Decreased glucose utilization in the brains of malnourished animals may explain the previously described alterations in lipid and protein synthesis resulting in permanent brain structural deficits.

In utero induction and development of brain β-hydroxybutyrate dehydrogenase (BDH). M. MICHAEL THALER and MAX M. CHAIT. *Univ. of Calif., San Francisco, Calif.*

Ketones become the major source of energy for brain metabolism during prolonged fasting. The energy-yielding conversion of β-hydroxybutyrate to acetoacetate is catalyzed by the substrate-inducible enzyme, BDH. The capacity of fetal brain for utilization of β-hydroxybutyrate, and effects of maternal starvation on development of BDH activity in immature brain were studied in rat fetuses, and in newborn rats and rabbits. In rats, BDH activity appeared on the 17th day of gestation, and tripled within 2 days. A second rise in BDH began 12 hours after birth, doubling activity by 48 hours. BDH developed more rapidly in fetuses from pregnant animals fasted for 3 days. At 21 days gestation, their activity was 42.5 ± 6.4 units compared with 24.7 ± 4.3 units in fetuses from fed controls. At birth offspring of fasted rats had approximately twice the BDH activity of normal newborns. When the former were nursed by fed animals, BDH activity decreased to normal values within 24 hours. Normal rabbits fasted for 24 hours after birth had 130% higher BDH activity than fed littermates. These results show that fetal and newborn brain can utilize ketones. The development of this capacity is accelerated by maternal or postnatal starvation. Thus, the immature brain appears extremely responsive to qualitative changes in nutrients before and after birth.

Neuropathological and ocular changes in the cerebrohepatorenal syndrome. JOSEPH VOLPE, DAVID WALTON, MARK ROGERS, and LEWIS HOLMES. *Harvard Med. Sch., Boston, Mass.* (Intr. by John W. Littlefield).

We have found in a four-month-old girl with the cerebrohepatorenal syndrome two abnormalities that may provide insight into the basic nature of the disorder. These are: (1) a profound defect of neuronal migration, and (2) iron storage in ocular structures. This girl had the following neurological findings: no visual responses with normal pupillary reactivity, no auditory responses, no suck, severe hypotonia, no reflexes and multifocal clonic seizures. Pathological findings included diffuse polymicrogyria and pachygyria, severely disordered deeper layers of cerebral cortex, tremendous aggregates of neurons in cerebral white matter, hypoplastic corpus callosum, dysplastic inferior olivary and dentate nuclei, numerous heterotopic Purkinje cells in cerebellar white matter, disordered cerebellar cortex (nodulus) and a dysgenesis of the grey matter of the lumbosacral spinal cord. Myelination was only slightly delayed for age, and spinal roots, peripheral nerves and muscle were normal. These neuropathological findings suggest that the primary genetic defect may involve the programming of neuronal migrational events. Also she had abnormal retinal pigmentation and glaucoma. Electroretinogram showed normal retinal signals but no measurable occipital signals. Her eyes showed reduplication of the pigment epithelium and iron deposits in the corneal epithelium and ciliary body. These unique iron deposits may be due to abnormalities of iron metabolism but not simply to increased serum iron (SI). She never had an elevated SI; 2 weeks before death, her SI was 122 μg%, TIBC 608 μg%.

Timing of intracranial bleeding in newborn infants. N. DYER, R. GUTBERLET, J. RAYE, G. FAXELIUS, S. SWANSTROM, A. BRILL, and M. STAHLMAN. *Vanderbilt Univ. Sch. of Med., Nashville, Tenn.*

