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ABSTRACTS

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1. Polygraphic studies (EEG, ECG, motor behavior, and respiration) in hypoglycemic newborns with particular reference to seizure activity. C. HOTES, F. J. SCHULTE, and H. LANGENSTRASSEN. *Univ. of Göttingen, Göttingen, Germany.*

Eleven newborn infants with blood glucose values below 20 mg/100 ml were studied by polygraphic recordings lasting 2–6 hr. Five infants were born at term and six were preterm. Two were infants of toxemic mothers, one was a triplet, and two were small for dates. Four suffered from perinatal brain damage and two had respiratory insufficiency. Hypocalcemia was present in three infants, hyperbilirubinemia in two infants. Six infants had convulsions, three were hyperexcitable, and two were hypotonic. Five infants had apnoic spells. All infants had only short periods of well defined sleep states, both active (rapid eye movement (REM) sleep) and quiet (non-REM sleep). Respiration was irregular and rapid. In six infants the EEG showed continuous seizure activity associated with convulsions or apnoic spells. In three infants the EEG was inactive either periodically or throughout the entire recording. Two EEG's were retarded by 3 weeks. All infants received intravenous glucose during the recording, with an elevation of blood glucose above 30 mg/100 ml. In six infants the elevation of blood glucose did not influence any one of the recorded parameters. Seizure activity as recorded on EEG, convulsions, and apnoic spells increased in three infants while glucose was injected. Only two infants showed prompt improvement of polygraphic and clinical findings. This effect, however, was either of short duration or could not be reproduced during successive periods of hypoglycemia. In conclusion, we think that polygraphic monitoring enables us to differentiate infants with symptomatic hypoglycemia from those with hypoglycemia as a symptom rather than as the cause of neonatal brain dysfunction.

2. Statistical analysis of the electroencephalographic response to controlled overbreathing in children with epilepsy. D. SCHEFFNER and L. STOLZIS. *Univ. Children's Hosp., Heidelberg, Germany.*

During hyperventilation (HV), theta and delta waves of three amplitude ranges were summed up for consecutive periods of 30 sec each. pH (P_{CO_2}) changes during HV are directly proportional to the frequency and depth of ventilation, provided that the respiratory system is intact. Results of correlating quantitative changes of the EEG and acid-base status of 58 children 6–13 years old suffering from generalized or focal epilepsy were compared with the results in 108 healthy children. Whereas in the latter there is an age-dependent increase in amplitude and a decrease in frequency with increased pH levels, children with epilepsy respond more readily but with less differentiation to HV, their interindividual variability differing widely. Thus it is not rational to conclude EEG changes from a given pH range. In contrast, a close relationship between EEG and acid-base status can be found in healthy children. Since our children suffer from epilepsy of early onset, we can only speculate whether lack of differentiated responses in children with epilepsy might be due to loss or immaturity of stabilizing brain function. There is no evidence so far that children with seizures acquired during school age show the same type of reaction. Therefore we suggest an immature homoiostasis toward HV (alcalosis, hypoxidosis) which is thought to be nonspecific rather than typical for children with epilepsy.

3. The Lennox syndrome: A clinical study of forty children. F. VASSELLA, H. SCHNEIDER, and K. KARBOWSKI. *Univ. of Berne, Berne, Switzerland.*

This type of epilepsy has to be suspected if a combination of various seizures patterns (atonic-akinetic seizures, grand mal, hemiconvulsions) is present in children of 1–6 years of age who are mentally retarded. Perinatal brain damage, tuberous sclerosis, intrauterine encephalitis due to toxoplasmosis and cytomegalic inclusion disease, and neurocutaneous melanoblastosis were the etiologic factors discovered in 6 children, the remaining 34 being classified as cryptogenic. Age dependency and the different etiologies lead to the assumption that this type of epilepsy is an unspecific reaction of the brain, during a certain developmental stage, to a generally severe damage.

The typical spike-wave variant was present at the first EEG examination only in one-fourth of the cases. In half of the patients, the EEG became characteristic only in the course of several months or even years. It is therefore postulated that a tentative label of Lennox syndrome should be supposed on clinical grounds alone. On the other hand, the diagnosis was suggested on EEG grounds in one-fifth of the patients.

4. Some causal factors in febrile convulsions. S. J. WALLACE and T. T. S. INGRAM. *Univ. of Edinburgh and the Royal Hosp. for Sick Children, Edinburgh, Scotland.*

Lennox (1960) described febrile convulsions in childhood as "the purest type of epilepsy." This view of febrile convulsions is not shared by many pediatricians who tend to regard febrile convulsions as relatively unimportant. They have, in fact, been compared in significance to rigors occurring with fever in adult patients. Ounsted *et al.* (1966), on the other hand, have emphasized that febrile convulsions may in themselves be a cause of brain damage, especially in predisposed patients. A series of 53 patients between 6 months and 7 years of age who presented in the Royal Hospital for Sick Children, Edinburgh, with convulsions associ-

ated with fever were studied in detail by Dr. S. J. Wallace. Careful family histories, accounts of the birth (supplemented by hospital notes), and details of the child's development and previous illnesses and the reasons for the admission associated with the convulsion were obtained from the parents. Compared with a control series, a higher proportion of patients suffering from convulsions had a history of being born after abnormalities of pregnancy, labor, and delivery; had a history suggestive of previous neurologic abnormalities; and had a history of virus infections associated with encephalitis (Wallace: 1970, 1971). The fertility of mothers of children suffering from febrile convulsions was studied in the same way as the fertility of mothers of children suffering from diplegic cerebral palsy and clefts of lip and palate (Drillien *et al.*: 1962, 1964; Drillien *et al.*: 1966). The significance and interrelationships of maternal subfertility, abnormalities of sibs, disorders of pregnancy, labor and delivery resulting in the birth of patients, evidence of preexisting neurologic abnormalities, and the presence or absence of indications of encephalitis at the time of the febrile convulsion are considered.

5. Recognition and assessment of the emotional and intellectual consequences of life in an institution. S. Doxiadis, A. Karagelli, and Y. Tryphonopoulou. *Bebies Centre Metera, Inst. of Child Hlth., Athens, Greece.*

The prevention of retardation or personality distortion, or both, cannot be any longer the only goal of the rearing of infants deprived of normal family life. The other and uppermost goal is the preservation and enhancement of the innate individuality of each child. For the evaluation of this, standard developmental tests are not sufficient. On 30 babies living in the residential nursery *Bebies Centre Metera,* we used three methods simultaneously for the study of their development and behavioral pattern from birth to 20 months: the Bayley tests (new forms), an individuality questionnaire filled out by the mother-substitutes, and interviews between the examiner and the mother substitute. With this approach, we found that initial individual patterns which persisted in the first 3 months of life showed a tendency for homogenization thereafter, while at the same time the rate of psychomotor development started to slow down in certain fields. It is only with the use of such multiple approaches to the assessement of the development of each child that we shall be able to recognize in time all risks and to make an early therapeutic intervention possible.

6. Immunoglobulin A and M levels in prematures with an infection of the gastrointestinal tract. C. Papadatos, G. Papaevangelou, D. Alexiou, and A. Skardoutsou. *Univ. of Athens, Alexandra Maternity Hosp., Athens, Greece.*

The purpose of this study is to present evidence that gastrointestinal (GI) infections of the premature initiate rapid immunoglobulin A synthesis. During an epidemic of gastroenteritis, it was decided to study all premature newborns with a birthweight of 1000–2000 g. On the basis of clinical and laboratory evidence, 17 of these newborns were considered healthy, while 11 developed a bacteriologically confirmed infectious process of the GI tract. There was a spectacular and statistically significant increase of IgA in infected *versus* noninfected prematures. These results support the concept of local antibody synthesis and suggest that the intestinal antibody system responds rapidly to local antibody stimulation resulting from the aquisition of a pathologic intestinal microbial flora. It is suggested that microorganisms causing localized infections of the GI tract stimulate immunoglobulin-producing sites of the intestinal wall. This results in rapid production of secretory antibody. In the course of this localized infection, replication of bacteria in the lymphoid tissue of the intestinal wall stimulates immunologically competent cells in direct proximity to the alimentary tract, causing increased serum IgA levels.

7. The immunoglobulins and coproantibody formation in infants after artificial colonization of the intestine with *Escherichia coli* O83 and lyzozyme administration. R. Lodinová V. Wagner, and V. Jouja. *Inst. of Care for Mother and Child, Prague-Podoli, Czechoslovakia.*

The development of immunoglobulins in stool filtrates and sera was followed in bottle-fed infants artificially colonized with a nonpathogenic *Escherichia coli* strain, infants treated with lyzozyme, and breast-fed infants.

Immuoglobulins were determined by radial immunodiffusion, antibodies against *E. coli* O83 by hemagglutination technique. In colonized infants, rather than in controls, an earlier occurrence of IgA and IgM and higher titers of antibody in stool filtrates and sera were found. The secretion of IgA in the intestine of lyzozyme-treated infants was decreased. The breast-fed infants showed high levels of IgA in stool filtrates, passively transferred from maternal milk. The artificial colonization represents a strong antigenic stimulus which caused a high and early antibody response in serum and intestinal mucosa. This accelerated immunologic reactivity might be the basis of a defense mechanism in infants who are not protected by passively transferred antibodies against enteral infections. Lyzozyme might influence the intestinal flora and decrease the production of secretory IgA in the intestine.

8. Elimination from plasma of gamma globulin fragments following substitution in immunologic deficiency. F. W. Bläker and K. Mai. *Univ. Kinderklinik and Inst. for Mikrobiol. and Immunol., Univ. of Hamburg, Hamburg, Germany.*

Investigations were performed to determine the duration of passive immunity needed to prevent infection in immunologically deficient children.

Pepsin-digested human gamma globulin was administered to patients with and without agammaglobulinemia. The elimination of the gamma globulin fragments and their antibody functions from the plasma were measured by means of single radial immunodiffusion tests and by tetanus antibody titration (passive hemagglutination). Two fractions could be identified, both containing antibody activity. One of them, obviously the main fraction, has a sedimentation constant of 5,3 S and a half-time of disappearance of 12 hr. The second, a minor fraction with a sedimentation constant of 3,5 S, is eliminated from the plasma with a half-time of 35 hr. Less than 5% of the administered amount was recovered in active form in the urine.

9. Inborn defect of immunological function: Absent antibody formation without decreased concentrations of serum immunoglobulins or of peripheral lymphocytes. A. Russell, G. Cividalli, and A. Simcha. *Hadassah Univ. Hosp., Hebrew Univ. of Jerusalem, Jerusalem, Israel.*

Presentation was of a boy of 10 years with profound systemic

salmonellosis but without serologic response. An underlying pattern of episodic if not chronic salmonellosis since 18 months emerged, accompanied by recurrent pneumonia and abscesses, together with chronic moniliasis and gross growth failure. He had delayed healing after chickenpox and vaccinia immunization. A sister and brother succumbed suddenly at 2 years and 5 months, respectively. While levels of three major immunoglobulins were normal, even increased, there was complete absence of circulating antibodies, greatly depressed delayed type skin hypersensitivity, and prolonged skin homograft rejection. Lymphocytes and plasma cells appeared normal morphologically and numerically, although *in vitro* lymphocyte transformation with phytohemagglutinin was markedly reduced. Neutrophils were normal in number and function. Evidence for a new partial immunologic deficiency syndrome compared with kindred states is apparent.

