Gross edema formed at higher differential pressures. Thus the pups developed minimal PE at lower TPAWP than would have been expected from their T.P. and COP. The data do not permit a choice of the several factors that might explain this finding. Similar susceptibility of the human fetus and newborn in relation to the adult would favor the development of PE during the perinatal period and might thus play a role in the pathogenesis of pulmonary problems of the newborn.

*173 The Effect of Thyroxin on Fatty Acid Biosynthesis in Brain.* JORGE GRIPPO and JOHN H. MENKES, UCLA Sch. of Med., Los Angeles, CA.

Fatty acid synthesis by chain elongation occurs in microsomal and mitochondrial fractions of rat brain. With myelination (13–16 days of age) the rate at which microsomal particles incorporate malonyl-CoA into saturated fatty acids characteristic for myelin is increased. The present study was undertaken to study control mechanisms of fatty acid synthesis in brain.

Daily injections of triiodo thyronine (60 $\mu$g/100 g body wt.) were given from age 1 day to 2 h prior to sacrifice. In the microsomal system incorporation of malonyl-CoA into fatty acids in 5–6-day-old animals was increased from $0.91 \pm 0.52$ m$\mu$M/mg protein to $2.25 \pm 0.39$ m$\mu$M/mg protein. The increase in precursor incorporation occurred almost entirely into saturated fatty acids. Thyroid had no significant effect on fatty acid synthesis by microsomal particles derived from animals sacrificed at other stages of development or from adult rats.

Incorporation of acetyl-CoA into both saturated and unsaturated fatty acids by mitochondria was slightly increased by thyroid in adult animals and at 3–6 days of age, but the differences were not significant.

These studies suggest that thyroid accelerates the normal maturational increase in microsomal fatty acid synthesis. This probably occurs by stimulating the synthesis of the enzyme system involved in the production of fatty acids characteristic for myelin.

*174 Mechanisms Responsible for the Sensitivity of Newborn Rats to Pregnanolone.* LESTER F. SOYKA, LASZLO GYERMEK and PATRICIA CAMPBELL, Stanford Univ. Sch. of Med., Palo Alto, CA.

The minimum lethal dose of pregnanolone, a potent pharmacologically active metabolite of progesterone, increased about 60-fold from birth to weaning. This was greater than the increase seen with non-steroid hypnotic drugs. The brain concentration of pregnanolone at the onset of hypnosis was 0.35 $\mu$g/g in 3-day-old and 7–10$\times$ higher in 23-day-old rats, indicating an elevated receptor threshold. Similarly, older rats awoke at a brain concentration 6$\times$ higher than that maintaining sleep in younger animals. Hepatic biotransformation to sulfate and glucuronic acid esters and more polar steroids was extremely rapid, even in 3 day olds. Seven minutes after i.p. administration of pregnanolone with radioactive tracer only 29 and 37% of the total cpm in blood and liver were present as free pregnanolone. Although metabolism was somewhat faster in older rats, the relative increase was not quantitatively important compared to the extent of newborn sensitivity. A number of metabolites were found in blood, brain and liver of which pregnanediol was a surprisingly small component. Esters in the liver (at 45 min postinjection) were predominantly sulfates. No conjugates were found in brain. Pregnanolone accumulation in brain, as a percentage of the injected dose, was slightly greater in newborns, though far less than predicted assuming uniform distribution. In almost all previous developmental studies, impaired hepatic metabolism has been of sufficient magnitude to explain accentuated pharmacologic responses. These studies may be the first to experimentally verify the concept of altered receptor threshold in the brain as a mechanism for the sensitivity of newborn animals to drugs.

*175 Familial Neuromuscular Disease and Non-ketotic Glycinemia.* GRANT MORROW III, ASLAN AKSU, WILLIAM BANK, L. P. ROWLAND and L. A. BARNESS, Dept. of Ped. and Neurol., Hosp. Univ. of Pennsylvania and Univ. of Pennsylvania Sch. of Med., Philadelphia, PA.

