1594 COMPARATIVE EFFICACY OF SEVERAL ORGANIC ACIDS IN INDUCING A REYE'S-LIKE SYNDROME IN RABBITS. Jerome V. Murphy, Tsae Fung Hwang, Kathleen M. Marquardt. The Medical College of Wisconsin, Milwaukee Children's Hospital, Department of Neurology, Milwaukee, Wisconsin.

Reye's syndrome (RS) has been associated with a defect in organic acid metabolism; patients with RS have elevated serum concentrations of propionate, isobutyrate, butyrate, isovalerate, valerate, and octanoate infusion in rabbits can produce many features of RS. To learn if the organic acids which were elevated in the serum of RS patients are etiologic in the disease, rabbits were infused with each one individually and in combination. Carotid, juglar and intracranial lines were placed in 2 kg rabbits under general anesthesia and the animals were allowed to recover overnight. Intracranial and arterial pressures, serum ammonia, EEG, EKG, and respiratory rates were followed in the restrained animal during the infusion of the specific organic acids at rates of 0.02-0.06 mM/min. To date, isovaleric and octanoic acids have been effective in reproducing symptoms of RS. Propionic acid was less effective and isobutyrate ineffective. (Butyrate and valeric acid are being studied.) These data suggest that only certain of the organic acids, which are elevated in RS, are etiologic factors in this disease.

1595 KINETICS AND ADVERSE EFFECTS OF IV GLYCEROL IN REYE'S SYNDROME. Milap C. Nahata, Benny Kerzner, H. Juhling McClung, Earl S. Sherard, and Milo D. Hilty, The Ohio State University College of Medicine, Dept. of Pediatrics and College of Pharmacy and Children's Hospital, Columbus, Ohio.

In severe cases of Reye's Syndrome, elevated intracranial pressure (ICP) is associated with poor prognosis. Little is known about the pharmacology of high dose IV glycerol as used in Reye's Syndrome.

Glycerol pharmacokinetics and adverse effects were studied in nine patients (age 9-20 yrs.) with Reye's Syndrome. Glycerol was administered by continuous infusion over 2 hours with half the dose given over the first 0.5 hour and the remainder over the next 1.5 hour. The dose was adjusted to keep ICP $\leq$ 15 mm Hg. At steadystate, serial blood samples were collected during glycerol infusion and analyzed by an enzymatic assay specific for glycerol. At 0.75-1.75 g/kg/2 hr glycerol doses, the serum levels ranged from 1.48-5.83 mg/ml. Total body clearance ranged from 1.99-5.1 ml/kg/min. Glycerol clearance was not related to SGOT, SGPT, and serum ammonia levels. Glycerol provided effective control of intracranial pressure in all patients. Temporary elevation of serum creatinine and BUN, and presence of hemolysis in two patients was thought to be related to glycerol. Our data demonstrate that a large intersubject variability in glycerol kinetics may account for varying glycerol dosage requirement to control ICP in patients with Reye's Syndrome.

1596 HYPERTYRAMINEMIA AND HYPERPROLACTINEMIA IN REYE'S SYNDROME:CORROBORATION OF THE FALSE NEUROTRANSMITTER HYPOTHESIS. Stephen L. Newman, Bahjat Faraj, Daniel B. Caplan (Spon. by Maurice D. Kogut) Wright State University School of Medicine, Dayton, Ohio and Emory University School of Medicine, Atlanta, Georgia.

Several explanations for the encephalopathy in RS including false neurotransmitter activity have been postulated. Our group has recently demonstrated preliminary evidence of a disturbance in tyrosine metabolism resulting in hypertyraminemia in 14 patients (Ped.64:76,1979). Additionally, we have observed hyperprolactinemia in three cases of stage IV RS (Lancet 2:1097,1979).

Utilizing the same radioimmunoassay techniques, plasma tyramines (TM) were measured on 16 additional RS patients. Plasma TM on admission were significantly elevated 6.65 ng/ml $\pm$ 1.86 (mean $\pm$ S.E.M., range 0.1-36.2) $p<0.003$ when compared to the control patients without liver disease (range 0.7-1.1 ng/ml). A double antibody RIA was utilized to measure daily serum prolactin in the same 16 RS patients. Mean peak serum prolactin levels for patients presenting in various stages of coma were: I 15.07(7-28), II 13.7(7-33), III 34.7(14-66), IV 50-6(13-73). The mean peak serum prolactins in patients presenting in stages III and IV were significantly higher than those presenting in stages I and II ($p<0.01$) and positively correlated with admission plasma TM ($p<0.04$ $r=0.61$).

