparation, 2.) fatty acids providing substrate, 3.) uncoupling of oxidative phosphorylation by 30-40%. The amount of uncoupling is additive, correlates with the amount of free fatty acids in the serum but is not inhibited by 1% defatted albumin as is oleate added to normal serum. The degree of stimulation/mcg of fatty acid is distinct from that of oleate or octanoate added to normal serum. RS serum stimulates respiration in the presence of antimycin and 3 mM ascorbate by 80-149%; oleate + normal serum causes a 0-10% increase. 3 mM medium chain dicarboxylic acids are not readily bound to 1% albumin and induce a 90-105% increase in antimycin/ascorbate respiration; they require intact mitochondria and exogenous substrate. Dicarboxylic acids are markedly elevated (1-3 mg/mg creatinine, N=12; controls $< .10$, N=40) in urine from our RS patients and unusual long and unsaturated dicarboxylic acids were reported in the serum of 2 RS patients (Amer. Soc. Mass. Spec. 31:98, 1983). Thus, dicarboxylic acids act as uncouplers and may be important in the general impairment of mitochondrial function in RS and other disorders where large amounts of dicarboxylic acids are present.

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NEUROBEHAVIORAL DEFICITS IN MODERATELY JAUNDICED TERM INFANTS. J. Tyson, F. Eubanks, T. Shimatsu, R.E. Lasky, A. Rupert, M. Porter, (spon. by C. R. Rosenfeld) Southwestern Med. Sch., Dept. Peds., and Univ. Tx. at Dallas, Dept. Comm. Disorders, Dallas, Tx.

We used Brazelton's Neonatal Behavioral Assessment Scale (NBAS) and auditory brainstem evoked responses (ABER) to evaluate moderately jaundiced term infants for neurobehavioral deficits. To evaluate behavioral deficits, an examiner blinded to jaundice by specially-tinted contact lenses, performed NBAS on 20 otherwise healthy, jaundiced infants (bilirubin=12-17 mg%) prior to phototherapy and 20 healthy controls matched for race, sex, age, delivery mode, and feeding method. Unexpected differences in gest. age and BW favored controls (39.9 vs. 39.1 wks; 3225 vs. 2938g) but had no significant effect on NBAS summary variables. NBAS mean scores consistently favored controls (28/37 NBAS items; $p < 0.01$). 20 more infants will be assessed to verify jaundice-related effects. To evaluate possible ABER deficits, 30 otherwise healthy, term jaundiced infants (total bilirubin 10-15 mg%) and 12 healthy, term controls were studied. ABER reliability was verified. Latency of Wave V but not Wave I in jaundiced infants exceeded controls ($p < .01$). Similar patterns were observed for ABER amplitudes. Response to phototherapy was variable. NBAS and ABER findings prior to phototherapy are similar to those reported at higher bilirubin levels with phototherapy. Bilirubin levels previously considered innocuous are probably associated with alterations in both brainstem function and infant behavior.