1612 BRAINSTEM AUDITORY EVOKED POTENTIALS IN NEWBORNS: Peripheral and Central Conduction Time. Leopold J. Streletz, Leonard J. Graziani, Hemant J. Desai, Susan F. Travis, Paul A. Branca and Diran O. Mikaelian, Jefferson Medical College of Thomas Jefferson University, Depts. of Neurol., Ped., and Otolaryngol., Philadelphia, PA.

Forty low risk newborn infants were studied with conceptual ages between 28 and 42 weeks. They were distinguished from high risk infants on the basis of neonatal medical complications. Brainstem auditory evoked potentials (BAEP) were recorded from vertex-ipsilateral and contralateral ear reference sites. Monaural 70 dBHL rarefaction clicks were presented at a repetition rate of 11 per second. Both ears were tested. The peak and interpeak latencies of waves I, III and V were measured in term and preterm infants. These intervals were analyzed in relationship to conceptual age in order to assess the relative contributions of the peripheral and central portions of the auditory system to the process of infant development.

Since it is expected that BAEPs will have increasing diagnostic and prognostic significance for the neurologic and otologic outcome of newborns, a short term study of these responses in relationship to risk factors is underway in our laboratory. This data forms, in part, a basis for comparison of auditory brainstem function in low and high risk infants. (Supported by USPHS Grant NS15254).

1613 LONG TERM FOLLOW UP OF NEONATAL SEIZURES DUE TO PERINATAL ASPHYXIA. Shyan Sun, Minerva Castillo, Kamtorn Vangvanichyakorn, Richard Koenigsberger. (Spon. by Franklin Behrle) CMDNJ-NJ Med. School, Dept. Neonatology, N.J.

Controversy exists as to whether neonatal seizures due to moderate degree of perinatal asphyxia requires long term anticonvulsant Rx. We reviewed all cases of neonatal seizures due to perinatal asphyxia from 1972-79. All were treated uniformly with Phenobarbital 10-20mg/kg I.V. & maintained at 10mg/kg/day for 3 days. If seizures recurred, patients were discharged on maintenance Phenobarbital. If seizures did not recur, patients were sent home without medication. All patients were seen at follow up clinic at regular intervals until presently. 2587 records were reviewed, 47 infants (35-43 wks GA) fitted the criteria of perinatal asphyxia (5 min Apgar score < 5(17), fetal distress (6), meconium aspiration (20) prolapsed cord (8) difficult delivery (6); other causes of seizures excluded). Infants less than 35 wks GA were excluded to avoid inclusion of IVH. Of all the 47 infants, 7 were lost to follow up, 12 required maintenance Rx. The remaining 28 infants who had no seizures beyond the 3rd day of life & discharged without medication, were found to our surprise to be seizure free for the follow up period (6 mos-8yrs, av. 42.5 mos) except for 2 infants who had seizures associated with fever, one at 9 mos, the other at 15 mos of age. These 2 infants had no recurrence of seizures and are not on therapy. From these data we concluded that perinatal anoxic seizures controlled within the first 3 days of life have excellent chances of being seizure free. Consequently, long term anticonvulsant therapy may not be necessary.

1614 FATAL VALPROIC ACID (VPA) HEPATOTOXICITY Donald A. Taylor, Katherine Deschryver, James P. Keating, Arthur L. Prensky, W. Edwin Dodson, Wash. U. Sch. Med., St. Louis Children's Hospital, Depts. of Ped., Neurol, and Path., St. Louis, MO; and Douglas J. Dove, So. Ill. U. Sch. Med., Depts. of Ped. and Neurol., St. John's Hosp., Springfield, IL.

More than 20 deaths due to hepatotoxicity associated with VPA have occurred in the USA. We report 2 autopsied cases of fatal hepatotoxicity associated with VPA. In both cases the signs of hepatotoxicity appeared after 3-4 weeks VPA therapy and in 1 case consisted of persistent elevation of serum phenytoin (PHT) level for 5 days despite stopping VPA and PHT. By light microscopy, the liver showed nodular architecture with pseudoductular proliferation of periportal hepaocytes in both cases. The remaining pericentral liver cells had a granular cytoplasm which on electron microscopy in 1 case was due to closely packed mitochondria. Fat globules were seen in some cells but the appearance was clearly distinct from that in Reye syndrome.

The earliest laboratory signs of VPA hepatotoxicity were derangements of hepatic synthetic and/or detoxification processes. The transaminases in our patients overlapped those in epileptic children without serious toxicity. Other parameters are needed to predict which patients might develop fatal hepatotoxicity. Unexplained fluctuations of anticonvulsant levels might be an early sign of significant VPA toxicity.

1615 PROGNOSIS IN CHILDHOOD EPILEPSY: A 15 TO 23 YEAR FOLLOWUP. Jean Holowach Thurston, Donald L. Thurston, Barbara B. Hixon, Amy J. Keller, Washington University School of Medicine, St. Louis Children's Hospital, Department of Pediatrics, Division of Neurology, St. Louis, MO.