10. Metabolic and morphologic studies of blood lymphocytes in the neonatal period. V. ANDERSEN, E. ANDERSEN, and B. FRIIS-HANSEN. *Rigshospitalet, University Hosp., Copenhagen, Denmark.*

The development of lymphatic tissue in the neonatal period as a consequence of antigenic stimulation has been studied in animal experiments. In lymphocytes, increased synthesis of RNA and protein and increased mitotic activity is found. In this study, blood lymphocytes of infants were examined at birth and at daily intervals thereafter. Their number and morphology were assessed, and the changes in RNA and DNA metabolism were studied through their *in vitro* incorporation of tritiated cytidine and tritiated thymidine, followed by autoradiography. The findings in normal infants were compared with the results obtained in newborns with infections.

11. Enzymatic studies on phytohemagglutinin-stimulated lymphocytes. S. NORDIO, A. MARCHI, and M. A. MARCHI. *Univ. of Trieste, Trieste, and Univ. of Genoa, Genoa, Italy.*

In a previous paper, the American Association presented first results of an investigation on the lysosomal enzyme activities of the phytohemagglutinin-stimulated lymphocytes of patients with celiac disease and a few other pathologic conditions with immunologic defects.

They continued these investigations by studying: (*1*) lysosomal enzymes (before and after treatment of the cultured lymphocytes with Triton) in relation to immunologic problems; (2) lysosomal and other enzyme activities in relation to cystic fibrosis of the pancreas and a few other inborn errors of metabolism (galactosemia, sulfatidosis, PKU). The sensitivity of the test of phytohemagglutinin-stimulated lymphocytes is increased by the enzymatic determinations. The interest of this new approach to immunologic and metabolic problems is emphasized.

12. Subacute sclerosing panencephalitis (SSPE): Differences between measles virus and viruses isolated from SSPE brain cells in culture. V. TER MEULEN, M. KATZ, M. Y. KÄCKELL, G. BARBANTI-BRODANO, and H. KOPROWSKI. *Univ. of Göttingen, Göttingen, Germany, and the Wistar Inst., Philadelphia, Pennsylvania, USA.*

Differences between measles virus and isolated SSPE viruses have been demonstrated previously in their infectivity for ferrets and hamsters. To compare some properties of these viruses *in vitro,* tissue cultures were infected with a wild strain of measles virus, the attenuated Edmonston strain, and two SSPE viruses. African green monkey kidney (AGMK) and human embryonic kidney cell cultures were found to be susceptible to the four viruses. When, however, human brain cell cultures, derived from patients with CNS diseases other than SSPE and from normal human embryos, were exposed to these viruses, they became infected only with the two types of measles virus and not with SSPE viruses. Kinetic experiments of SSPE viruses of different passage levels suggest that a large proportion of incomplete virus particles inhibiting infection accounts for the resistance of the brain cells. AGMK cells infected with the four viruses showed positive cytoplasmic staining by fluorescence microscopy in the presence of SSPE sera and early and late measles convalescent sera. When SSPE sera and early convalescent measles sera were used, immunofluorescence was also observed in the nuclei of the infected cells, except in those cells infected with the Edmonston strain of measles virus. Cells infected with SSPE viruses exhibited only two types of intranuclear fluorescence: speckled and inclusion type. These data suggest that the SSPE viruses are not identical with measles virus, and that host response to them differs.

13. Gestational and growth characteristics of a neonatal population in Greece. S. N. PANTELAKIS, T. VALAES, and C. PAPADATOS. *Inst. of Child Hlth. and Univ. Maternity Hosp. "Alexandra," Athens, Greece.*

Thirteen thousand nine hundred twenty-six consecutive births during a 2-year period (1966–1968) in "Alexandra" Maternity Hospital, Athens, were studied in terms of the reproductive and socioeconomic characteristics of the mothers and the intrauterine growth of their newborns. Eighty-four per cent of the mothers belonged to the lower socioeconomic group and 48% were primiparae; 10.5% of the newborns were preterm and 6.5% postterm, and the gestational age distribution curve was displaced toward shorter gestation by 3–4 days in comparison with the distribution in the British Perinatal Mortality Survey. A definite slowing of growth rate was evident after the 37th week of gestation. This slowing of growth during the last 3 weeks of pregnancy, and the tendency toward shorter gestation might be an indication of limited capacity of the maternal environment to support fetal growth in this population.

14. Amniotic fluid total hydroxyproline and intrauterine growth. B. A. WHARTON, J. W. FOULDS, I. D. FRASER, and C. A. PENNOCK. *Inst. of Child Hlth., London, England.*

In normal pregnancy, amniotic fluid total hydroxyproline concentration rose to a peak around the 28th week before falling steadily to term, while a creatinine concentration was at first constant and then rose rapidly to maximum values at term. The total hyproxyproline/creatinine ratio reached a zenith around 17 weeks and then fell rapidly. Total hydroxyproline concentrations tended to be lower in those pregnancies producing small for dates babies and those at particular risk of intrauterine growth retardation. The total hydroxyproline/creatinine ratio in the first urine passed by babies was a little higher than the amniotic fluid from the pregnancy concerned. After birth, the urinary ratio rose rapidly. There is some evidence that changes in amniotic fluid total hydroxyproline and total hydroxyproline/creatinine ratio are related to intrauterine growth. Further information, particularly from other animals, is required. A determination of amniotic fluid-total hydroxyproline may eventually prove to be clinically useful when considering in-

duction of labor for preeclampsia, or maternal loss of weight toward term, but a more intensive study during this period of pregnancy will be necessary before firm, clinically useful conclusions can be made.

15. Late effect of early malnutrition on physical and mental development: Follow-up after 22–42 years. G. Berglund and E. Rabo. *Univ. of Gothenburg, Göteborg, Sweden.*

The remaining 180 of the 203 patients treated for hypertrophic pyloric stenosis during the years 1922–1942 at Children's Hospital, Göteborg, were interviewed and their height and intelligence test results at the time of registration for military service have been investigated.

Comparison of their heights with the mean height of the male population showed slight differences. Comparisons with the heights of their brothers showed that the patients were shorter than the brothers. The difference was more pronounced when the patients had suffered a more severe malnutrition. At the intelligence test, only those who had suffered the most severe malnutrition demonstrated slightly lower values. The adaptability test demonstrated that the greater the malnutrition, the lower the score.

16. Reduced nicotinamide adenine dinucleotide (NADH)-dependent diaphorase isoenzymes in the newborn. G. Weippel, M. Pantlitschko, and W. Kosse. *Univ. of Vienna, Vienna, Austria.*

There are two isoenzymes of the NADH-dependent diaphorase (methemoglobin reductase) in the adult, with an activity of 30% (*A*) and 70% (*B*). In the newborn we find the same two isoenzymes with another relative activity. In consideration of the lowered activity of the whole enzyme in the newborn (70% of the adult) the activity of the *fraction A* is the same as in adults, 30%, and *fraction B* has only 40%, contrary to 70% in adults. Therefore, the cause of the diminished activity in the whole enzyme is only the lowered activity of the *isoenzyme B*. Method: cellulose acetate electrophoresis. The enzyme with NADH reduces dichlorphenol-indophenol (DCIP) and DCIP reduces dimethylthiazolyl-tetrazoliumbromide under the action of phenazin-metasulfate as H^+-transfer substance to formazan. Formazan was measured spectroscopically.

17. *Diazepam metabolism in premature infants.* P. L. Morselli, N. Principi, G. Tognoni, and F. Sereni. *Instit. di Ricerche Farmacologiche M. Negri and Univ. of Milan, Milan, Italy.*

While it is well known that in newborn animals the activity of liver drug metabolizing enzymes is defective and the rate of metabolism of foreign compounds greatly impaired, very few data are available for newborn infants. Investigations were performed in order to evaluate in newborn and premature infants the rate of metabolism of diazepam (DZ), which in mature subjects undergoes demethylation, hydroxylation, and conjugation. Plasma and urinary levels of DZ and its metabolites were measured by gas chromatography. 0.3 mg/kg DZ (intramuscularly, single dose) led to higher plasma clearance, in comparison with values obtained in children. No significant differences in plasma levels of *N*-demethyl-diazepam were observed. While in children significant amounts of hydroxylated and conjugated metabolites (*N*-methyl-oxazepam and oxazepam) were present, not even traces of such compounds were detected in urine of premature infants. Biochemical and clinical implications in terms of developmental pharmacology are considered.

18. Interaction between human placental alkaline phosphatase and ABO system polymorphisms. E. Bottini, P. Lucarelli, P. Pigram, R. Palmarino, G. F. Spennati, and M. Orzalesi. *Natl. Res. Council, Cntr. of Evolutionary Genetics, Rome, Italy, and Yale Univ., New Haven, Conn., USA.*

Placental alkaline phosphatase (Pl) shows an electrophoretic polymorphism determined by three common alleles, as well as by other rarer ones at an autosomal locus. The gene is normally active during intrauterine life only, and the enzyme, produced by the fetal part of placenta, is present at an early stage of pregnancy in the maternal blood stream. Considering that an association with the ABO system has already been described for another alkaline phosphatase, namely the intestinal one, our present investigation was undertaken with the purpose of finding out a possible interaction between the Pl polymorphism and the ABO one during intrauterine life. Recently, Beckman reported that the six common phenotypes of placental alkaline phosphatase show different enzymatic activities both in pregnancy serums and in placental extracts. Nine hundred three placentas, collected during the period from September 1968 to September 1970 at the Yale-New Haven Hospital and belonging to a white population of European origin, were examined. The results have shown that, in the newborn babies incompatible with the mother in the ABO system, the incidence of Coombs' test positivity or jaundice (as referred to the single common Pl phenotypes), or both, are correlated in a linear fashion with the enzyme activity associated to the various Pl phenotypes in the sense that the lower the enzyme activity, the higher is the incidence of these signs. Several other lines of evidence found in the course of our investigation favor the hypothesis of a complex interaction involving ABO and Pl polymorphisms at various stages of intrauterine life. Because the intensity of action, at the level presently considered, appears in a fairly evident relation with the enzyme activity associated to the alleles of one of the interacting systems, a quite reasonable basis does exist for further investigation of the interaction mechanism.

19. The influence of glucagon and phenobarbital on enzymes of carbohydrate metabolism in the developing rat liver. J. Schaub and F. Freska. *Children's Hosp. of the Univ. of Munich, Munich, Germany.*

In rat liver the following enzymes are measured from the 15th fetal to the 20th neonatal day: G6PDH, 6PGDH, PGM, PGI, FDPase, phosphorylase, F6PK, HK, α-glucosidase, G6Pase, glycogensynthetase *a* and *b*. Glucagon was injected either into the abdomen of each fetus after opening the abdominal wall of the mother or intraperitoneally to each newborn rat. Phenobarbital was injected three times in an interval of 24 hr either to the littermates or to the newborn intraperitoneally.