A family of Lebanese extract is described in which 3 of the 4 children (all males) have neuromuscular disorders and a primary aminoaciduria. The symptoms in those affected began in early childhood and are slowly progressive. In the 2 older siblings (age 22 and 24), the neurological disorder implied dysfunction of both spinal cord and peripheral nerves: weakness, wasting and loss of reflexes of distal muscles, combined with hyperactive reflexes, and spasticity of other muscles. EMG and muscle biopsy indicated denervation but conduction velocity of peripheral nerves could not be estimated because action potentials were not evoked by stimulation. Symmetrical upper motor neuron disease with clonus, spasticity, bilateral Babinski signs, and increased deep tendon reflexes were the clinical picture in the 10-year-old sibling. Examination and EMG in the mother and unaffected 14-year-old sibling were normal. The syndrome has features of both Friedreich's ataxia and Charcot-Marie-Tooth disease.

Urinary amino acids were measured on 6 members of the family. The combination of massive isolated glycinuria and neuromuscular disease was found only in the 3 affected males. Amino acid quantitation of the propositus revealed a plasma glycine of 0.817 $\mu$M/ml (normal 0.150–0.300) and urinary excretion of 1720 mg/day (normal $<200$). None of the patients were clinically acidotic and urinary organic acids were normal. Propionate metabolism in white cells of the entire family was normal. This is the first known example of an inherited neuromuscular disorder associated with a specific amino acid abnormality. (Supported in part by USPHS grants nos. AM-02231 and HD-04837.)

*176 A Syndrome of Hypopituitary Dwarfism, Hypoplasia of Optic Nerves, and Malformation of Prosencephalon: Report of 6 Patients.* SELNA L. KAPLAN, MELVIN M. GRUMBACH and WILLIAM F. HOYT, Dept. of Ped. and Ophthal., Univ. of California, San Francisco, CA.

We have suggested that 'idiopathic' hypopituitary dwarfism (IHP) is a heterogenous disorder of disparate pathogenesis [New Engl. J. Med. *278:* 57, 1968]. Among a group of 36 children with sporadic IHP (16 isolated GH and 20 multiple pituitary deficiencies) in whom mass lesions were excluded, 6 patients (3F, 3M) had a distinctive clinical entity of dwarfism, optic nerve dysplasia, and midline abnormalities of the prosencephalon. The findings included: congenital diabetes insipidus in 2; bilateral hypoplasia of optic nerves with small optic discs in 6; pendular, dysjunctive nystagmus in 5; bilateral amblyopia in 3; inconstant, irregular field defects in 5; and documented growth

hormone deficiency in 6 with multiple tropic hormone deficiencies in 4/6. In 3 of 4 patients, in whom a PEG was performed, absence of septum pellucidum, thin optic nerves and chiasm, abnormal fornices, irregular lamina terminalis, and an abnormally shaped 3rd ventricle with small inferior pointing diverticulum from the optic recess were demonstrable. The sella turcica and suprasellar cistern were normal. EEG dysrhythmias were noted in 2 of 4 patients tested; I.Q. was normal or mildly subnormal in 6. No evidence of ocular abnormalities or dwarfism was noted in the parents or sibs of the 6 patients. Hence, sporadic hypopituitary dwarfism is not uncommonly associated with a characteristic congenital malformation of the prosencephalon. The hypopituitarism is ascribable to a diencephalic defect which results in deficiency of hypothalamic hypophysiotropic factors and in some cases vasopressin.

177 *Two Types of Congenital Cysts of the Posterior Fossa: A Comparison of Their Clinical and Pathological Characteristics and Their Embryogenesis.* JEROME S. HALLER, SAMUEL M. WOLPERT and EDWARD F. RABE, Tufts Univ. Sch. of Med., New England Med. Center Hosps., Depts. of Ped., Neurol., and Radiol., Boston, Mass.

Two types of cystic lesions can occur in the posterior fossa of infants and children. In one type there is a cystic dilatation of the 4th ventricle known as the Dandy-Walker (D-W) syndrome, and in the second type, a cyst or cysts overlie the cerebellum. This is referred to as a posterior fossa extra-axial cyst (PFEAC). These two entities may be differentiated clinically as will be illustrated by presentation of the findings in 2 infants with PFEAC and 2 with D-W syndrome. The pattern of skull transillumination is distinctive for each entity, although the differences are subtle, and can enable the clinician to suspect the correct diagnosis immediately. Arteriographic and air contrast findings show similar abnormalities in the supratentorial region in both conditions but distinctive differences are present in the infratentorial region. The histology of the cyst wall in PFEAC differs from that in D-W syndrome. Inferences drawn from a comparison of the arteriographic and histologic findings in these 4 cases with the appearance of certain brain structures at different stages of human embryogenesis indicate that both conditions are congenital abnormalities occurring before the 3rd fetal month but affecting the leptomeninges in one instance (PFEAC) and the cerebellar anlage in the other (D-W syndrome).

