kg/min) were administered to 7 infants with IRDS. In three patients the drug was infused directly into the pulmonary artery through an umbilical arterial catheter guided through the ductus arteriosus. A second umbilical catheter was placed in the aorta for pressure recording and blood sampling. In four other infants, the drug was infused into the superior vena cava.

In each of the 3 infants who received infusion into the pulmonary artery, a decrease in pulmonary artery pressure of 6 to 25 mm Hg was observed, accompanied by small increases in pH and $PaO_2$ and decrease in $PaCO_2$. The gradient established between aortic and pulmonary pressure persisted for periods up to 45 minutes but then disappeared while the infusion was still in progress. Clinical improvement was seen in only one of these infants and in none of the four who received infusion in the superior vena cava. It would therefore appear that acetylcholine is capable of promoting vasodilation of the pulmonary arterioles but is ineffective in treatment of IRDS. (APS)

89 *Hypoglycemia in Infants with Erythroblastosis Fetalis.* CYNTHIA T. BARRETT*, THOMAS K. OLIVER, Jr., FREDERICK G. HAZELTINE* and JEROLD F. LUCEY, Department of Pediatrics, University of Washington, Seattle, Wash., and University of Vermont, Burlington, Vt.

Hyperplasia of the Islets of Langerhans is usually found in fetuses in infants who die as a result of erythroblastosis fetalis (EF) and the pancreas contains levels of insulin comparable to those found in infants of diabetic mothers (IDM). The clinical counterpart of these observations, hypoglycemia, is believed to occur rarely if at all in infants with EF. During the last 18 months we have observed hypoglycemia (< 30 mg/100 ml in term infants; < 20 mg /100 ml pre-term) in 11 infants. Borderline levels have occurred in 2 others. Five of the infants developed hypoglycemia prior to exchange transfusion (ET). Recently 16 consecutive infants with moderate to severe EF have had frequent blood glucose measurements following ET. 6 (30 %) developed symptomatic hypoglycemia with borderline values in 2 others. 9 infants had multiple measurements of blood glucose in the 3 h period following ET and 4 of these had simultaneous measurements of serum immuno active insulin. Serum insulin was elevated in all 4 infants. Glucose disappearance constants ($K_t$) were calculated for the first hour following ET and compared to $K_t$ values for normals and IDM following IV glucose tolerance tests. The infants with EF who developed hypoglycemia had significantly greater $K_t$ values than did the normals; their values approximated IDM. Because of the necessity for prompt treatment, blood glucose should be measured frequently in infants with EF both after birth and after ET. Intravenous glucose or fructose should be effective in prevention of hypoglycemia. (APS)

90 *Vascular Responses to Oxygen Breathing in the Newborn Infant.* NICHOLAS M. NELSON*, CHRISTOPHER H. NOURSE*, BETTTY L. PRIESTLEY*, RUTH B. CHERRY* and CLEMENT A. SMITH, Department of Pediatrics, Harvard Medical School, Boston, Mass.

During the course of measurements of pulmonary function in newborn infants breathing 60–100 % oxygen, we have previously noted frequent, rapid and significant decreases in hematocrit and hemoglobin levels. The present investigation has been designed to confirm and elucidate this finding. 14 newborn infants varying in gestational age from 36–37 weeks, in birth weight from 2.7–4.6 kg and in postnatal age from 1–18 h breathed 60 % $O_2$ by demand valve for periods of 60–70 min. Hematocrit (Hct), hemoglobin (Hb), total protein (TP) and blood gases were followed throughout and blood volume (CO method) was measured in 3 infants. Within 10 min of onset of $O_2$ breathing prompt decreases of Hb, Hct, TP were seen reaching levels of 20 % below control values by 60 min. These changes promptly reversed upon resumption of air breathing. TP changes were seen to be more consistent and marked than changes in Hct or Hb. The response was seen with arterial $O_2$ tensions of as low as 116 mm Hg. Total blood volume increases of 40–60 ml/kg were noted during $O_2$ breathing in 3 infants. These data suggest auto-infusion of tissue fluid from some vascular bed in response to $O_2$ breathing; this may imply an increase in precapillary resistance with consequent decrease in capillary pressure and derangement of the Starling equilibrium. Preliminary investigations indicate that bradycardia and increased peripheral vascular resistance are involved in this phenomenon. (APS)

91 *Otic Lesions and Congenital Hypothyroidism.* GERALD J. BARGMAN* and LYTT I. GARDNER, State University of New York, Upstate Medical Center Syracuse, New York.