A striking effect of glucagon is seen on the two forms of glycogensynthetase. During fetal and neonatal life, the enzyme is significantly inhibited by the hormone. A small effect is seen on PGM: this enzyme is activated during development. The effect of glucagon on the other enzymes measured is not significant. The most striking effect of phenobarbital is seen on phosphorylase. The activity, either measured with the optical test or with phosphorus release is decreased 1.5-fold during the neonatal period. The independent form of glycogensynthetase is de-

creased 1.5-fold during the 5th and 20th neonatal day. The lysosomal α-glucosidase is activated 1.5-fold by phenobarbital before and after birth.

20. Ontogeny of iminoglycine transport in the kidney. K. BAERLOCHER, C. R. SCRIVER, and F. MOHYUDDIN. *Univ. Children's Hosp., Zurich, Switzerland, and McGill Univ., Montreal Children's Hosp. Res. Inst., Montreal, Quebec, Canada.*

In human and rat kidney glycine, L-proline and L-hydroxyproline are transported by three different systems: a common system with high capacity and low affinity which is shared by all three amino acids and two specific systems, one for proline and one for glycine, both with high affinity and low capacity. Since human and rat newborns show a transient hyperexcretion of these amino acids in urine, one may ask whether it is a decrease in the activity of all systems or rather a transient deficiency in one of the systems which accounts for the "immaturity." Therefore, we investigated developmental aspects of the iminoglycine transport *in vitro* by means of kidney cortex slices in 1-, 2-, and 3-week-old rats. Initial rates of uptake are reduced in the newborn kidney at low substrate concentration when compared with the adult kidney; during longer incubation newborn kidney slices accumulate more substrate reflecting reduced rate of efflux. Kinetic analyses reveal the absence of the low K_m systems for proline and glycine in the 1-week-old rat. At 2 weeks, the low K_m-proline system appears, and at 3 weeks the low K_m-glycine system. Cyanide and anoxia inhibit the available high K_m transport. The deficiency of transport is therefore due to a lack of carrier and not of the coupling of the carrier to energy. V_{max}'s for proline and glycine uptake on the present high K_m carriers increase equivalently with age. Thus, changes in specific activity of membrane sites and in total membrane activity characterize transport ontogeny in kidney.

21. Fructose in the diet of diabetic children. H. K. ÅKERBLOM, I. SILTANEN, and A.-K. KALLIO. *Children's Hosp., Univ. of Helsinki, Helsinki, Finland.*

The object of the study was to evaluate whether fructose can safely be used as a sweetening agent in the diet of diabetic children. At first, short term effects of fructose were studied in 26 hospitalized diabetics by administering fructose 1 g/kg body weight at breakfast and comparing for 3 hr postcibal levels of blood glucose to those of control days, when a corresponding amount of calories was given at breakfast in a regular diet for diabetics. The postcibal hyperglycemia was significantly smaller on "fructose" days as compared with control days at 30, 60, 90, and 120 min. For the time being, we are studying whether a longer lasting use of fructose has any effect on the control of childhood diabetes. Ten subjects took at home every 2nd week a diet containing 1.5 g fructose/kg/24 hr, alternating for 1 week with a regular diet for diabetics with the same amount of calories. The children were studied for 4 weeks, and the dose of insulin remained constant. Glucosuria was recored twice daily by "Clinitest" and ketonuria by "Ketostix," and at the end of each week 24-hr glucosuria was measured. No significant differences were found in glucosuria and ketonuria between control and "fructose" weeks, suggesting that fructose could be used as an alternative for sweetening of food for diabetic children. If fructose is used, a corresponding amount of other carbohydrates should be deducted from the diet.

22. Therapeutic ketolysis in ketoacidosis without use of insulin. J. R. BIERICH, K. RAGER, and G. BRÜGMANN. *Univ. Kinderklinik, Tübingen, Germany.*

It is our future object to remove the ketone bodies in ketoacidotic patients by means of substances which stimulate the TCA cycle. Here our animal experiments are reported. Groups of 10 rabbits each (5, 48 hr fasted; 5, alloxan diabetic) were infused with (*1*) lactate, (*2*) pyruvate, (*3*) malate, (*4*) alanine, and (*5*) asparagine; 0, 30, and 300 min postinfusion, serum was examined for: glucose, FFA (according to Duncombe), acetoacetate (AA), β-hydroxybutyrate (OH-but), and pyruvate, using the enzymatic method according to Bergmeyer and Bernd. Results of fasted animals which showed no severe ketosis are not reported here. AA and OH-but were enhanced 30 times in nontreated diabetic rabbits and decreased after infusion of each substance used. Decrease was maximal after lactate (to 30 and 35%, respectively, of the starting values of AA and OH-but) and pyruvate (to 35%). Ketolysis was always connected with hyperpyruvatemia.

23. Secretin induces renal bicarbonate loss in man. O. OETLIKER, H. B. HADORN, and A. CHATTAS. *Univ. of Berne, Berne, Switzerland.*

The gastrointestinal hormone secretin stimulates bicarbonate excretion in the pancreas and the liver. A number of hypotheses have been put forward to explain the mechanism of action of this hormone [1]. In a search for targets of secretin, we tested its influence on bicarbonate reabsorption in the kidney: in three patients who underwent "renal bicarbonate titration studies" [2], the handling of bicarbonate, sodium, titratable acid, and ammonia by the kidney was tested before and after adding secretin to an infusion of sodium bicarbonate. Under the influence of secretin (80 U/hr/m) more bicarbonate was excreted and the excreted fraction of filtered sodium was significantly higher than in the control period. By contrast, less titratable acid and ammonia were excreted in the presence of secretin.

The data are interpreted to indicate that secretin inhibits sodium reabsorption and hydrogen ion excretion, and thereby increases bicarbonate loss in the human kidney.

1. Grossman, M. I.: Lancet, *i:* 1088 (1970).
2. Oetliker, O., and Rossi, E.: Pediat. Res., *3:* 140 (1969).

24. A compensated hemolytic process in rats due to a decreased lipid exchange between plasma and erythrocyte membranes. P. HÜRTER. *Univ. of Hamburg, Hamburg, Germany.*

Hypolipemia (decreased plasma cholesterol, phospholipids, and FFA, and altered patterns of FFA and fatty acids esterified with phospholipids) in rats was induced by applications of CPIB (ethyl-*p*-chlorphenoxyisobutyrate) (200 mg/kg body weight/24 hr). Due to decreased lipid content of plasma, the active and passive incorporation of cholesterol and phospholipids into the erythrocyte membrane were reduced. The continuous lipid loss of the membrane could not be compensated for. An increased hemolytic process and a compensatory increased erythropoiesis could be demonstrated: erythrocyte count decreased by 10% and ^{51}Cr life span decreased by 50%; there was an increase of MCV, MCD, MCSA, and MCH, and a decrease of MCHC. The membranes of young erythrocytes contained significantly more phospholipids and cholesterol. The patterns of the fatty acids esterified with the phospholipids were altered according to those in the plasma.

25. Glycogenosis *type I:* A membrane disease? R. GITZELMANN and M. A. SPYCHER. *Univ. of Zürich, Zürich, Switzerland.*

An ultrastructure study of parenchymal cells obtained from the liver and from a stemmed liver tumor of a patient suffering from glycogenosis *type I* revealed gross abnormalities of the endoplasmic reticulum, *i.e.,* of the cellular organelle with which the enzyme glucose 6-phosphatase is normally associated. An uncommon type of "vesiculation" of the rough ER was found [1]. The structural lesions may be causally related to a primary effect of the mutation on some membranes as was recently postulated for radiation-induced glucose 6-phosphatase deficiency in albino mice. If this were indeed the case, glycogenosis *type I* would seem to fit into the concept of "enzyme integration mutants" [2].

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26. Glycogen metabolism in normal and glycogen-rich red blood cells. S. W. MOSES and N. BASHAN. *Central Negev Hosp. and Negev Univ., Beer-Sheva, Israel.*

Evidence for active glycogen metabolism involving synthesis and breakdown, present in both normal and glycogen-rich erythrocytes, obtained from patients with glycogen storage disease *type III,* was provided by incorporation studies of glucose-U-^{14}C into erythrocyte glycogen. The kinetics of glycogen synthesis and breakdown was studied by varying incubation conditions. Incorporation rates showed a pH maximum at 7.6. Sodium was found to stimulate incorporation rates more than potassium. Phosphate requirement was established and sodium fluoride has an inhibitory effect on this reaction. Studies employing β-amylolysis showed that the main metabolic activity of erythrocyte glycogen affects its outer tiers, both in normal and glycogen-rich erythrocytes. The characteristics of erythrocyte glycogen synthetase were studied and are considered.

27. Clinical, biochemical and histologic observations in a case of so-called "I-cell disease." W. NÜTZENADEL, K. H. LICHTE, K. SCHÄRER, and A. K. ROSSNER. *Children's Hosp. of Univ. of Heidelberg, Heidelberg, Germany.*

In 1968 Leroy and De Mars described two children with numerous cytoplasmic inclusions in cultured fibroblasts, mental retardation, and Hurler-like clinical features. Spranger and Wiedemann reported in 1970 six additional cases. We observed a child with identical changes of the cultured fibroblasts and a similar clinical course. At the age of 2 months the legs were swollen and x-ray examination revealed periostal new bone formation and signs of atypical rickets at the end of lower metaphyses of the femur. Later, the skeletal disturbance became more severe, with generalized decalcification and deformities of many bones. The child suffers from severe mental retardation, myoclonic seizures, and a progressive limitation of joint mobility. Other striking clinical findings are a peculiar face, an extremely hypertrophic gingiva, a hoarse voice, and a pale, tight and firm skin. Laboratory data are normal except for the increase in excretion of phosphate in urine and alkaline phosphatase in the serum. In liver tissue, some lysosomal hydrolases are high and the content of mucopolysaccharides seems increased. The histologic studies of liver, kidney, and bone marrow show only slight alteration in the sense of a storage disease. The investigation of brain tissue by light and electron microscopy gives a picture similar to that of orthochromatic leukodystrophy. Biochemically, the content of lipids in the white matter and that of the glucolipids in the gray matter of the brain are somewhat low. Our studies concerning the estimation of enzymes and the chemical nature of the stored material in the fibroblasts are in progress.

28. The skeletal abnormalities in patients with homocystinuria due to cystathionine synthase deficiency. D. P. BRENTON. *Univ. Coll. Hosp. Med. Sch. and Galton Labs., Univ. Coll., London, England.*

The purpose of this communication is to describe the skeletal abnormalities of 22 patients and to correlate them with other clinical and biochemical features. Skeletal abnormalities were mild in 10, moderate in 5, and severe in 7. The long bone metaphyses and the vertebrae have a characteristic appearance in severe homocystinuria. These appearances are illustrated together with details of percentile heights and body proportions, and so forth. Mental retardation seems to be more common in patients with severe skeletal abnormalities. Two patients without lens dislocation and three with dislocations occurring after the age of 10 years had mild skeletal features. Patients with mild skeletal and other clinical features nearly always show a good biochemical response to pyridoxine, but the response of severely affected patients is less predictable.