178 *Quantitative RISA Subarachnoid to Plasma Transport and Subarachnoid Perfusion Tests in Children with Progressive Macrocephaly and Suspected Hydrocephalus.* THOMAS H. ROCKEL and EDWARD F. RABE, Tufts Univ. Sch. of Med., New England Med. Center Hosps., Dept. of Ped. and Neurol., Boston, Mass.

A measure of the adequacy of lumbar subarachnoid to plasma CSF transport is obtained by determining quantitatively the percent of $^{12}$/I RISA in the plasma 24 h after its lumbar subarachnoid injection. This was done in 35 infants and children ranging in age from 5 weeks to 14 years. The ability of the CSF circulation to dispose of normal saline perfused into the lumbar subarachnoid space at a rate of 0.76 ml/min for 30–60 min was determined by CSF pressure measurements at 5-min intervals during the perfusion of a sedated patient. This was done also on 17 of the 35 patients. Patients with normal external CSF circulation transported 38.5±10.2% (2 S.D.) of the injected RISA; patients with communicating hydrocephalus, 16.1–25.4%; those with obstructive hydrocephalus, 31.5–45.8%; and macrocephalic achondroplastic dwarfs, 29.9–53.1%. The pattern of perfusion test CSF pressures could be divided into 3 distinct forms: normal, uncompensated abnormal and partially compensated abnormal. In every instance save one, the results of the two tests on the same patient agreed. This patient with hydrocephalus and porencephaly had a normal RISA transport test but an abnormal uncompensated perfusion pattern. From these data we conclude, (1) that both tests are needed to evaluate the adequacy of the external CSF circulation, and (2) the external circulation can be normal when the internal circulation (ventricles to cisterna magna) is obstructed.

179 *Failure of Exchange Transfusion to Prevent Minimal Cerebral Damage When Employed so as to Maintain Serum Bilirubin Concentrations Below 18 and 20 mg/100 ml.* LOIS H. JOHNSON and THOMAS R. BOGGS, Dept. of Ped., Pennsylvania Hosp., Philadelphia, PA.

The occurrence of minor cerebral deficit in the absence of gross neurologic damage as a result of neonatal hyperbilirubinemia has been suspected for some time [DAY and HAINES, Pediatrics *00:* 000, 1954]. Recently ODELL (J. Pediat. *00:* 000, 1970] has documented the presence of such damage by means of psychometric and neurologic evaluations at age 5 to 6 years in a group of jaundiced infants treated with exchange transfusion. Damage was found to correlate with degree of saturation of the serum proteins with bilirubin (as measured by his salicylate saturation index). We are confirming these results in a similar study using our HABA technique (Program SPR 1966, COLEMAN, Jr. 50 L serum, cc $30 \times 10^{-5}$ HABA, $PO_4$ buffer) as a measure of serum binding reserve.

Analysis of the first group of infants being recalled at age 4 years for detailed psychometric, speech and hearing and neurologic examinations suggests that jaundiced infants whose HABA binding levels fall below 50% are likely to suffer some degree of measurable damage which infants whose binding levels remain above this level will escape (Chi square = 6.04, $p = 0.014$, $n = 41$). Correlation of damage with bilirubin/albumin molar ratio was good. As in the study of ODELL, correlation with serum bilirubin concentration was poor.

The data clearly indicate that if minimal as well as major cerebral damage as a consequence of neonatal jaundice is to be prevented more exchange transfusions will have to be done or some alternative or additional form of therapy will have to be used. Phototherapy in conjunction with exchange transfusion gives promise of providing increased protection without increased therapeutic risk. Its ability to do so should be subjected to the scrutiny of long-term follow up studies.

180 *Effects of Hyperoxia on the Nucleic Acid Contents of Developing Brain.* GILMAN D. GRAVE, CHARLES KENNEDY and LOUIS SOKOLOFF, Lab. of Cerebral Metabolism, Nat. Inst. Mental Health, Bethesda, MD.

Prolonged exposure of the newborn to elevated concentrations of oxygen may initiate pathologic changes in the retina, but, except for inhibition of capillary