Intracranial hemorrhage is a frequent finding at autopsy in very immature infants. Because of the possibility of therapy in whom DIC seems to be present, it was thought important to be able to time the intracranial bleed to see if it had already occurred before therapy could have been initiated. Infants at high risk for intracranial bleeding have been transfused as early in the course of their illness as possible with red cells tagged with ^{50}chromium. ^{50}Cr is a stable tracer which can be activated in vitro to ^{51}Cr and counted. If the infant died and had an intraventricular clot in which >70% of the red cells were tagged, it was assumed that bleeding occurred after tagging. If the clot contained <30% tagged cells as compared to the sample of blood taken at tagging or just prior to death, it was assumed that bleeding had occurred prior to tagging. 28 such tagged infants have died and had intracranial clots analyzed for ^{50}Cr. 16 infants had HMD, 7 extreme immaturity, the remainder died of other disorders. 18 were <1250 g. B.Wt., 23 were <32 wks. gestation. Median age of tagging was 6.3 hrs. while median age at death was 33.2 hrs. ^{50}Cr concentrations in clot samples indicated that 25 infants had clearly bled after tagging and only 2 had already had their major bleed before tagging. 4 infants presumably had some bleeding before tagging, but continued to bleed afterwards. Investigations of the possible exchange of ^{50}Cr tag after clot formation did not indicate significant exchange between tagged circulating red cells and those in the clot. 12 infants had clear-cut DIC, 11 possible, and 5 had no evidence of DIC. All but 1 without DIC had grossly abnormal second stage clotting values. It is concluded that most of these infants' intracranial hemorrhages occurred after birth and after their disease process was clearly established.

In vitro studies of *post mortem* neural tissue in subacute sclerosing panencephalitis (SSPE). JOHN F. GRIFFITH and SAMUEL L. KATZ. *Duke Univ. Med. Ctr., Durham, N. C.*

Brain and spinal cord from 2 cases of SSPE were obtained within one hour of death and cultures were established from multiple sites including frontal, temporal and parietal lobes, pons, cerebellum and cord. These were serially passaged and remained viable for many months. Their growth rates, cytologic detail, and survival varied depending on the region of brain sampled. Only certain of these cultures, derived from specific neuroanatomical sites showed evidence of measles antigen or yielded a viral agent when appropriately studied.

Cell cultures derived from cortical regions showed intranuclear and intracytoplasmic inclusion bodies even before a monolayer had formed. These inclusions were both type A and B, and in one case the cells showed significant hemadsorption in a distribution indicating the presence of viral antigen in terminal processes.

Two cell types could be identified in early cultures from the cortex but with passage, one of these, a small round cell with a hyperchromatic nucleus, disappeared and the other, a larger cell, seemed to elongate and divide rapidly, resulting in the fibroblastic monolayer. The cells derived from the cerebellum and spinal cord were slower to grow, had a shorter survival and different morphology.

Despite widespread pathologic changes in both brains, cytopathology developed only in the cultures of the frontal lobe in

the first case and to date, after 3 months, this is the only region showing similar changes in studies of the second patient. An agent, immunologically identified as measles virus has been isolated from one of these specimens. This study underscores the importance of post mortem cultivation of neural tissue in all patients with chronic CNS disease.

Effect of elevated blood tyrosine on intellectual development of premature infants. JOHN H. MENKES, DORIS W. WELCHER, HELENE LEVI, EVELYN R. STERN, JOSEPH DALLAS and NEIL E. GRETSKY. *UCLA Sch. of Med., Los Angeles, Calif.; Johns Hopkins Sch. of Med., Baltimore, Md.*

Blood tyrosines were followed from birth to nursery discharge in 71 premature infants fed a high-protein formula supplemented by 60 mg/day of ascorbic acid. In 89% tyrosine concentrations were abnormal, and in 38% the maximum observed was 5.0 mg% or higher. Maximum blood tyrosine correlated with gestational age ($p < 0.05$) but not with birth weight.

On a follow-up study performed at 15 months, infants with high tyrosine levels had no increase in neurological abnormalities. Between 7 and 8 years a second follow-up was done on 64 children. This included a WISC and tests for psychomotor function. Two children had died in the interval and six others were too retarded for full testing. The full scale IQ of all children correlated with birth weight ($p < 0.01$). The mean IQ of high and low tyrosine subjects was 85.9 and 86.2, respectively. When infants were grouped by birth weight a significant difference was detected in subjects weighing 2000+ gm.

	Full IQ	Verbal	Performance
High tyrosine (5)	85.4 ± 5.5	90.4 ± 6.1	82.4 ± 6.2
Low tyrosine (11)	95.0 ± 14.0	93.4 ± 13.2	97.8 ± 14.2
p =	<0.1	n.s.	<0.02

Significant differences were recorded in scores on object assembly ($p < 0.05$), picture assembly ($p < 0.05$), and picture completion ($p < 0.10$). We observed no effect of high tyrosine levels on intellectual performance of smaller infants, who, on the whole, are a greater risk for other complications of prematurity.