29. Renal functions in hypophosphatasia. K. MÉHES and L. KLUJBER. *Univ. Med. Sch., Pécs, Hungary.*

In a previous study of hypophosphatasia, we reported impaired tubular reabsorption of phosphates in two homozygous patients (ESPR Meeting, Stockholm, 1970).

Since then, altogether 5 homozygotes and 16 heterozygotes have been observed, partly as a result of a screening program, in our clinical material. The diagnosis of the juvenile type of hypophosphatasia was confirmed by decreased alkaline phosphatase activity in the blood and urine, and by the excretion of phosphoethanolamine. In all these patients, renal functions proved to be normal, but the tubular reabsorption of phosphates was significantly impaired in the homozygotes, and slightly, but consistently, reduced in the heterozygotes. This feature was found to be unchanged under a variety of conditions including phosphorus loading and phosphorus-free diet. Calcium loading tests of two homozygotes showed normal response of the parathyroid gland. Examinations of amino acid and glycosaminoglycan excretion revealed normal patterns.

Although the exact pathomechanism is still unknown, the impaired tubular reabsorption of phosphates seems to be a characteristic feature of the disease, and might be useful even in the detection of heterozygotes.

30. Protein synthesis in human leukocytes. Dependency of amino-acid incorporation on intra- and extracellular concentrations of amino acids in cell suspensions and cell-free systems. K. WINKLER, G. HELLER-SCHÖCH, and R. NETH. *Universitäts-kinderklinik Hamburg Eppendorf, Germany.*

The incorporation rate of labeled amino acids into protein of human leukocytes is inhibited *in vitro* by the presence of other

amino acids in the culture medium. It is shown that this inhibition is not caused by reduced protein synthesis, but is the consequence of the known competitive inhibition of amino acid uptake by intact cells. In the presence of high concentrations of phenylalanine, no inhibition was demonstrable in cell-free systems of human tonsils, neither in aminoacyl-tRNA synthesis, nor in mRNA-dependant binding of aminoacyl-tRNA to ribosomes, nor in the peptidyl-transfer reaction. Correspondingly, the incorporation rate in the 30,000 × *g* supernatant of homogenate of human tonsils was unchanged by high concentrations of phenylalanine. In conclusion, it is assumed that direct inhibition of translational processes of protein synthesis does not play an essential role in the pathogenesis of phenylketonuria. However, a reduction of protein synthesis by other mechanisms, *e.g.*, substrate deficiency or reduced RNA synthesis, is not excluded and may take part in the pathogenesis of phenylketonuria as is suggested by the results of other authors.

31. The statistical distribution of amino acid concentrations in plasma. H. WICK, T. BRECHBÜHLER, C. BACHMANN, and R. BAUMGARTNER. *Univ. Children's Hosp., Basel, Switzerland.*

The Gaussian distribution of normal values of amino acids is usually taken for granted. A large sample ($n > 50$) for phenylalanine and tyrosine was collected. These amino acids follow a log-normal distribution more closely than a lin-normal distribution. Preliminary results with other amino acids showed that some may be symmetrically distributed while others are not. It would be of great practical importance if one could ascertain an asymmetric behavior, as it would prevent unnecessary and disturbing examinations in many normal children.

32. Importance of physical forces and the control of tubular sodium reabsorption. A. APERIA, O. BROBERGER, and S. SÖDERLUND. *Karolinska Inst. and S:t Göran's Children's Hosp., Stockholm, Sweden.*

The purpose of the present study was to establish the importance of physical forces: *i.e.*, peritubular, hydrostatic, and oncotic pressure for the control of tubular sodium reabsorption in experimental animals and in man. (*1*) The effect of variations in renal artery perfusion pressure on the tubular sodium reabsorption has been examined in the *in situ*-perfused dog kidney. Renal artery perfusion pressure increases suppressed tubular sodium reabsorption in the entire nephron but predominantly in the proximal tubule. This effect was, however, abolished by increases in peritubular capillary oncotic pressure which was accomplished by renal artery albumin infusion. The results clearly demonstrate the importance of physical forces in the control of tubular sodium reabsorption. (*2*) Deviations from normal conditions in peritubular physical forces is to be expected in patients with abnormal renal artery perfusion pressure and in patients with high hematocrits, since high hematocrits will increase the filtration fraction and thereby the peritubular capillary oncotic pressure. For this purpose, the control of sodium reabsorption was studied by determining the elimination of an acute sodium load in patients with (*A*) various levels of renal artery perfusion pressure, *i.e.*, before and after operation of coarctatio aorta, and (*B*) children with high hematocrits: infants and children with cyanotic heart diseases. Glomerular filtration rate, PAH clearance, and sodium reabsorption were determined in each study. A significant correlation could be found both between renal artery perfusion pressure, filtration fraction (changed as a function of hematocrit), and tubular sodium reabsorption. Clinical importance of physical forces for the control of sodium reabsorption is thereby established.

33. Control of sodium homeostasis in children with recurrent urinary tract infections and reduced glomerular filtration rates. A. APERIA, U. BERG, and O. BROBERGER. *Karolinska Inst. and S:t Göran's Children's Hosp., Stockholm, Sweden.*

Basal sodium excretion and rapid response to oral and intravenous sodium loads have been studied in children with recurrent urinary tract infections and a wide range of glomerular filtration rate. Basal sodium excretion related to body surface was remarkably stable in all children studied and was thus independent of glomerular filtration rate. The rapid response to an oral or an intravenous sodium load was reduced in patients with low filtration rates. The urinary sodium excretion rate following oral sodium load was correlated to the glomerular filtration rate with high statistical significance. In patients with high filtration rates, saline infusion resulted in a rather prompt inhibition of tubular sodium reabsorption with consequent increase in urinary sodium excretion. In patients with low filtration rates, inhibition of tubular sodium reabsorption following intravenous saline load was much less pronounced. During the transition from hydropenia to water diuresis without extra sodium supply, both the patients with low and with high filtration rates increased the absolute as well as the fractional sodium excretion concomitantly with an increase in the filtered load of sodium. The results are compatible with, but do not prove the existence of, an additional natriuretic factor that keeps the basal sodium excretion constant in the diseased kidney.

34. Sandhoff's disease: Total deficiency of hexosaminidase (A and B) as cause for accumulation of globoside G_{M2} and asialo G_{M2}. W. KRIVIT, H. SHARP, P. SNYDER, and R. DESNICK. *Univ. of Minnesota, Minneapolis, Minnesota, USA.*

Sandhoff in 1968 noted hexosaminidase activity to be totally deficient in a patient with clinical symptomatology of Tay-Sachs disease. The differences between these diseases is apparent from the following:

	Sandhoff	Tay-Sachs
Enzyme deficiency	A and B absent	A absent B increased
Substrate accumulated	Globoside G_{M2} and asialog$_{M2}$	G_{M2} and asialog$_{M2}$
Racial predilection	Non-Jews	Jews
Hepatosplenomegaly	Moderate	None

Individual case reports from several centers indicate that frequency of Sandhoff disease is much greater than had been considered. We have established the above enzyme deficiency and substrate accumulation in two siblings in a family of non-Jewish ancestry. Since the enzyme is present in normal plasma, an attempt at enzyme replacement by plasma infusion was made. The level of enzyme rose in proportion to amount infused. Hepatic tissue obtained by percutaneous biopsy was assayed for enzymatic activity before and after plasma infusion. The conclusions from these studies are that the new diagnostic techniques and therapeutic ventures have increased importance

in correctly diagnosing the underlying defect of degenerative central nervous system disorders.

35. Recherche d'une consommation intra-vasculaire par une étude *in vivo* de la cinétique du fibrinogène ^{125}I et des plaquettes ^{51}Cr. M. Dechavanne, F. Berthoux, J. P. Thouverez, J. J. Viala, and D. Germain. *Labor. Ctr. Hématol. Hôpital E. Herriot, Lyon, France.*

Le but de ce travail est de mettre en évidence une consommation intra-vasculaire subaigüe ou chronique, en étudiant simultanément la cinétique des plaquettes du malade, marquées au ^{51}Cr selon la technique d'Aster et Jandl, et celle d'un fibrinogène lyophilisé marqué auparavant au ^{125}I selon la technique de MacFarlane. Dans huit cirrhoses avec splénomégalie et thrombopénie, le taux quotidien du fibrinogène dégradé est normal, le pourcentage maximum de plaquettes circulantes très abaissé, et le $T_{1/2}$ plaquettaire modérément diminué. Ainsi la thrombopénie n'est pas la conséquence d'une consommation intra-splénique, mais elle traduit l'augmentation du pool plaquettaire splénique. Par contre, dans deux hépatites virales aiguës, le taux quotidien de dégradation du fibrinogène est très augmenté et le $T_{1/2}$ plaquettaire très diminué. Ces arguments plaident en faveur d'une consommation intra-vasculaire dans les hépatites.

36. Fibrin degradation products in the urine of children with renal disease. T. M. Barratt, C. Chantler, and H. Ekert. *Inst. of Child Hlth., London, England.*

Fibrin degradation products (FDP) were assayed by the tanned red cell hemagglutination inhibition technique in the sera and urine of children with renal disease, and were related to other parameters of proteinuria. Urinary FDP excretion was greater in individuals with poorly selective proteinuria; within the poorly selective group there was also a significant correlation between FDP excretion and albumin excretion. No correlations were observed with tubular proteinuria, hematuria, or serum FDP levels. Urinary FDP may arise from intravascular coagulation confined to the kidney or from fibrinogen filtration and fibrinolysis in the urinary tract; the data presented are compatible with either hypothesis.

37. Coagulation abnormalities in acute meningococcemia: Results of early heparinotherapy. J. Dubois, P. Fondu, and D. Blum. *Univ. Libre of Bruxelles, Brussels, Belgium.*

Coagulation abnormalities were related to the clinical state of 48 patients with meningococcemia (shock, preshock, or absence of any cardiocirculatory abnormalities).

Characteristic coagulation abnormalities, *i.e.*, prolongation of prothrombin time secondary to depression of *factors VII* and X, prolongation of partial thromboplastin time, and diminution of platelet count were already observed in most cases of preshock, but in a few cases were already present before any symptom of circulatory abnormalities. Severely decreased fibrinogen levels and platelet count are only observed in major cases (shock). Twenty-nine patients were subjected to early heparin therapy according to following criteria: shock, preshock, and or presence of multiple coagulation defects. No hemorrhagic complication was observed in treated patients. Only three deaths were recorded; two of them concerned children with severe shock when admitted.

These results, compared with data of the literature and with our former experience in the treatment of meningococcemia without the use of heparin, seem to demonstrate the usefulness of early anticoagulant therapy in children with meningococcemia.

