lung liquid, and lung lymph, information was obtained about the separate capillary and alveolar components of the barrier. The results show that for both parts of the barrier the permeability constants for water-soluble/fat-insoluble molecules increase with diminution in size, and that the alveolar component is much less permeable than the capillary component (*e.g.*, 1,000-fold difference for sucrose). Preliminary studies suggest that the same size dependence holds for fat-soluble molecules, and that for a given size, permeability constants increase with fat solubility. There was no difference between the mature and immature fetuses.

38. Early stages of hyaline membrane disease. N. FRENCK, A. TORRADO, J. M. CHOFFAT, and L. S. PROD'HOM. *Hôpital Cantonal Universitaire, Lausanne, Switzerland.*

In 78 preterm infants with HMD, the initial PaO2 values, in 100% O2 (hyperoxya test), were lower than expected for age in the first 4 hr of life, then dropped and stayed low for 24 to 72 hr and started to rise. It was also shown that the shorter the gestational age, the earlier the rise and the limit seems to be at 33 weeks gestation. The drop in PaO2 could be explained by intrapulmonary shunt through increased atelectatic areas or by extrapulmonary shunting (fetal shunts).

The functional residual capacity (FRC), was measured by the close circuit helium dilution method, as an index of pulmonary aeration, in six preterm babies with HMD and was found to be 50% lower than expected value, already before the 4th hr of life, and remained low without any significant change for the first 24 hr. Thus, it can be speculated that the drop in PaO2 is due to extrapulmonary shunting through the foramen ovale and ductus arteriosus and not to an increase in atelectasis.

39. Fibrinolytic system in infants of low birth weight and/or short gestational period. H. EKELUND and O. FINNSTRÖM. *General Hosp., Malmö, and Univ. of Umeå, Sweden.*

The aims of this investigation were: (*1*) to study fibrinolytic activity and the development of the different factors of the fibrinolytic system from early "prematurity" up to term and (*2*) to study the changes, if any, of these factors in infants with postnatal asphyxia, idiopathic respiratory distress syndrome (IRDS), and intracranial hemorrhages. The material consisted of 197 infants in the 25th to 43rd gestational week. Approximately half of the material served as a "control material" to the rest of the infants with postnatal asphyxia and IRDS. Blood was obtained from a catheter in the umbilical artery or vein. Serial sampling was performed in one part of the material. Determinations were made of: fibrinolytic activity on fibrin plates, fibrinolytic split products (FSP) in serum and in serum with addition of ϵ-aminocaproic acid (EACA), fibrinogen, plasminogen, antiplasmin, α_2-macroglobulin, inhibitors of urokinase activation of plasminogen. Plasminogen and α_2-macroglobulin increased significantly with increasing length of gestation, while the other factors were at the same levels as in full term newborns throughout. Fibrinolytic activity was demonstrated even in the smallest infants and also in infants which developed IRDS. It was high in some infants with severe hypoxia. FSP in serum-EACA were studied by serial sampling and were found in infants with severe hypoxia and acidosis. The various factors of the fibrinolytic system are sufficiently developed in preterm infants which are capable of producing fibrinolytic activity. The findings argue against the assumption that IRDS is due to a primary deficiency of the fibrinolytic system. It rather lends support to the hypothesis of an increased fibrinolysis in infants with hypoxia and acidosis.

40. Studies by direct calorimetry of thermal balance in the first day of life. G. RYSER and E. JÉQUIER. *Lausanne, Switzerland.*