In an effort to elucidate the relation, if any, between thyroid abnormality and congenital deafness in Pendred's syndrome, an experiment was designed to study the effects of hypothyroidism on middle and inner ear hearing structures, including the auditory nerve and its central projection, in developing chick embryos. Propylthiouracil (PTU), 2 mg, was injected into the albumin of fertile chick eggs on the 10th incubation day. Single doses of l-thyroxine (range 1 to 100 $\mu$g) were inoculated in a similar manner, either alone or with PTU. Control inocula included sterile saline or water. After hatching, each chick was examined for obvious malformations. The thyroid glands, middle and inner ear mechanisms, auditory nerve and brainstem were studied grossly and with different histologic staining techniques. When compared to controls, chicks exposed to PTU on their 10th incubation day exhibited: increased mortality, delayed hatching, reduced size, incomplete yolk sac absorption and death within 5 days unless exogenous thyroid hormone was provided in the first 24 to 47 h post hatch. Specific, consistent, morphologic alterations were observed in their thyroid glands as well as in the sensory hair cells and spiral ganglion of the cochlea. Preliminary results indicate if 50–75 $\mu$g of l-thyroxine is given simultaneous with (or as long as 120 h after) the PTU injection of the 10 th incubation day, one cannot detect the groos defects, marked thyroid lesions or abnormal histology in cells of the cochlea and its ganglion. A relationship between embryonic thyroid gland function and the hearing mechanism of the chick embryo, is suggested. (SPR)

92 *Mechanism of Myelin Formation During Development.* NORBERT HERSCHKOWITZ* and GUY M. MCKHANN, Stanford Univ. Sch. of Med., Palo Alto, Cal.

Myelin is formed by a satellite cell which wraps around the axon to form a continuous spiral of membrane. This membrane has a distinctive lipid and protein composition when compared with other membran-

ous structures. The myelin components may be synthesized at the level of the forming membrane, or transported into the membrane following synthesis by some other intracellular organelle.

The synthesis of sulfatide, a membrane lipid, by 9[5] and 17-day-old rats was determined after a single intraperitoneal injection of $^{35}S$-sulfate into the sulfatide of whole brain, myelin, non-myelin organelles, and 105,000 × g supernatant of brain was followed. At times when there was no further *de novo* synthesis of lipid, the amount of labelled sulfatide in myelin continued to increase while that of non-myelin membranes decreased. The transfer of sulfatide from non-myelin structures to myelin appeared to be mediated by soluble lipoproteins which were isolated from supernatant, characterized, and found to contain labelled sulfatide.

*In vitro* studies, indicated that isolated myelin contained galactocerebroside sulfokinase, the enzyme involved in the synthesis of sulfatides. Thus, isolated myelin contains some membranous components capable of synthesizing myelin lipids.

These studies suggest that a lipid component of myelin is both transported into the forming membrane by a carrier lipprotein and synthesized by the myelin membrane. The relationship between these two mechanisms of formation of myelin components during development will be discussed. (SPR)

93 *Physico-chemical Properties of Ceruloplasmin from Normal and Wilson's Disease Subjects.* NEIL A. HOLTZMAN* and MICHAEL A. NAUGHTON*, Johns Hopkins Univ. Sch. of Med., Baltimore, Md. (introduced by Robert E. Cooke).

Although most patients with Wilson's disease have low levels of serum ceruloplasmin, an occasional patient presents with a normal level. This variation might be due to differences in the structure of ceruloplasmin. To investigate this possibility, physico-chemical properties of ceruloplasmin from a Wilson's disease patient with normal levels of ceruloplasmin, from a second, unrelated, patient with low levels and from normal subjects were compared.

Highly purified ceruloplasmin from the patient with normal levels was chromatographed on hydroxylapatite. The major component obtained had the same electrophoretic mobility (at pH 5.6, 6.4, 8.9), tryptic peptide map, oxidase activity, copper, amino acid and sugar composition as the major component from normal subjects. The minor hydroxylapatite component from the patient had the same electrophoretic mobility (at pH 5.6), tryptic peptide map and oxidase activity as the minor component from normal subjects. The major and minor ceruloplasmin components were found to differ from each other by only one peptide spot. Ceruloplasmin from the Wilson's disease patient with a low serum ceruloplasmin concentration had the same chromatographic and electrophoretic characteristics as normal ceruloplasmin. Thus it appears that ceruloplasmin in Wilson's disease is structurally normal.