38. Disseminated intravascular coagulation and respiratory distress syndrome in the newborn. U. Bleyl. *Univ. of Heidelberg, Heildelberg, Germany.*

Disseminated intravascular coagulation (DIC), an "intermediary mechanism of disease," is a common event in cases of intrauterine and perinatal asphyxia and consequent respiratory distress syndrome. More than 80% of autopsy cases with pulmonary hyaline membranes in the newborn showed fibrin-rich multilocular microthrombi, especially in the liver, the lungs, and the suprarenals. As a consequence of fetal and maternal birth complications, hypoxemia and acidosis can induce inadequate capillary perfusion and generalized plasmatic hypercoagulability. Circulating plasmatic fibrin monomers and intermediates polymerize intravascularily to disseminated microthrombi, and, after extravasation, polymerize extravascularily to pulmonary hyaline membranes. Hyaline membranes as well as DIC must be considered as morphologic equivalents of generalized disorders of microcirculation with inadequate capillary perfusion, and as morphologic symptoms of shock. Moreover, DIC in the respiratory distress syndrome indicates that pulmonary hypoperfusion must be considered as a symptom of shock, too. Pulmonary hypoperfusion as a typical event in the shock of the newborn and the adult does not only favor the extravasation of fibrin monomers and intermediates into the alveoli, but also induces a marked reduction of the synthesis of the surfactant. Pulmonary hyaline membranes and pulmonary atelectasis are both characteristics of shock-induced respiratory distress.

39. Coagulation studies in the premature infant using micromethods on capillary blood. Preliminary results. A. Hurlet, A. Minkowski, and F. Josso. *Ctr. de Recherches Néonatales du C. H. U. Cochin and C. H. U. Necker-Enfants Malades, Paris, France.*

Methods for clotting factors assays on capillary blood were developed. Accuracy of these assays is good, provided that blood collection is performed very early after the puncture, especially for *factor V* and *VIII* assays.

Factor I, II, VII + X and *VIII* assays combined with platelet count were performed in about 100 premature infants on the 1st, 2nd, 3rd, and 10th days of life. It was sought to define tentatively correlations between the results of these tests and prematurity, possible dysmaturity, and the number of days after birth.

A decrease of the level of blood-clotting factors, especially *factors I* and *V*, is often observed in "sick" premature infants, even in the absence of any hemorrhagic tendency.

Several cases of hemorrhagic syndromes related to prematurity have been analyzed. An attempt at prevention of the disseminated intravascular coagulation in the newborn is discussed.

40. Humoral factors in coagulation disturbances of newborn pathology. I. Virág and D. Boda. *Univ. of Szeged, Szeged, Hungary.*

According to many observations, humoral factors (hormones, vasoactive substances, biologically active metabolites) play an important role in neonatal adaptation disturbances. On the other hand, severe and multiple blood coagulation disturbances have

been demonstrated in the same pathologic conditions. The possibility exists that the activity of the blood-clotting factors are influenced by humoral factors, and the abnormalities in the blood coagulation are partly due to accumulated metabolites. Astrup's thromboplastin activation test, standard methods for determining prothrombin complex time and isolated prothrombin activity, and also von Kaulla's thrombin titration method were employed to see whether serum ultrafiltrate of hypoxic guinea pigs influences the coagulation process of normal test plasma. Profound alterations were found: thromboplastin activation was inhibited, the coagulation times in Quick systems and the thrombin times were prolonged. These effects were frequently normalized by prior treatment of the pathologic ultrafiltrate by hydrogen peroxide. Essentially the same was found with the ultrafiltrate of pathologic newborn sera. Our data suggest the existence of humoral effects in hypoxic animals. Such a mechanism in infants is presumably not specific, but an adaptation involved in acute pathologic processes. The investigation of humoral effects may represent a new direction in this field requiring further study.

41. Studies on hypercoagulability of cord and neonatal blood. G. Digilio, M. Orzalesi, G. Marzetti, A. Torroni, and D. Del Principe. *Univ. of Rome, Rome, Italy.*

The recalcification time (RT), screening tests on RT, and a modified thromboplastin generation test (TGT) were performed on cord blood and on blood of normal and hemorrhagic infants in the first days of life. In cord and in normal newborn plasma a significant shortening of RT was observed in the first 48 hr of life as compared with normal adult plasma. A progressive prolongation of RT was observed from the 2nd to the 14th day after birth. The RT of normal adult plasma was markedly shortened by the addition of 1:10 cord or newborn plasma. Such effect did not appear after treatment of cord blood with ethyl ether or chloroform, or after absorption on $BaSO_4$. The TGT performed with cord plasma, absorbed on $BaSO_4$ and diluted 1:10, showed a more rapid formation and greater activity of hematic thromboplastin as compared with normal adult plasma. These results suggest the presence of a procoagulant substance in cord and newborn blood; 62.5% of 24 hemorrhagic newborn infants showed the same above-mentioned hemocoagulative patterns. In the remaining hemorrhagic infants, in association with very severe deficits of many coagulative factors or presence of a circulating anticoagulant, a prolongation of RT or screening tests, or both, was observed.

42. Erythro-kinetics of the perinatal period. L.-E. Bratteby. *University Hosp., Uppsala, Sweden.*

The production and life span of the erythrocytes determine their rate of destruction and change in number per time unit. In the present study the change in amount of circulating erythrocytes before and after birth was estimated from measurements of red cell volume (RCV) using a ^{51}Cr-technique. Measurements of RCV were performed in newborn infants of a gestational age varying from 222 to 295 days. Repeated RCV estimations were performed in infants aged 0–138 days. The destruction of the erythrocytes present at birth was studied as the survival in adult recipients of cord red blood cells labeled *in vitro* with diisopropyl-^{32}-fluorophosphate. In the nonkinetic steady state, present during the perinatal period, calculation of the erythrocyte mean life span and distribution of life spans around the mean (life span frequency function) is complicated and possible only if the changes in red blood cell production and destruction are known. In the present study, calculation of red cell production and destruction during the last 2 months of fetal life, the mean life span, and the life span frequency function was made possible using the information of the change in circulating RCV during the last 2 months of fetal life and the cord red blood cell disappearance. The erythrocyte production at a gestational age of 220 days varied between 1.5 and 2.8 ml, and at 280 days between 3.5 and 6.8 ml or 3.6–4.2% and 2.5–3.5%, respectively. The mean destruction was at the same period 0–0.5 ml and 1–4 ml, respectively. The mean life span of the erythrocytes present at birth varied between 45 and 70 days. The frequency function was skew, with the majority of cells dying before the mean life span. The results are considered in relation to data obtained from the literature.

43. Normal and abnormal synthesis of hemoglobin A and F in the newborn. J. H. P. Jonxis. *State Univ. Hosp., Groningen, The Netherlands.*

Reticulocytes and bone marrow of newly born infants are still able to synthesize hemoglobin A and F during *in vitro* experiments. The rate of synthesis of hemoglobin A and F can therefore be determined in reticulocytes by incubation *in vitro* with ^{14}C-leucine. During these *in vitro* incubation experiments, the rates of synthesis of hemoglobin A and F can be determined over a certain period. In normal newborns the hemoglobin A synthesis is greater than that of hemoglobin F. In babies of a gestational age of less than 35 weeks, 80% of the synthesized hemoglobin is hemoglobin F. In most babies with increased hematopoiesis, the switchover from hemoglobin A to hemoglobin F is rapid. When, however, the erythropoietic stress is excessive, the hemoglobin F synthesis increases again.

When the synthesis of hemoglobin F decreases, an unequal labeling of the α-F and γ chains is found, indicating the presence of a pool of γ chains. The synthesis of both hemoglobins can be reactivated by adding fresh plasma or already used dialysed plasma to the medium. The presence of a low molecular weight inhibitor of hemoglobin synthesis in the plasma is postulated.

44. Acid lysis of thalassemic erythrocytes. F. Schettini, A. Mautone, and L. Cavallo. *Univ. of Bari, Bari, Italy.*

Acid lysis of red cells is probably a very indicative index of chemical changes in the membrane and of Cl^- and water content of the cell.

Acid lysis of erythrocytes from thalassemic major and trait, from iron-deficiency anemia, from newborns, and from normal children, was studied by an automated procedure (Fragiligraph model D-2). Acid lysis was obtained by submitting the red cell suspension (pH 7.4) to a progressively increasing H ion concentration by dialysis against an isotonic solution of pH 2.45.

Red cells of thalassemia major, of newborns, and of iron-deficiency anemia were more resistant ($P = 0.01$) to the acid lysis and the behavior of thalassemic major cells was intermediate between iron deficiency and newborn cells. In the cells of thalassemic trait only the time from the start to the initial lysis augmented.

The rate of acid lysis became progressively smaller through the series: normal = thalassemia trait > iron-deficiency anemia > newborns = thalassemia major ($P = 0.01$).

The reduction of the acid fragility is probably the result of the

particular properties of the red cell membrane of newborns, of thalassemic major, and of iron-deficiency anemia.

45. Heinz body formation in red cells of newborn infants. E. KLEIHAUER and E. KOHNE. *Univ. of Ulm, Ulm, West Germany.*

During the administration of oxidizing agents, red cells of newborn infants are known to be highly susceptible to formation of Heinz bodies. This phenomenon cannot be explained either by the type of hemoglobin or by the enzyme pattern typical for fetal erythrocytes.

Studies on Heinz body formation by β-acetylphenylhydrazine in an *in vitro* system yield the following results. (*1*) Heinz body formation is not different in red cells before (fetal cells) and after (adult cells) exchange transfusion. (2) Heinz body formation is enhanced in adult red cells after suspending in human newborn plasma. (*3*) The susceptibility to form Heinz bodies is not restricted to a short postnatal period.

Heinz body formation is altered by environmental factors, most probably by changing the properties of the red cell membrane.

46. Excretion of erythropoietin and erythropoiesis inhibitors in normal infants and in infants with neonatal polyglobulia. R. LINDEMANN and S. HALVORSEN. *Rikshospitalet, Oslo, Norway.*

A dual regulation of erythropoiesis through stimulators (ESF) and inhibitors (EIF) has recently been suggested. ESF and EIF have been separated in urine from different haematologic disorders [1]. It is suggested that the EIF is a chalone [2]. In this study the excretion of ESF and EIF from normal newborn babies and from infants with neonatal polyglobulia has been investigated.

Urine from normal newborn babies, from infants born to diabetic mothers, and from infants with high packed cell volume was collected the first days of life. The urine was divided into volumes corresponding to 6-hr excretion. The 6-hr volume was passed through a Sephadex G-100 column, and the EIF fraction was collected and tested. ^{59}Fe incorporation in RBC of exhypoxic, polycythemic and ESF-stimulated mice has been used as assay method [1]. Urine from normal newborn babies showed no ESF activity. A marked inhibitory effect on erythropoiesis was, however, observed the first days after birth. Urine from infants born to diabetic mothers, however, showed no inhibitory effect. The possibility of a causal relationship between the increased erythropoiesis and the lack of inhibitors in the latter infants are considered.