Coagulation abnormalities in patients with hydrocephalus and ventricular-jugular (V.J.) shunts. MARIE STUART, JAMES STOCKMAN, SCOTT MURPHY, JOAN URMSON, MARY AMES, and FRANK OSKI. *Univ. of Pennsylvania Sch. Med., and Children's Hosp. of Philadelphia, Pa.*

The presence of silastic prostheses and tubing in the circulation is now recognized to produce alterations in hemostasis. Stimulated by the observation of severe disseminated intravascular coagulation in a child with a clotted V.J. shunt and the recognition that obstruction to such catheters is one of the undesirable complications of its use in children with hydrocephalus, coagulation studies were performed in 25 asymptomatic children with V.J. shunts. Prothrombin and partial thromboplastin times, Factor V and VIII levels and platelet counts were normal in all. In 2 of the patients the thrombin time was prolonged and in 1 of these patients significant increases in the level of fibrin split products were demonstrable. In 4 patients platelet survivals, using Cr^{51} labeled platelets, were performed. In 2 the survival was significantly reduced. Patients in whom coagulation abnormalities or shortened platelet survival were present developed obstructive complications in their shunts. It would appear that catheter problems can be anticipated by performance of coagulation studies. The use of aspirin and dipyridamole, agents which inhibit platelet aggregation in vivo, may provide a means of eliminating the complication of shunt obstruction.

Prognosis in childhood epilepsy: A follow-up study of 148 cases in which therapy had been suspended after prolonged anticonvulsant control. JEAN HOLOWACH, DON L. THURSTON, and JAMES L. O'LEARY (Intr. by Philip R. Dodge). *Wash. Univ. Sch. of Med., St. Louis, Mo.*

One hundred and forty-eight unselected epileptic children, seizure-free for 4 years on anticonvulsant medication, were followed for 5 to 12 years after drug withdrawal to determine the frequency of seizure recurrence and to discern any prognostic criteria. Thirty-six children (24%) had a recurrence of seizures. Sixty-one per cent of recurrences took place during the first year of gradual discontinuation of therapy. Drug withdrawal at puberty (9–15 yrs) was not associated with increased risk. An analysis of the records revealed no relation of relapse to sex, race, heredity, or seizure frequency. The prognosis was very good in children who had an early age of onset with prompt control (relapse rate 13%). There was at least a two-fold increase in relapse in cases with a late onset, with prolonged duration of seizures, and evidence of neurologic, psychologic, and electroencephalographic abnormalities. The most striking correlate to relapse was seizure type.

Best results were obtained in children with grand mal (relapse rate 8%), febrile seizures (12%), and uncomplicated petit mal (12%). In psychomotor attacks the relapse rate was 25%. The highest recurrence was in children with Jacksonian seizures (53%) and those who had seizures of more than one type (40%). It was concluded that these data suggest unquestionable criteria for drug withdrawal in epileptic children after prolonged seizure control with a favorable outcome in a large percentage of selected cases.

CHILD DEVELOPMENT I: BEHAVIORAL SCIENCE AND EPIDMIOLOGY

Perinatal mortality, economic and racial influences on the sex ratio. RICHARD L. NAEYE, LESLIE S. BURT, DAVID L. WRIGHT, and WILLIAM A. BLANC. *Pennsylvania State Univ. Coll. of Med. and Columbia Univ. Coll. of Physicians & Surgeons, Hershey, Pa., and New York, N.Y.*

An excess of fetal and neonatal deaths in male offspring is found in man, domestic animals and some insects. In humans, the male disadvantage is reportedly less when perinatal infant mortality is high, i.e. in nonwhites and the socioeconomically disadvantaged. The present study offers some explanations. In an analysis of 2735 consecutive newborn autopsies, the ratio of males to females was 1.28:1 which differs significantly from the 1.05:1 ratio for all U.S. live-births. Within this series the ratio for stillbirths was 0.95:1 and for live-births 1.45:1. Most disorders which were present in both stillborn and liveborn infants had a much lower male:female ratio in the former group. The ratio for infants of poor families was 1.17:1, nonpoor 1.40:1, whites 1.34:1, blacks 1.22:1, Puerto Ricans 1.22:1, and Mexican-Americans 1.23:1. The ratio for liveborns with infections of antenatal