These findings of hyperprolactinemia and significantly elevated plasma TM in the severely encephalopathic patients indirectly confirm evidence of a "false neurotransmitter" contribution to the encephalopathy. Hyperprolactinemia may select a subpopulation of RS patients with potential to benefit from attempts to correct neurotransmitter disturbance with agents such as L-dopa or bromocriptine.

● 1597 DIAGNOSTIC ACCURACY OF NEONATAL BRAIN IMAGING: A POST-MORTEM CORRELATION. Karen Pape, Stephen Bennett-Britton, Wanda Szymonowicz, David Martin, Charles Fitz, Laurence Becker. (Spon. by P.M. Fitzhardinge). Research Institute, Hospital for Sick Children, Departments of Pediatrics, Radiology and Pathology. University of Toronto, Toronto.

During an 11 month period of a prospective study of < 1250 gm appropriate for gestational age infants, 31/87 (36%) died. Autopsies were performed on 24 and revealed 2 (8%) with germinal layer hemorrhage only, 15 (63%) with intraventricular+germinal layer hemorrhage and 7 (29%) without either hemorrhage. During life all infants were scanned through the skull in coronal and axial planes using real-time linear array ultrasound (U/S). Transfontanelle static sector U/S and CT studies were done after death prior to autopsy. The table shows correlation of autopsy findings with these scans.

	N	False		Agreement	
		Negative	Positive		
Sector U/S (Postmortem)	14	1	1	14	(88%)
Linear-array U/S	24	4	4	14	(67%)
CT (Postmortem)	14	2	5	7	(50%)

Although the differences are not statistically significant, the results suggest that greatest accuracy is obtained by ultrasound imaging through the fontanelle. It is noteworthy that no method of brain imaging was 100% accurate in detecting hemorrhage.

● 1598 MUSCLE RELAXANTS-A POTENTIAL DANGER TO INFANTS AT RISK FOR INTRAVENTRICULAR HEMORRHAGE Joyce L. Peabody (Spon. by June Brady) Children's Hospital and Cardiovascular Research Institute, Univ. of California, San Francisco.

Goldberg recently reported an increased incidence of intraventricular hemorrhage(IVH) in infants receiving muscle relaxants(MR). The mechanism is unknown. We studied 11 infants (BW 850-2800gm) before and during administration of curare or pancuronium. The effects of an increase of 4cm. peak inspiratory pressure (↑PIP) and of leg raising(LR) were tested. Intracranial pressure(ICP) was measured. Cerebral blood flow (CBF) was assessed by a doppler technique and expressed as pulsatility index (PI=systolic-diastolic/systolic) (Bada). Our results (Mean$\pm$SD):

	PI	ICPcmH$_2$O	ΔICPcmH$_2$O$\vec{c}$↑PIP	ΔICPcmH$_2$O$\vec{c}$LR
off MR:	.70$\pm$.13	11.2$\pm$5	1.6$\pm$2.6	3.9$\pm$2.1
on MR:	.56$\pm$.12	11.7$\pm$7	2.9$\pm$1.8	8.4$\pm$3.3
	($p<.01$)	(NS)	($p<.01$)	($p<.01$)

During MR, PI decreased, consistent with an increase in apparent CBF. There was no significant change in ICP due to MR alone. However, there was a significantly greater increase in ICP during ↑PIP and LR. Both observations suggest a loss of autoregulation during MR.

We conclude, muscle relaxants affect cerebrovascular dynamics and may be dangerous in infants at risk for IVH, particularly when high PIP is required.

1599 IDENTIFICATION OF INTERMEDIATE FILAMENT AGGREGATES IN CULTURED SKIN FIBROBLASTS FROM PATIENTS WITH GIANT AXONAL NEUROPATHY Sergio D.J. Pena (Spon. by Charles R. Scriver). McGill University, Montreal Neurological Institute, Departments of Neurology/Neurosurgery and Pediatrics, Montreal, Canada.

Giant axonal neuropathy (GAN) is a severe childhood disease affecting the peripheral and central nervous systems. It is characterized by segmental axonal ballooning due to large neurofilament masses, and abnormal aggregates of filaments in a variety of other cell types. Recently, I described a new technique for visualization of cytoskeletal components in cultured fibroblasts with the arylmethane dye coomassie blue R250 (Cell Biol Int Rep 4: 149, 1980). Application of this technique to skin fibroblasts cultured from two patients with GAN revealed in 90 to 95 per cent of cells large cytoplasmic clumps of filaments which had the immunochemical and cytochemical characteristics of intermediate (8-10 nm) filaments. Besides providing definitive evidence for a genetic etiology for GAN, these fibroblast abnormalities should prove to be a simple and useful handle for prenatal diagnosis and for investigations of the pathogenesis of this disease. Moreover, they may provide a unique opportunity to unravel the assembly mechanisms and determine the cellular functions of intermediate filaments.