1. Lindemann, R.: Lancet, *i:* 781 (1970).
2. Skjælaaen, P., and Halvorsen, S.: Acta Pædiat. Scand., (1971).

47. Leukocyte blood picture in newborn babies during and after exchange transfusion. M. XANTHOU, K. TSOMIDES, D. NICOLOPOULOS, and N. MATSANIOTIS. *Univ. of Athens, Athens, Greece.*

Serial leukocyte counts were done on 12 full term and 8 premature jaundiced babies during exchange transfusions and daily thereafter up to the 9th day, in order to study changes in each cell type. The main changes were found to be: (*1*) a marked reduction in all cell types during the procedure, with a statistically significant difference in absolute values before and after; (2) significantly lower values of the polymorphonuclear neutrophils and eosinophils in the baby's blood at the end of the transfusion compared with those of the donor's blood, the monocytes and lymphocytes showing no statistically significant change; (*3*) a remarkable rise in each cell type, reaching 6 times the value found at the end of the procedure, within the week following the transfusion, a rise which was highly significant ($P < 0.001$), the highest absolute values of polymorphonuclear neutrophils being well above the upper normal limits (7.000/mm^3) for the age studied; (*4*) a similar response in full term and premature babies and following one or multiple transfusions. In conclusion: it was found that the numbers of circulating leukocytes decrease during the exchange transfusion, to rise again soon after the procedure to the preexchange levels and to increase further within the following week, reaching very high values.

48. Neonatal diabetes becoming permanent. S. OSEID, O. SØVIK and Ø. AAGENÆS. *University Hosp., Rikshospitalet, Oslo, Norway.*

Two siblings, a boy now 4 years old and a girl now 15 months old, have been studied. The boy showed a steady increase in blood sugar levels from 48 mg/100 ml 6 hr after birth to 590 mg/100 ml 6 days later. Insulin treatment was started on the 6th day, and was continued for nearly 3 months.

He was dysmature with a birthweight of 1840 g. Immunoreactive insulin (IRI) levels were at a low normal level before treatment. Fasting blood sugar levels have remained normal after treatment was discontinued, there is no glycosuria, and blood sugar values following a glucose stimulus are in the normal range. However, both on oral and intravenous testing, there is a very sluggish and diminished IRI response. The sister was also dysmature, birthweight 1440 g. She showed a similar increase in blood sugar levels without ketonuria, and insulin treatment was started after 12 days. Her fasting blood sugar levels have gradually subsided and were in the range of 120–160 mg/100 ml when insulin treatment was stopped in November 1970. Her glucose tolerance is still grossly abnormal, but she is now well controlled on tolbutamide. Fasting IRI levels have always been in the low normal range. The results of repeated oral and intravenous glucose loadings after stop of treatment are in accordance with findings in prediabetic individuals.

49. Metabolic effects of feeding in the newborn pig. J. GENTZ, B. PERSSON, and M. KELLUM. *Karolinska Inst. and S:t Göran's Children's Hosp., Stockholm, Sweden.*

Newborns of different species increase their oxygen consumption ($\dot{V}O_2$) during the first days of life. In newborn piglets the influence of feeding and of starvation on $\dot{V}O_2$, expired carbon dioxide, rectal temperature (RT), and on different parameters indirectly reflecting the utilization of substrates such as respiratory quotient (RQ) and levels of blood glucose, free fatty acids (FFA), glycerol, and ketone bodies were studied. Feeding led to a significant rise in "minimal $\dot{V}O_2$" and RT during the first days of life; their major increase occurred during the first 24 hr. Starvation led to insignificant variations in "minimal $\dot{V}O_2$" and RT in newborn animals, while in older (1–9 days) previously fed piglets $\dot{V}O_2$ and RT decreased progressively with starvation, finally reaching values similar to those of the newborns. During starvation in all groups, the changes in FFA glycerol and ketone

bodies suggested limited lipid mobilization and utilization; the changes in glucose and RQ values indicated increased protein catabolism and ability of gluconeogenesis. The rises in $\dot{V}O_2$ and RT following a fixed milk load were greater in newborn than in older previously fed animals, and the increases were related to the pretest $\dot{V}O_2$ also when this had been lowered by starvation in previously fed animals of different ages. A tentative explanation for how feeding effects the rise in "minimal $\dot{V}O_2$" during the first days of life is given.

50. Changes in total body water of premature infants in the first 4 days of life. A. I. MURDOCK. *Hammersmith Hosp., London, England.*

The presently practiced feeding schedule in the premature nursery provide 60, 90, 120 and 150 ml/kg birth weight/24 hr intake of milk (62 Kcal/100 ml) from the 1st to the 4th day in order. Changes in body composition were studied using an antipyrine dilution technique for measuring total body water (TBW) on *day 1* and *day 4*. Ten infants of mean birth weight 1905 g (range 1140–2640) received a mean intake of 105 ml/kg/24 hr (range 94–120 ml/kg/24 hr). TBW increased in six infants and decreased in one. The mean change in TBW was +5 ml/kg birth weight ($P > 0.002$) over the 4-day period. The main change in dry weight was −52 g/kg birth weight ($P > 0.001$) (Dry weight = body weight − TBW). Fluid balance studies and measurements of respiratory metabolism with urea nitrogen determinations allowed calculation of change in body water and change in dry weight resulting from the sum of dietary input and tissue breakdown for heat production in five babies. The results obtained were comparable to those from antipyrine studies. The data show that the feeding regime provides sufficient water but inadequate calories for solid tissue growth.

51. Experimental investigation about peculiarities of pathophysiology of shock in early age. G. HOLLMANN, H. D. SCHMIDT, A. E. URBAN, J. SOLC, D. KNORR, A. SUWATANAWIROY, VARELA-CIVES, and R. SCHADWINKEL. *Kinderklinik, Univ. München Kinderspital, Munich, Germany.*

Puppies in experimental hemorrhagic shock show reactions which can be observed also in shock of newborn and early infancy. In 23 puppies aged 14–21 days and in 20 adult dogs, standardized hemorrhagic shock is performed by the method of Wiggers modified by Schmier *et al.* In a constant environmental temperature of 31°, the heart rate, respiratory rate, and rectal temperature decrease in puppies and increase in adult dogs. The stroke volume in puppies is significantly higher than in adult dogs. The concentrations of H^+, K^+, Ca^{++}, Mg^{++}, adrenaline, and noradrenaline increase more quickly and reach a higher level than in adult dogs. Shock tolerance in puppies is significantly lower than in adult dogs.

These different reactions in shock find possible explanations either by regulatory mechanisms which are effective only in this period of age or by a sudden breakdown of the vital regulatory mechanisms. Aldosterone seems to be much more important for homeostasis in shock of early age than in adults. Plasma level of aldosterone in puppies is 3 to 2 times higher than in adult dogs.

52. Endotoxine-induced circulatory changes in the rabbit. F. WYLER and K. WEISSER. *University Children's Hosp., Basel, Switzerland.*

The circulatory responses of unanesthetized rabbits were studied 60 and 150 min after administration of endotoxine. Arterial pressure, blood gases, blood pH, and cardiac output (indicator-dilution method) were repeatedly measured. Distribution of cardiac output, organ blood flow, and local vascular resistance were calculated after repeated injections of nuclide-labeled microspheres (50 μ diam.) into the left ventricle.

In spite of a considerable fall in total cardiac output, arterial pressure was well maintained, owing to generalized vasoconstriction. Vascular resistance increased most markedly in the spleen, kidneys, and skin. The effects of endotoxine in the rabbit were compared with those in the monkey, where maintenance of cardiac output and generalized vasodilatation contrasts with the findings in the rabbit. A similar lack of vasoconstriction was observed when the endotoxine was given to rabbits under halothane anesthesia.

53. Acid-base balance during prolonged normoxic hypercapnia in the newborn. K. P. RIEGEL, D. CHRISTEL, and J. SCHÖBER. *Universitäts-Kinderklinik, Munich, Germany.*

In a 2-year period, seven newborns, birth weight 1020–4400 g, developed hypercapnia (P_{CO_2} 40–110 Torr) despite artificial ventilation, while other parameters (*e.g.*, P_{O_2}a, glucose, and electrolyte metabolism) could be kept in normal ranges. In five infants hypercapnia was present for weeks. Although mechanical ventilation did not prevent fluctuations of P_{CO_2}, there were stable periods of hypercapnia for days in any case. Such periods were selected to define limits of maximal compensation. A first stage of (partial) compensation is reached after 48–72 hr, complete compensation within 5–7 days, depending on the degree of hypercapnia. The ability to defend H ion homeostasis increases with age and duration of hypercapnia. According to the Henderson equation, the bicarbonate concentration necessary for full compensation can be expressed as $[HCO_3^-] = 24.47\ R$ ($R = P_{CO_2}/H$ ratio). This can be used to calculate $\Delta[HCO_3^-]$ for diagnosis and therapy.

	$R = b \cdot P_{CO_2}$ (Torr) $- a$		
	1 week	*2 week*	*< 2 weeks of life*
N	71	35	195
Slope *b*	0.00642	0.01281	0.01027
Intercept *a*	0.8355	0.5117	0.7860
r	0.59	0.82	0.87

54. Effect on plasma osmolality of rapid intravenous alkali in newborn infants with respiratory distress. A. MARINI, F. CATTANEO, and V. BARBARANI. *"L. Mangiagalli," Univ. of Milan, Milan, Italy.*

Newborns with respiratory distress (NRD) are often treated with rapid intravenous alkali (RA). This therapy may induce a significant increase of plasma osmolality (PO).

We studied PO after RA with THAM (0.3 M) or sodium bicarbonate (NaB) in NRD. Basal values of PO match with those known for the newborn. Both THAM and NaB induce a marked increase of PO after 3 min; after 20 min in NaB cases, PO returns to normal, while a further increase is seen in THAM cases. The slow administration of alkali does not influence PO. Changes in PO are not only related to the amount and the kind of alkali, but also to the age (gestational, hours of life) and to the predicted extracellular fluid.

Alkali	Osmolality, mOsm/liter		
	Initial	3 min	20 min
THAM	284 (267–292)[1]	303 (270–318)	307 (283–332)
NaB	293 (285–302)	325 (310–342)	295 (278–311)

[1] Values expressed as mean. Numbers in parentheses indicate range.

55. Biochemical studies during partial perfusion of newborn infants. B. J. N. Z. DANESH and C. H. M. WALKER. *Univ. of Dundee, Dundee Royal Infirmary, Dundee, Scotland.*

It has been suggested that an extracorporeal-assisted circulation with artificial oxygenators might be used to maintain life in newborn infants with severe cardiopulmonary distress. Such a procedure can in itself lead to further biochemical disturbances such as water and electrolyte retention, rise in plasma potassium, and development of lactic acidosis. To control these and to correct the initial respiratory and metabolic imbalances, an artificial kidney has been used in conjunction with an oxygenator in the extracorporeal circuit. The partial perfusion of six newborn infants has indicated that the metabolic disturbances can be controlled efficiently by this system. The gas-exchange capacity of the artificial "kidney-lung" is also more than sufficient, but, owing to the limited blood flow obtainable from one umbilical or femoral catheter, ventilation by this means alone could not be adequately maintained. An alternative to large vessel cannulation (*e.g.*, carotid) is the coincident use of artificial ventilation during perfusion.

