†1711 ENERGY STATE OF THE BRAIN IN EXPERIMENTAL NEONATAL STATUS EPILEPTICUS-R.C. Vannucci & F. Vasta, UMDNJ-Rutgers Medical School, Department of Pediatrics, New Brunswick, N.J.; D.G. Fujikawa, B.D. Dwyer & C. G. Wasterlain, Veterans Administration Medical Center, Department of Neurology Sepulveda, California

Cerebral metabolic responses to status epilepticus (SE) were investigated for the first time in neonatal primates. Ten 14-day old Marmoset monkeys were anesthetized with ketamine & monitored for systemic BP, blood gases & glucose. An IM injection of bicuculline produced tonic-clonic convulsions without hypoxemia, hypoglycemia or hypotension for 30 min,; thereafter, brains were quick frozen & prepared for regional NADH reflectance fluorometry & ATP bioluminescence. Micro-samples of forebrain were analyzed for ATP (C-2.66, SE-2.04), P-creatine (C-3.45, SE-0.92), Glucose (C-3.57, SE-0.20) and Lactate (C-1.23, SE-10.05)mmol/kg. Similar alterations in metabolite levels were noted in diencephalon and in deep cerebral cortical structures. NADH fluorometry produced patchy relatively symmetrical areas of enhanced fluorescence in boundary zones between anterior & middle cerebral arteries of cerebral cortex, in cingulate gyri & diencephalon. Regional ATP was decreased globally in SE animals. Furthermore, ATP levels were not statistically different in brain regions with high or low NADH fluorescence. Thus, glycolytic intermediates & high energy reserves are disrupted in brains of neonatal Marmosets sustaining SE. The insult follows in part a vascular distribution. Whether or not the altered energy state is severe enough to be associated with brain damage is under investigation. (Supported by Research Service of the Veterans Administration and by NIH #NS-13515 and #HD-15738.

●1712 GLUCOSE SUPPLEMENTATION DOES NOT ACCENTUATE HYPOXIC-ISCHEMIC BRAIN DAMAGE IN IMMATURE RATS: BIOCHEMICAL MECHANISMS-R.C. Vannucci, F. Vasta & S.J. Vannucci, UMDNJ-Rutgers Medical School, Department of Pediatrics, New Brunswick, N.J. 08904.

Previous investigations from our laboratory have shown that hyperglycemia during the course of hypoxia-ischemia (H-I) does not increase brain damage in immature animals as occurs in adults (Voorhies et al 1982). To clarify biochemical mechanisms responsible for this age specific paradox, we subjected 7-day postnatal rats to unilateral common carotid artery ligation followed by the hypoxia produced by the inhalation of 8% oxygen for 2hr (Rice et al, 1981). Experimental animals received 0.1 ml. 50% glucose sc 15 min prior to onset of hypoxia, which increased blood glucose to 350 mg/dl for 2 hr. Glucose in the cerebral hemisphere ipsilateral to the carotid occlusion was exhausted by 20 min of H-I in control (saline injected) rats but not until 2 hr in glucose-treated animals. Brain lactate and puruvate increased to a greater extent in the glucose-treated animals but only at 20 and 60 min, such that L/P ratios were comparable at 2 hr. Declines in ATP and P-creatine occurred earlier in control animals, but by 2 hr low levels were seen in both groups. Total adenine nucleotides also were depleted to the same degree. The findings indicate that despite an early protective influence of glucose on brain glycolytic intermediates & high energy reserves during cerebral H-I, the effect is short lived even with continuing hyperglycemia. Limited glucose entry into the immature brain at any blood glucose level retards anaerobic metabolism during H-I; which, in turn, leads to a disruption of the energy state of the tissue and ultimate brain damage. (NIH #HD-15738).

1713 SERUM CREATINE KINASE BRAIN SPECIFIC ISOENZYME (CK-BB) IN TERM ASPHYXIATED INFANTS. Rose M. Viscardi, Steven M. Donn, Donald A. Giacherio, Gary W. Goldstein, Depts. of Pediatrics, Pathology, and Neurology, University of Michigan Medical Center, Ann Arbor.

Asphyxiated term infants (A) are at risk for early-onset seizures, persistent encephalopathy, abnormal EEG's and long-term sequelae. CK-BB is elevated in preterm infants with IVH and term infants with post-asphyxial neurologic injury. We correlated CK-BB with other laboratory and clinical assessments of asphyxia in the neonatal period and with outcome at 3-6 months. Criteria for asphyxia was one or more of: Apgar (5 min) $\leq$ 5; need for resuscitation beyond 5 min; abnormal neurologic exam by 24 h of age with a history suggestive of perinatal asphyxia. Serum total CK and BB fraction were measured from umbilical cord blood and samples were drawn at 6-12 h and 24-36 h in 8 normal and 13 A infants. Sarnat encephalopathy staging was done daily and EEG's were obtained on days 1 and 7 for A infants. CK and BB values were not affected by route of delivery or duration of labor. Differences were seen in CK-BB measurements at 6-12 h for:

	CK-BB (U/L)		CK-BB (U/L)	p
Apgar < 5	48 ± 53	Apgar ≥ 5	8 ± 8	< 0.05
Seizures	62 ± 72	No seizures	15 ± 21	< 0.05
Sarnat II/III	62 ± 72	Sarnat O/I	15 ± 21	< 0.05
Abnormal outcome	62 ± 72	Normal	15 ± 21	< 0.05

The CK-BB peak at 6-12 h rather than in cord blood suggests that the asphyxial insult was more closely related to intrapartum period than chronic intrauterine events. The best predictors of poor prognosis are a low Apgar at 5 min and neonatal seizures. CK-BB is a useful biochemical marker of significant asphyxia.