Penicillamine administered to the patient with normal ceruloplasmin concentration caused an increased excretion of copper. Concommitantly, ceruloplasmin activity became undetectable in his plasma and reappeared only after the drug was discontinued. This finding suggests that in Wilson's disease, the sensitivity of the ceruloplasmin synthesizing system to copper may be diminished. (SPR)

94 *Effect of Hypertonicity on the Metabolism of Brain in Vitro.* JEAN F. SOTOS, S. ADDANKI*, P.D. REARICK* and F. D. CAHILL*, Depts. Ped. & Physiol. Chem., Ohio State Univ. Col. of Med. & Children's Hosp. Res. Fndn., Columbus, Ohio

Hypertonicity of body fluids whatever the cause—hypernatremia, uremia, hyperglycemia—alters CNS function with alteration of sensorium, coma and death. Also, hypdtonicity induces acidosis (SOTOS *et al.:* Pediatrics *26:* 925; *30:* 180). The mechanism of the alterations is unclear. Rat brain slices where incubated in Krebs-Ringer phosphate buffer containing glucose-UL-C-14 or pyruvic acid-2-C-14 as substrates in 100 % $O_2$ atmosphere (ADDANKI *et al.:* Ann. Biochem. *13:* 458 [1965]). Using glucose as substrate, increases in tonicity due to NaCl, sucrose or glucose (340 to 1000 mOsm/kg $H_2O$) caused decreases in $O_2$ consumption (97 to 100 %). The same hypertonic media did not change $O_2$ consumption of rat brain homogenate. Urea up to 1000 mOsm had no effect on $O_2$ uptake of slices. The $C^{14}O_2$ evolved decreased to 80 and 10 % of control with hypertonic media containing 450 and 900 mOsm of either NaCl or sucrose with glucose as substrate. These changes were due to decreased Krebs cycle activity, since similar values were obtained when pyruvic acid-2-C-14 was used as substrate. No effect was seen with urea solutions at 450 mOsm, decreasing to 81 % of control at 900 mOsm. Studies conducted with glucose 1-C-14 or 6-C-14 did not show any significant change on the activity of the hexomonophosphate shunt. The different values can be accounted for by the different osmotic effect of the solutions. The lactic acid production increased 160 % of the control with NaCl hypertonic media. These observations bear on the pathogenesis of (acidosis and) CNS alterations observed in clinical conditions with hypernatremia, hyperosmolar non-ketotic diabetic coma and experimental uremia. This investigation was supported by USPHS grants NB 05114 and FR-78. (SPR)

95 *Continuous Recording of Cerebral Ventricular Fluid Pressure in Hydrocephalic Children.* PATRICIA HAYDEN*, ELDON FOLTZ and* DAVID B. SHURTLEFF, Univ. of Wash. Med. Sch., Seattle, Wash. (introduced by Ralph Wedgwood).

To quantitate physiologic variations in and the effect of chemical agents on cerebral intraventricular pressure a technique for continuous pressure recording via an indwelling ventricular catheter and strain gauge transducer has been developed. Pressure studies for periods up to 10 days have been made on 12 hydrocephalic children ranging in age from 3 weeks to 5 years. Baseline recordings extending over 24 to 96-hour periods revealed multiple patterns of rhythmic variation with mean pressures ranging from 280 to 50 mm of water. Other physiologic parameters studied included respiratory rate and pattern, electrocardiogram and scalp venous pressure. Serum and ventricular fluid electrolyte and osmolar concentrations have been monitored. Ten of 11 children given oral isosorbide showed an immediate decrease in ventricular pressure ranging from 53 to 100 % of baseline similar to the effect of mannitol and urea. Ventricular wave form flattened during periods of pressure reduction. Five patients studied were also given acetazolamide, urea and mannitol. Acetazolamide increased ventricular pressure 2 to 3 fold with a concommitant exaggeration of pressure wave form. This hypertensive effect was immediate and persisted 2 to 4 hours before returning to