56. Acid-base status of CSF in recurrent neonatal apnea. E. D. BURNARD. *Women's Hosp., Sydney, Australia.*

Acid-base relations between blood and CSF were measured in nine babies (six small prematures, three approaching term) early in the course of recurrent apnea and in the absence of pulmonary or other disease; ages were 1–6 days. A mild decompensated acidosis was found in the blood, but the babies were in a steady state at the time of the CFS examination as judged by trivial difference between the blood then and the specimen 6 hr before. The CSF was alkalotic relative to the blood. In eight controls the normal relation was found.

	pH		P_{CO_2} mm Hg		HCO_3 mEq/liter	
	Apnea	Control	Apnea	Control	Apnea	Control
CSF	7.33	7.38	49	37	24	20
Blood	7.31	7.44	45	36	20	24
Difference	0.02	−0.06	4	1	4	−4
	($P < 0.05$)		(NS)		($P < 0.01$)	

The differences between blood and CSF, by comparison with the controls, was significant for pH and highly so for bicarbonate. Chloride was 10–15 mEq/liter higher in CSF than blood in both groups. All babies lived.

An explanation of the findings is not obvious. However, recurrent apnea is a poorly understood syndrome. CSF alkalosis, arising from some temporary anomaly in transport at the blood-brain barrier, might be a factor in depressing respiratory drive.

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

Intracranial hemorrhage is a frequent finding at autopsy in very immature infants. Because of the possibility of therapy in infants in whom DIC seems to be present, it was thought important to be able to time the intracranial bleed to see whether 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 chromium-50. ^{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 had occurred after tagging. If the clot contained <30% tagged cells as compared with the sample of blood taken at tagging or just prior to death, it was assumed that bleeding had occurred prior to tagging. Twenty-eight such tagged infants have died and had intracranial clots analyzed for ^{50}Cr. Sixteen infants had HMD, seven extreme immaturity; the remainder died of other disorders. Eighteen weighed <1250 g, 23 were <32-week gestation. Median age of tagging was 6.3 hr, while median age at death was 33.2 hr. ^{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 afterward. 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. Twelve infants had clear-cut DIC, 11 possible, and 5 had no evidence of DIC. All but one 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 was clearly established.

58. Evoked EEG responses in newborns with asphyxia and IRDS. A. HRBEK, P. KARLBERG, I. KJELLMER, and T. OLSSON. *Univ. of Göteborg and Chalmers Univ. of Technol., Göteborg, Sweden.*

A group of mature and premature newborn infants with asphyxia or IRDS were examined. Photostimulation and electrical pulses applied to the nervus medianus were used. Visual (VER) and somato sensory (SsER)-evoked responses were recorded simultaneously on an EEG apparatus and on a tape recorder. Responses were averaged with a PDP 12-digital computer. The first results are presented.

In both pathologic states the evoked responses differed conspicuously in form and amplitude from responses in normal subjects. Above all, the initial fast components were affected. The recovery of the responses was very fast in IRDS and slower in asphyctic newborns and was dependent on the severity of asphyxia. In IRDS, a relationship to the oxygen supply was observed. In both disorders studied, VER were much more affected than SsER. The later ones also recovered earlier. The reported preliminary results are encouraging for the clinical application of the evoked responses in neonates.

59. Prolonged intravenous fat administration in low birth weight infants and the effect of heparin. A. GUSTAFSON, I. KJELLMER,

R. Olegård, and L. Victorin. *Univ. of Göteborg, Göteborg, Sweden.*

In a previous report (European Soc. Ped. Research, Stockholm, 1970) newborn low birth weight infants were given a single intravenous load of 0.1 g/kg body weight of fat emulsion (Intralipid, Vitrum). From the elimination curves a disappearance rate corresponding to a fat tolerance of some 6 g/kg body weight/24 hr was calculated. At higher single fat dose (0.5 g/kg body weight) a difference was observed betweeen light for date infants and preterm infants with birth weights appropriate for gestational age. In the light for dates, an early appearing and longlasting increase of the pre-β-lipoprotein fraction was observed. Concomitantly, the removal rate of exogenous fat decreased. In the present study repeated injections of Intralipid were given hourly during 8 hr, 0.15 g fat/kg body weight/hr, corresponding to half the calculated maximal removal capacity. The preterm infants (birth weight appropriate for gestational age) rapidly cleared their plasma after each injection. In the light for date infants, the plasma concentration of total lipids rose continuously. Forty minutes after the last injection the concentration of plasma total lipids had risen twice as much in the light for date group as in the appropriate for date group. The injection of heparin accelerated the fat removal in the light for dates. This would indicate an inefficient activity of the lipoprotein lipase in the untreated light for date infant.

60. Exercise studies in children with aortic stenosis. M. R. H. Taylor. *Inst. of Dis. of the Chest, London Univ., London, England.*

Studies were performed in children with aortic stenosis to determine their exercise tolerance and cardiopulmonary response to exercise. These tests were performed using a bicycle ergometer. The indirect (CO_2) Fick method was used to determine cardiac output. It was found that some children could reach a normal maximum work load despite severe aortic stenosis. It was also found that in severe aortic stenosis cardiac output was lower than normal at high levels of work. It is concluded that exercise testing provides a method of following the progress of children with aortic stenosis and gives useful information for clinical management.

61. Adriamycin in the treatment of neoplastic diseases of childhood. Effect on lymphoblastic transformation and chromosomes. L. Massimo, F. Dagna-Bircarelli, P. G. Mori, and F. Cottafava. *Univ. of Genoa, Genoa, Italy.*

Adriamycin is a new antitumor antibiotic, isolated by Di Marco *et al.* in 1967 from *Streptomyces peucetius caesius*. It is similar to daunorubicin: it interferes with nucleic acid metabolism and inhibits their synthesis. The American Association report a group of 16 children suffering from solid tumors, in an advanced stage, treated with adriamycin (6 neuroblastoma, 3 reticulosarcoma, 2 rhabdomyosarcoma, 2 Ewing sarcoma, 2 malignant teratoma, and 1 adenocarcinoma). The highest effectiveness was seen in neuroblastoma, in rhabdomyosarcoma, and in malignant teratoma, where improvement of general condition, decrease in tumor size, and disappearance of pain occurred. Toxic effects consisted of mouth ulcers (4/16), alopecia (6/16), leukopenia (7/16), and vomiting (2/16) and they appeared to be correlated with the single and total dose of the drug. The treatment schedule suggested is a daily dose of 0.5 mg/kg in 3-day courses for two or three times. Research performed only in the seven children never treated before for the neoplasia showed that lymphoblastic transformation with phytohemagglutinin is not modified, while a moderate increase of chromosome fragmentation and a high number of aneuploid cells occur after the treatment with adriamycin.

62. Congenital osteosclerosis in athyreosis. H. Andersen. *Childrens Hosp., Fuglebakken, Copenhagen, Denmark.*

A few cases of osteosclerosis in severely hypothyroid children have been reported. Various etiologic factors: renal failure, hypervitaminosis D, disturbances in parathyroid and calcitonin secretion, and so forth, have been considered. The condition seems not to have been observed at birth. Therefore, and to point out also that prenatal changes, presumably in the cartilage, may play a role in this disorder, an athyreotic child with normal serum calcium, phosphorus, and alkaline phosphatase and in whom dense bones were demonstrated immediately after birth is considered.

63. Two possibly unrecognized clinical syndromes. R. A. Pfeiffer. *Inst. of Human Genetics, Münster, West Germany.*

I wish to demonstrate two separate syndromes: (*1*) A variant of pseudopseudohypoparathyroidism in two unrelated children. Both children exhibit short stature, mild mental retardation, and visual impairment due to an infantile glaucoma. There is brachymetacarpy III–V, with cone-shaped epiphyses. The boy in 1956 exhibited also an idiopathic scoliosis, the girl in 1961 suffered from valvular aortic stenosis. (*2*) Multiple anomalies in two unrelated boys. Both children exhibit macrocephaly, a flat short (puglike) nose with anteverted nostrils, slight protrusio bulborum, small abnormally shaped ears, hypertrophy of the gingiva, bifurcation of the terminal phalange of the thumb, irregularly shaped phalanges, hypoplasia of the scrotum, and a normal-sized penis partially hidden in the suprapubic fat. The elder patient (1962) was mentally normal. He also showed nonprogressive osteopetrosis. Anomalies of the lumbar vertebrae have recently appeared.

64. Studies on mulibrey-nanism. J. Perheentupa and S. Leisti. *Children's Hosp., Univ. of Helsinki, Helsinki, Finland.*

In 1970 we reported on a previously unknown syndrome of proportionate prenatal-onset dwarfism with these characteristics: triangular face with bulging forehead, low nasal bridge, mildly hydrocephalic appearance, long-shaped sella turcica, thin hypotonic extremities, funny high-pitched voice, hepatomegaly, abnormal dispersion of retinal pigment with yellow dots, and slightly or moderately dilated brain ventricles (Perheentupa *et al.* Acta Paediat. Scand. suppl., *206:* 74). The name was coined from the words muscle, liver, brain and eye. Mulibrey is distinct from Russel-Silver dwarfism.

We have now studied 11 affected children. The geographical distribution of the ancestors suggests genetic etiology, but familial occurrence has not been observed. All except one of the patients were below or at the 10th height and weight percentile for gestational age at birth. The present height was 2.5–6.4 (mean 4.5) SD and the weight 3.4–5.9 (mean 4.2) SD below the mean for age. Liver edge was 2–8 cm below the costal arch at midclavicular line. Several of the patients had liver biopsy with normal histology. Of the six boys, five had varying degree of fibrous

bone dysplasia of tibia. Several of the children had large naevi flammei.

The only metabolic abnormality thus far revealed has been fasting hypoglycemia with acetonuria. This is associated with small glycemic response to glucagon test, undiminished urea excretion, and normal gluconeogenesis from alanine. As we have demonstrated similar patterns of fasting hypoglycemia in other types of primordial dwarfs, we are suggesting that this derangement is an unspecific permanent sequela of intrauterine stunting.

65. Renal-retinal dysplasia, encephalopathy and glycolipid storage. P. DURAND, O. BUGGIANI, G. PALLADINI, B. BERRA, and C. BORRONE. *G. Gaslini Inst., Genoa-Quarto; Inst. of Neurol. and Mental Dis., Univ. of Genoa, Genoa; Inst. of Comp. Anat., Univ. of Rome, Rome; and Inst. of Biol. Chem., Univ. of Milan, Milan, Italy.*

An 8-year-old girl with renal dysplasia, similar to juvenile nephronophtisis, tapeto-retinal degeneration, gradually increasing mental deterioration, waking incoordination, obesity, and ictiosis is reported.