In a 5 to 12 yr followup, 36 of 148 epileptic children (24%) who had been seizure-free for 4 yrs on anticonvulsant medication (ACM) relapsed after drug withdrawal (W) (N Engl J Med 286:169, 1972). This report concerns a 15 to 23 yr followup of the same children. There were only 5 new relapses, increasing the relapse rate to 28%. Fifty-four percent of the relapses occurred in the first yr after W of ACM; 83% before 5 yrs (91% of the jacksonian cases relapsed within 2 yrs). There was no significant overall relation of relapse to sex, race, heredity, age at onset of seizures, age at W of ACM (puberty) or total number of seizures. Seventy-four percent of EEGs showed paroxysmal activity (focal or non-focal) at the time of W of ACM; the presence and degree of EEG abnormalities were not significantly related to relapse. Relapse rates varied significantly among seizure types (jacksonian, 58%; multiple seizure types, 43%; psychomotor, 31%; grand mal, 14%; petit mal, 12%; simple febrile seizures, 12%); among those with and without neurologic and/or psychologic deficits, 43% vs 23% ($P<0.05$); and in those with a seizure duration of more than 6 yrs, 89% vs 22% with a shorter duration ($P<0.001$).

The data suggest helpful prognostic clues as to the likelihood of relapse after W of ACM and its timing. With the exception of those who have jacksonian or multiple seizure types, most epileptic children "outgrow" their seizures (84% in this study).

1616 REYE'S SYNDROME SERA: EFFECT ON RESPIRATION. James H. Tonsgard, Godfrey S. Getz (Spon. by Peter R. Huttenlocher). Pritzker School of Medicine. Univ. of Chicago. Depts. of Pediatrics, Neurology, and Pathology.

The effect on the respiration of isolated rat liver mitochondria of sera from 6 patients in profound coma due to Reye's syndrome (R.S.) was assessed. Respiration was measured polarographically with 5 mg of mitochondrial protein. Active respiration was initiated with 3mM of glutamate and 0.1 mM ADP. 10λ of 5x concentrated control or R.S. serum was added to the resting state. R.S. serum initially produced a profound stimulation of respiration (5.65 ± 0.18 nmol O_2/mg protein, control = 2.11 ± 0.15, $p<0.0001$) lasting 1-3 minutes with a slight increase in respiration thereafter. This effect was diminished but not ablated with the addition of 1 mM EgTA to the incubating medium. Increasing [EgTA] to 30 mM or adding 5 nmol ruthenium red to inhibit calcium uptake did not further diminish the initial stimulation of respiration. Stimulation by R.S. sera occurred in the presence of rotenone and antimycin, suggesting that the effect was beyond Site I and II in the respiratory chain. Respiration was also stimulated in the presence of rutamycin, suggesting that R.S. sera might transiently uncouple oxidative phosphorylation. These findings confirm Aprille's observations (Science 197:908, 1977) in part, except that the effect of R.S. sera on respiration was transient. Entry of calcium into the mitochondria plays some role in this phenomenon, but the principal effect appears to be secondary to a transient stimulant of respiration or a weak uncoupler of oxidative phosphorylation that is consumed or inactivated within 1-3 minutes.

● **1617** LACTIC ACIDOSIS IN REYE'S SYNDROME. James H. Tonsgard, Peter R. Huttenlocher. Pritzker School of Medicine. Univ. of Chicago. Depts. of Pediatrics and Neurology.

Plasma lactate was measured in 22 children with Reye's syndrome (R.S.) and was compared with the neurologic state at time of sampling. A five stage coma scale was used (lethargy, stupor, light coma, decorticate state, decerebrate state). Mean plasma lactate for the 5 stages was 1.94 (± 0.33), 3.38 (± 0.33), 4.94 (± 0.82), 10.5 (± 0.87), and 12.38 (± 0.71) respectively (normal range 0.4-1.4 meq/L). Separation between all except the second and third groups was highly significant ($p<0.0005$) and a linear trend due to the clinical state was noted ($F_{1,22}=137.9$ $p<0.0001$). Plasma pyruvate, measured in 6 cases, was elevated in proportion to lactate, with a normal mean lactate-pyruvate ratio of 16:1. Lactate values could not be explained by differences in glucose load. All patients demonstrated a metabolic acidosis which was compensated in most cases. Plasma lactate accounted for most of the observed base deficit in a majority of our patients (mean of 81%, range 10 to 100%). Blood ammonia correlated with severity of the encephalopathy early in the course only ($p<0.05$). It has been suggested that lactic acidemia in R.S. is related to tissue hypoxia or hypoperfusion (Shannon et al., Pediatrics 56:999, 1975). This did not appear to be the case in our patients. Lactic acidemia was an invariable finding even in mild cases, and is best explained on the basis of dysfunction of mitochondria, leading to a defect in pyruvate metabolism. It is an excellent objective parameter of severity of the illness in R.S.