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 $mEq/m^2/24$ 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. Karaklis. *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

families are needed for the statistical approach to the problem. In order to obtain the most information regarding maternal or paternal nondisjunction, the simultaneous determination of color blindness, Xg blood group, and G-6-PD deficiency, known to have polymorphic frequency in Greece, have been studied in 10 patients with XO Turner's syndrome and their available parents. Four families were informative. In the first the patient was Xg (a+) and the mother Xg (a−). In the second the patient and the father were G-6-PD deficient, while the mother was normal. Clearly in these two families the single X was of paternal origin. In a third family the patient was color-blind and the mother had normal color vision, and in the fourth the patient was Xg (a−) while her mother was Xg (a+). Unfortunately, in both cases the father was dead and since these two sex-linked characters cannot be detected in the heterozygous state the origin of the single X could not be located. Clearly the inclusion in this type of study of an X-linked trait which can be detected in the heterozygous condition is advantageous, as has been shown in the first family.

47. Clinical and experimental relationship between liver lymphatics and bile flow. O. Aagenaes, H. Sigstad, B. Cuderman, W. Krivit, and H. Sharp. *Univ. of Oslo, Norway, and Univ. of Minnesota, Minneapolis, USA.*

A syndrome with cholestasis in infancy and recurrent cholestasis and edema in the lower extremities in adulthood was presented in this Society in 1967. Further studies in our now 22 patients with this syndrome have shown that these children have abnormal lymph vessels in the legs before development of edema, and the cause of the edema is probably a congenital lymph vessel hypoplasia. A liver lymphangiography with Au^{198} in one adult patient with no cholestasis at time of examination failed to show the normal clearance of the radioactive gold to the thoracic lymph nodes. To study the relationship between liver lymph flow and bile flow, an experimental animal model was devised: all lymph nodes draining the liver were obstructed in cats while control animals were sham-operated. In one group of cats, the bile flow was studied shortly after the lymph obstruction, in another group 1 day later, and in yet another group 2 days later. The bile flow was the same in the lymph-obstructed and the sham-operated groups of cats studied on the day of lymph obstruction; in the lymph-obstructed cats studied 24 hr after lymph obstruction the bile flow was about 70% higher and the bile acid excretion more than 100% higher than in the sham-operated group. Forty-eight hours after the lymph obstruction, the bile flow was only slightly elevated in the lymph-obstructed group. Following the bile flow study an electron-dense material (lanthanum) was injected in the common bile duct, and biopsies from different parts of the liver were studied in the electron microscope. The injected lanthanum could be traced from the bile canaliculi to the intercellular spaces and to the Disse's spaces. The findings of this intimate relationship, both anatomically and functionally between the liver lymphatics and the biliary tree, compared with the clinical findings of abnormal peripheral lymphatics and an abnormal liver lymphangiography, indicate that a lymph anomaly in the liver may be the cause of the cholestasis in these patients.

48. Value of color scintiscanning in the diagnosis of cerebral, renal, and hepatic neoplasias in pediatrics. G. C. Mussa, M. Martini Mauri, and D. Bacolla. *Univ. of Turin, Italy.*

New high sensitivity apparatus and particularly the discovery of pure gamma-emitting, low energy, short half-life radioisotopes have brought the use of radioisotope techniques, especially scintiscanning, within the orbit of paediatric diagnosis. Here, a series of color scintiscans is presented, the children in question having been admitted for suspected cerebral, renal, and hepatic neoplasias. Tc^{99m} was used for the cerebral scans, colloidal Tc^{99m} sulfide for the hepatic, and Chlormerodrin Hg^{197} for the renal. The cerebral scintiscanning was performed on 25 children with suspected intracranial neoplasia. Seventy-six per cent of all cerebral tumours encountered were correctly localized. Within this percentage, the success rate with supratentorial tumors was 100% and with subtentorial 61.5%. Renal scintiscanning proves to be of particular value in the diagnosis of primary and metastatic tumors. While urography is an important tool for evaluating the morphology of the excretory cavities of the kidney, scintiscanning studies parenchyma conditions. Using colloidal Tc^{99m} which is localized by choice in the hepatosplenic reticuloendothelium, it is possible to detect the presence of primary hepatic tumors or metastases, if any. Findings showed that: (*1*) there are no particular contraindications to the use of scanning because the technique is free from toxicity, harmless, painless, and easy to use; (*2*) in pediatric age and, above all, in the early months of life, scanning makes it possible to solve diagnostic problems which in its absence would require much more laborious, traumatizing techniques; (*3*) with scanning, the effects of antiblastic therapy may be followed up over a period of time.

49. Changes in angiotensin II-like activity in arterial blood induced by hemorrhage in immature and adult rabbits. F. Broughton-Pipkin, J. C. Mott, and N. R. C. Roberton. *Nuffield Inst. for Med. Res., Oxford, England.*

The conclusion [1] that the presence of the kidneys may be more important in the regulation of arterial pressure in immature than adult rabbits suggested the desirability of measuring changes of angiotension II-like activity in arterial blood in response to hemorrhage. Angiotensin II-like activity was measured by the shortening of a rat's ascending colon, irrigated intraluminally with pronethalol 1 mg/ml/min. The colon was superfused with arterial blood from the rabbit in an external circuit, from which the blood was returned to a jugular vein [2]. The colon was calibrated by infusion of Hypertensin (Ciba) before withdrawal of 25% of the rabbit's calculated blood volume. After 30 min, the blood volume was restored with dextran and the calibration were repeated. Angiotensin II-like activity developing during hemorrhage in 6 adult rabbits was equivalent to 0.31 ± 0.07 ng/ml Hypertensin, whereas that in 10 immature rabbits averaged 1.76 ± 0.41 ng/ml ($P < 0.025$). Although Hypertensin is inactivated slightly less rapidly in immature rabbits, the difference is insufficient to account for the very much greater rise in angiotensin II-like activity seen during hemorrhage in immature than in adult rabbits.

1. Mott, J. C.: J. Physiol., *202:* 25 (1969).
2. Vane, J. R.: Brit. J. Pharmacol. Chemother., *35:* 209 (1969).

50. Clinical and genetic examinations in hypophosphatasia. K. Méhes and L. Klujber. *University Med. Sch., Pécs, Hungary.*

A 5-year-old boy with typical clinical and biochemical findings of hypophosphatasia of the late infantile-juvenile type has been observed. The patient's acid-base regulation and renal functions, such as glomerular filtration, concentration and acidifying capacity, proved to be normal; however, the tubular reabsorption of phosphates was impaired.

The paternal grandparents of the propositus were second and the maternal grand-grandparents third cousins. As to serum