●1714 EFFECT OF THEOPHYLLINE ON THE CEREBRAL BLOOD FLOW (CBF) RESPONSE TO HYPOCAPNIA IN NEWBORN PIGLETS. L. Craig Wagerle, Barry Lawson, and Maria Delivoria-Papadopoulos. Univ. of PA. Sch. of Med., Dept. of Physiology, Phila., PA. 19104

Cerebral hypocapnic vasoconstriction is limited such that CBF no longer decreases when $PaCO_2$ falls below 20-25 torr, presumably because tissue hypoxia resulting from hypoperfusion counteracts the CO_2 induced vasoconstriction. This study examines the effect of theophylline (T), an adenosine receptor antagonist, on the CBF response to hypocapnia in newborn piglets. Twelve piglets (2-5) days, ventilated under 30% N_2O anesthesia, were divided into two groups; one received T, 10 mg/kg i.v. (n=5) while controls received saline (n=7). CBF (microspheres), blood gases, pH, and blood pressure were measured during baseline ($PaCO_2$=40) and following sequential hyperventilation for 10 min, to $PaCO_2$'s of 31 (HV1), 23 (HV2), and 14 torr (HV3). In control pigs, CBF decreased from baseline (55±7) to 47±6 and 38±5 ml/min/100g during HV1 and HV2 with no further decrease at HV3, 38±5 ml/min/100g (mean±SEM). In T pigs, CBF decreased from 54±4 to 41±5 and 36±5 during HV1 and HV2 and decreased further to 28±4 ml/min/100g during HV3, $p < 0.01$. T enhanced vasoconstriction at low $PaCO_2$ in all brain regions. Additional studies in 6 piglets (α-chloralose), with a cranial window implanted over the left parietal lobe, examined the response of pial vessels to topical adenosine before and after T. Adenosine (10^{-5} M) caused 31% increase in pial vessel caliber, 151±21 μm (12 vessels) to 199±26 μm. T caused pial vasoconstriction (135±18 μm) but had no effect on adenosine-induced vasodilation (176±20 μm, 30%). These data show that T enhanced hypocapnic vasoconstriction at doses where cerebral vessel response to adenosine was not inhibited, suggesting that T acts by a mechanism other than adenosine receptor inhibition.

† 1715 NEW METHODS FOR THE DIAGNOSIS OF VARIANT FORMS OF NEUROLIPIDOSIS. David A. Wenger, Tooru Kudoh, Koji Inui, Shinsuke Fujibayashi and Martha Sattler. University of Colorado School of Medicine, Department of Pediatrics, Denver.

Most lysosomal storage diseases can be diagnosed by measuring the activity of a specific enzyme in an easily obtainable tissue sample. This can open the way to carrier identification in family members and prenatal testing when requested. A number of children and young adults with mental retardation, seizures and other clinical findings but normal enzyme values have been diagnosed as having a defect in sphingolipid catabolism by new techniques. Two additional types of patients with GM2 gangliosidosis have been identified. One type has a defect in hexosaminidase A (Hex A) not detectable with the usual fluorogenic substrate. The use of a sulfated synthetic substrate in the assay can make the diagnosis. Patients with a second variant type of GM2 gangliosidosis have normal Hex A levels but appear to be missing a required heat stable activator protein. Patients suspected of having GM2 gangliosidosis despite normal Hex A activity can be diagnosed by examining 1 ml of cerebrospinal fluid for gangliosides. Patients with normal arylsulfatase A activity have been demonstrated to excrete sulfatides and be unable to degrade ^{14}C-sulfatide presented to their cultured cells. Their deficiency in a required sphingolipid activator protein (SAP-1) has been demonstrated using monospecific antibodies (Ab) in easily obtained tissue samples. When cultured cells from these patients were given ^{35}S-methionine, and after 24 hrs they were lysed and treated with Ab, very little SAP-1 was produced.

1716 VISUAL EVOKED POTENTIALS (VEPs) IN ASPHYXIATED NEONATES. Hilary Whyte, Kwei Chin, Rosemary Menzies, Margot Taylor. (Spon. by P.R. Swyer). Research Institute, Hosp. for Sick Children, Dept. of Pediatrics, University of Toronto.

In order to determine the prognostic utility of VEPs in asphyxiated infants we studied 14 neonates (34-42 wks) with Apgars ≤6 at 5', excluding those with other complicating features (eg., jaundice, hydrocephalus). VEPs were recorded from Oz (reference Fz) in response to red LED stimulation within 24 hours of admission. Infants with Apgars ≤3 had 1-3 repeat testings within their first week.

Three infants with mild to moderate asphyxia (Apgar 4-6 at 5') had normal VEPs. The recordings were well defined and reproducible.

Eleven infants had severe asphyxia (Apgar ≤3 at 5'). Three had consistently normal VEPs. In one case, the initial VEP was abnormal, reverting to a normal pattern by 5 days. The remaining 7 infants had markedly abnormal and poorly replicating or flat VEPs which persisted. Normal or rapidly improving VEPs correlated well with clinical recovery in the neonatal period. Severely abnormal VEPs carried a poor prognosis. Six infants died in the neonatal period and the one survivor has severe persistent neurologic abnormality. This preliminary data suggests that repeated VEPs are a useful addition to the clinical evaluation of the asphyxiated neonate.