Using a gradient layer direct calorimeter, total heat losses were measured in 73 full term newborns in three different environments: ambient temperature (T_a) of 30, 32, or 34°. The relative humidity of the air was kept constant at 50%. Esophageal temperature (T_{int}) and mean skin temperature (T_s) were continuously recorded. All experiments lasted at least 1 hr, and the data were obtained when the newborn was quiet. The mean total heat loss (± SEM) was at 30°: 41.85 ± 1.29 cal/kg/min; at 32°: 35.40 ± 0.71 cal/kg/min at 34°: 27.80 ± 0.85 cal/kg/min. Total heat loss was proportional to the difference between T_s and T_a. Evaporative heat loss was very constant in these three conditions (even when T_{int} was higher than 37.0°), with a mean of 6.58 ± 0.13 cal/kg/min. This value is a measurement of insensible perspiration. The heat storage (ΔS) was calculated using the following formula: ΔS = weight (kg) × specific heat of body mass (0.84 kcal/g.C) × [(0.6 × variation of T_{int}) + (0.4 × variation of T_s)]. ΔS was negative at T_a of 30° (body cooling), and positive at T_a of 34C (body warming). Regression analysis showed a mean heat loss of 36.26 cal/kg/min when the newborns were in thermal equilibrium ($S = 0$) this value corresponds to a calculated $\dot{V}O_2$ of 7.52 ml O_2/kg/min. This occurred in most babies at 32° (neutral environment). The skin thermal conductance [C = cutaneous heat loss/($T_{int} - T_s$) × body surface], which is an index of cutaneous blood flow, increased sharply in most babies when T_s reached 35.8° and T_{int} 37.0°. These data indicate that the thermoregulatory mechanisms on the 1st day of life are limited: at low T_a (30°), vasoconstriction and very likely that increase in metabolic rate are not large enough to prevent a fall of T_{int}. At high T_a (34°), vasodilatation occurs, but sweating is not elicited.

41. Oxygen transport capacity in the neonatal period. A KOIVIKKO, E. LÄNSIMIES, and J. KLOSSNER. *Children's Hosp. and Univ. of Turku, Finland.*

The oxygen consumption of resting lambs is from 8 to 13 ml/min/kg during the 1st week of life. Assuming a cardiac output of 300 ml/min/kg and a hemoglobin of 13 g/100 ml, it may be seen that about one-third of the oxygen transport capacity is used at rest. In the present study lambs 2–7 days old were subjected to shivering during hypothermia. The animals were breathing 100% oxygen and were anesthetized with chloralose. Oxygen consumption, dye dilution curves, pressures of the central arteries, and arterial SO_2 and acid-base balance values were registered. The oxygen consumption of the lambs increased to a maximum of 35 ml/min/kg during shivering. Cardiac outputs increased from about 300 ml/min/kg to 500–700 ml/min/kg in the lambs with the highest values of oxygen consumption. The arterial oxygen saturation did not change at the cardiac output values. These results were also observed when the body temperature had been lowered to about 30°. About one-third of the oxygen carried by the arterial blood was extracted by the organism. Decreasing values of standard bicarbonate were often associated with lowered cardiac outputs. Correction of metabolic acidosis increased cardiac outputs but did not influence the oxygen consumptions. It may be concluded that shivering increases the oxygen consumption and cardiac output in the

neonatal lambs. Metabolic acidosis counteracts the cardiac response but does not influence the rate of oxygen consumption.

42. Effect of hypercapnia on a blood-brain barrier in fetal and neonatal sheep. C. A. N. Evans, J. Reynolds, M. Reynolds, N. R. Saunders, and M. B. Segal. *University College, London, England.*

Penetration of sucrose from blood into brain which is very slow in the adult has been used to investigate the development of the blood-brain barrier (BBB) in fetal and neonatal sheep. Approximately constant blood levels of ^{14}C sucrose have been maintained by an intermittent intravenous injection technique over 1½ hr, after which cerebrospinal fluid and brain were removed, their ^{14}C activity was measured and compared with that in the blood during the 1½-hr injection period. Fetuses as young as 100 days gestation have a barrier to ^{14}C sucrose which is similar to that found in adult animals. However, fetuses at term (140 days) and newborn lambs show an increase of about 300% in sucrose penetration when made severely hypercapnic (arterial $pCO_2 > 90$ mm Hg). A smaller effect occurs at lower levels of pCO_2. The effect of CO_2 is also less in older animals. In other experiments, acidosis induced by slow intravenous infusion of ^{2}N-lactic acid has little effect on sucrose penetration, although arterial pH was as low as that in the hypercapnic animals. Asphyxia produced by intermittent cord occlusion in the fetus or underventilation in newborn lambs did not affect sucrose penetration unless arterial pCO_2 showed a sustained rise above about 60 mm Hg. A possible explanation for the effect of hypercapnia is that the increase in cerebral blood flow which occurs in hypercapnia may cause more sucrose penetration because of the increased surface area for exchange across the BBB. Krypton-85 clearance has been used to estimate superficial cortical blood flow. Preliminary observations suggest a correlation between cortical blood flow and sucrose penetration into cortical tissue since both appear to be proportional to arterial pCO_2. Other possibilities being considered are (*1*) a direct effect of CO_2 upon the permeability of the barrier, (2) an increase in the size of the brain extracellular space.

43. Plasma amino acid ratio in infants born after pregnancies complicated by toxemia, placental infarction, impaired umbilical circulation and chronic maternal diseases. J. Mestyán. *Univ. of Pécs, Hungary.*

The ratio of the plasma concentration of glycine + serine + glutamine + taurine to the concentration of leucine + isoleucine + valine + methionine has been studied by Whitehead's method using paper chromatography. The mean postnatal rise in the ratio was found to be significantly higher than that observed previously in infants born to mothers with uncomplicated pregnancies. The higher ratio observed in the different series of examinations was due to a pronounced opposite response in the plasma level of the two groups of amino acids included in Whitehead's ratio test. The results will be discussed in relation to conditions interfering with uteroplacental functions.

44. Combined cortical and medullary adrenal hyporesponsiveness in hypoglycemia of infancy and childhood. R. P. Zurbrügg, H. U. Tietze, K. A. Zuppinger, E. E. Joss, and H. Käser. *Univ. of Berne, and Swiss Ctr. for Clin. Tumor Res., Berne, Switzerland.*

In contrast to healthy subjects a group of children with hypoglycemic attacks do not respond with an appropriate increase in urinary epinephrine (E) during the insulin tolerance test, ITT (Broberger *et al*, 1959, 1961). The significance of the E deficiency regarding the disturbance of blood glucose regulation is still uncertain. Therefore, the possible importance of growth hormone (GH) and especially cortisol (F) was evaluated under various stimuli. The eight patients investigated were suffering from hypoglycemia with an insufficient or virtually absent urinary E response.

During ITT the clinical signs of hypoglycemia were lacking. The mean plasma glucose fell to a significantly lower minimum and the rise toward normalization, as expressed by the recovery index, was significantly slower. There was no impairment of GH response.

The most impressive finding during ITT was a deficient response of plasma F which could be shown to be independently impaired from the lacking E excretion. F and E response to intravenous glucagon was also found to be impaired in the same group of patients.

The simultaneous and independent occurrence of both an adrenomedullary and adrenocortical disturbance gives evidence for an impairment of hypoglycemia-sensitive centers for E as well as F regulation located most probably in the hypothalamus. In addition, a delayed response to metopirone, a lack of sweating during hypoglycemia and a positive history for birth injury in all patients also are in favor of a central nervous system dysregulation.

45. Incomplete renal tubular acidosis with hypercalciuria in siblings. K. Schärer. *Children's Univ. Hosp., Heidelberg, Germany.*

Two female siblings were first seen at the age of 7 and 9 years with a recent history of pyelonephritis. On admission, polyuria, hypercalciuria (up to 10 mg/kg 24 hr), and advanced nephrocalcinosis were noticed. Growth was normal. Renal function studies revealed leukocyturia, proteinuria, moderately decreased glomerular filtration rate, impaired concentrating capacity, an acidification defect (minimal urinary pH 5.4 3 days after 150 mEq/m²/24 hr of NH_4Cl), a normal HCO_3 threshold, and a low citrate excretion. Under basal conditions, acidosis was never observed. Potassium metabolism and amino acid excretion were normal. Radiological examination showed slight osteoporosis. In a kidney biopsy patchy interstitial fibrosis and glomerular sclerosis were reported. Increased calcium absorption by the gut was excluded by following the calciuria during prolonged starvation and the activity of Ca^{47} (200 nCi *p. os*) in the whole body and in the stools. Phosphate reabsorption in the kidney rose as in normal subjects after a Ca infusion, but insufficiently after administration of parathyroid hormone. Treatment with a diet low in Ca resulted in a fall of the Ca excretion with a negative Ca balance. By a salt restricted diet, given over 6 months, the balance increased considerably and the calciuria became normal. Hydrochlorothiazide provoked hypocalcemic tetany. The father of the siblings is a past stone former, has a high Ca excretion, but can acidify his urine normally. It is believed that these girls present an incomplete familial form of (distal) tubular acidosis distinct from other types of tubular acidosis and from idiopathic hypercalciuria.

46. Origin of the X chromosome in patients with XO Turner's syndrome. S. N. Pantelakis and A. Karakelis. *Aghia Sophia Children's Hosp., Athens, Greece.*

The frequency of maternal *versus* paternal origin of the single X chromosome in cases of XO Turner's syndrome has not been decided with certainty. Additional data from informative