Histochemical analyses of the liver, spleen, intestine, lungs, myocardium, kidneys, and brain showed a not identified glycolipid storage. The lipid-bound NANA content of the brain was normal, but ganglioside pattern was different from the normal value: GD2 was considerably greater, and GD1b and GT1 were significantly increased with diminution of GD1a and GM1. The activity of some lysosomal acid hydrolases was increased. The double cousin of the propositus had a tapeto-retinal degeneration and mental retardation.

A possible defect in the synthesis, also, of tubular cell lipoprotein membrane in hereditary renal-retinal dysplasia is emphasized.

66. Small intestine disaccharidic inundation. J. C. MAMELLE. *Hôpital Sainte-Eugenie, Lyon, France.*

We observed eight infants with the nonincidental association: hiatal hernia, dwarfism, mental defect, complex melituria, and osteoporosis possibly complicated with nephrolithiasis (J. C. Mamelle, Pédiatrie, *26:* 129, 1971). This association is the result of the small intestine disaccharidic inundation by pyloric incontinence or hypervagotony. Then follows an early exaggerated postprandial hyperglycemia which induces hyperinsulinism with poststimulating hypoglycemia. The melituria of exogenous origin (mono- or disaccharides, or both) is a simple magnification of a physiologic state. The deficiency of calories and proteins secondary to hyperinsulinism is possibly responsible for dwarfism, diffuse osteoporosis, and mental defect. The treatment, at the same time curative and preventive if established early enough, avoids sequels; it consists in slowing down the gastric emptying rate with a thickener. With extent, this syndrome is to be searched after in every infant with or without an esophago-gastric malformation and suffering from growth failure with delayed bone age, especially if he has endured a pyloroplasty or pylorotomy, or both (three esophageal atresiae and one hypertrophic pyloric stenosis). Thus every pyloroplasty must be pondered upon. At last the small intestine disaccharidic inundation syndrome is an etiology of functional hypoglycemia with hyperinsulinism.

67. The influence of stress on growth hormone concentrations in full term newborn infants. P. STUBBE and H. WOLF. *Univ. of Göttingen, Göttingen, Germany.*

This study was performed to evaluate the influence of stress on growth hormone (GH), glycerol, and glucose levels in the blood of full term newborn infants at 1, 4, and 7 days of age. Two teams of infants were investigated consisting of three groups with 10 infants each. The first team had intravenous glucose loadings and consequently a series of heel-pricks. The second team had heel-pricks only without glucose infusion. The results of the second team were thought to be the consequence of skin-pricking representing a stressful procedure, of which vigorous crying was one sign. Skin pricks alone were followed by continuously increasing blood glucose concentrations, whereas the GH response varied within the 1-, 4-, and 7-day-old infants, increasing first and then decreasing. After glucose injection, the GH concentration showed a different slope, decreasing initially, and seemed to be contrary to the stress team. The variations of growth hormone concentrations during an intravenous glucose loading procedure were corrected for the influencing stress effect and were found to be more pronounced when stress was taken into account. The influence of a stressful procedure was more evident in 2- than in 4-day-old infants and almost was to be neglected at 7 days of age. The different GH responses within such a short period of 1–7 days may be evidence of adaptive changes in the early postnatal period of life.

68. Plasma growth hormone in neonates. G. B. FORBES, A. POJEROVA, R. LAWRENCE, and D. SCHALCH. *Univ. of Rochester, Rocester, N. Y., USA.*

Plasma growth hormone (GH) levels are high in neonates, but there is great variability which is largely unexplained. In 39 fasting full term infants aged 6–8 hr, we found a range of 3–82 ng/ml (average 18) and at 23–31 hr, 9–86 ng (average 31). A number of possible factors were studied in an attempt to explain the variability, and certain trends were found. Boys tended to have lower levels than did girls, circumcision done shortly after birth raised the GH level ($P < 0.05$), and an Apgar score of less than 8 or subnormal body temperature, or both, tended to lower it. Feeding of cow's milk raised the level within 30 min, whereas feeding of plain water lowered it ($P < 0.05$). Type of delivery and maternal premedication had no effect, nor did the fasting level of blood glucose. A subsample of 11 infants was carefully observed for 0.5 hr before sampling: status before sampling had no effect, but vigorous crying during the sampling procedure resulted in higher levels.

69. Plasma glucose, insulin, cortisol, and growth hormone responses to glucagon stimulation in newborns. P. C. SIZONENKO, G. ZAHND, L. PAUNIER, G. LACOURT, and I. J. KOHLBERG. *Clin. Universitaire de Pédiatrie, Geneva, Switzerland.*

In order to investigate hormonal control of plasma glucose in neonates, intravenous glucagon stimulation tests were performed at dosage of 300, 30, 3 μg/kg in normal newborns aged 1–3 days, after a 3-hr fast. Response of plasma glucose (G), insulin (IRI), cortisol (F) and growth hormone (GH) were compared with that of control children aged 5–10 years, tested at 30 and 3 μg/kg. Fasting mean G levels, lower in neonates, were followed by a similar rise in all groups (29–39%). IRI levels increased to 108–153 μU/ml at 3 min after injection of glucagon, as compared with a mean fasting value of 10 μU/ml. No statistical differences between the five groups were observed. A prolonged response

occurred with higher dosage. Fasting F levels were higher in newborns (20–36 μg/100 ml), and a similar rise for F was observed in all groups (10–47%). No significant rise of serum GH was observed in control children (1–5.5 ng/ml). In newborns, GH rose considerably after glucagon (from 19.5–64 to 71.6–152 ng/ml). Presently, there is no evidence of dose-response effect of glucagon in any of the groups, with regard to the four parameters investigated. No striking differences were noted between neonates born by vaginal delivery and those born by cesarean section. The remarkable response of GH to glucagon in newborns disappears in the first weeks of life. The capacity of the pituitary to secrete GH should be further evaluated in neonatal hypoglycemia.

70. Relation of lipid to carbohydrate metabolism in infants of diabetic mothers. M. KELLUM, J. GENTZ, and B. PERSSON. *Karolinska Inst. and S:t Görans Children's Hosp., Stockholm, Sweden.*

Hypoglucosemia and low free fatty acids (FFA) have been described in infants of diabetic mothers, but because these data are limited, a study was done in 38 infants of insulin-dependent diabetic mothers (IDM's) and 15 infants of gestational diabetic mothers (IGDM's) with cold exposure minimized and where maternal pregnancy care was intensive, similar, and well defined. Results are compared with those of 22 normal infants (NL's) (Persson and Tunell, Acta Pediat. Scand., in press). Plasma glucose (GLK), FFA, glycerol (GLYC) and β-hydroxybutyrate (BHB) were determined five times during the first 2 hr of life. Seventy, thirty, and twenty percent of IDM's, IGDM's and NL's, respectively, had asymptomatic hypoglucosemia. Hypoglucosemic infants were not distinguishable by FFA values and GLK was not correlated to FFA or GLYC except (for FFA) in IGDM's at 2 hr. After 30 min, BHB was similar and low in all groups. The majority of IDM's but only few IGDM's had low FFA relative to GLYC when compared with normals, suggesting decreased lipid mobilization despite comparable lipolysis. Insulin-dependent diabetic mothers with and without decreased lipid mobilization were compared: in the former group, k_G was higher, GLK was suggestively lower, and maternal prepregnancy insulin doses were higher. Since other measures of maternal diabetic control were comparable, the results suggest that the determinants of abnormal lipid and carbohydrate metabolism in IDM's may be more complex than "maternal hyperglycemia-fetal hyperinsulinism."

71. Factors influencing the accumulation of bilirubin in amniotic fluid in Rh hemolytic disease. K. POLÁČEK and A. ZWINGER. *Inst. for the Care of Mother and Child, Prague-Podoli, Czechoslovakia.*

The significant negative correlation ($r = -0.63$) between hemoglobin and bilirubin concentration in the cord blood was found in newborn infants with Rh hemolytic disease when hydropic fetuses were excluded. The significant positive correlation ($r = 0.62$) between cord blood bilirubin and mild or moderate increase of optical density at 450 μm was also found, but there was no such correlation ($r = 0.31$) when the peak of optical density exceeded the value of about 0.1. It is suggested that in mild cases of fetal hemolytic disease the accumulation of biliary pigment in amniotic fluid is due to the increase of bilirubin content in the fetal extracellular fluid which again is correlated with the fall of hemoglobin. In severe cases of fetal disease, the high binding capacity of amniotic fluid is the main cause of accumulation of bilirubin in the amniotic fluid.

72. Renal response to an oral sodium load and in full term infants. K. THODENIUS, A. APERIA, O. BROBERGER, and R. ZETTERSTRÖM. *Karolinska Inst. and S:t Göran's Children's Hosp., Stockholm, Sweden.*

In the newborn infant, renal function is known to be restricted with regard to filtration rate and concentrating and acidifying capacity. Our knowledge about the ability to control sodium homeostasis is rather limited. Since filtration rate is about 20–30% of that of the 2-year-old child (values related to body surface as well as to weight), it can be expected that the ability to excrete sodium is also restricted. Knowledge of the control of sodium homeostasis in the newborn infant is of importance for the calculation of optimal amounts of saline in formula and intravenous infusions. In this communication a study of the control of sodium homeostasis in full term infants is reported. The urinary elimination of an oral saline load was determined after saline had been given as 1–2% solution of a diluted ordinary formula in a total amount of 55 or 110 mEq/m² body surface. The study was carried out during a constant and fairly high fluid intake. Urine was collected at approximately hourly intervals. The average sodium excretion per hour was calculated. The results were compared with those found in children 2–15 years old, some of them having reduced filtration rate. The following results were obtained. (*1*) The elimination rate of sodium is extremely low even when related to the filtration rate. (*2*) There is no significant increase in the sodium elimination rate between *day 1* and *day 10*. (*3*) In contrast to sodium, the excretion of water increases significantly from *day 1* to *day 10*. (*4*) There is no increase in the elimination rate when the amount of saline is doubled. (*5*) There is an inverse significant correlation between hematocrit and the ability to eliminate sodium. Several possibilities explaining the low sodium elimination rate may be suggested. The results provide information about the maximal sodium tolerance of the infant kidney.

73. Human postnatal gland development: Ductular transport of Na^+, K^+, H^+ and HCO_3^- in the single sweat gland of the newborn. D. KAISER, E. DRACK, and E. ROSSI. *Univ. of Berne, Berne, Switzerland.*

Development of electrolyte transport in human eccrine glands can best be studied in the single sweat gland. Using nanoliter analytical techniques, tubular handling of electrolytes was investigated from 0–96 hr of life. Sodium concentration [Na^+] varied with sweat rate (V, nanoliters per minute) according to: $[Na] = 2.5\ V + 55.0$ on 1st day and approached final values not before 4th day: $[Na] = 2.5\ V + 22.0$. From these data a synchronous +35% increase in tubular sodium reabsorption (R_{Na}) from: $R_{Na} = 92\ V + 144$ (10^{-6} mEq/min, 1st day) to: $R_{Na} = 125\ V + 144$ (4th day) could be calculated. Changes for potassium were parallel so that the Na/K ratio remained unchanged at 3.0, which suggests no involvement of adrenal hormones in postnatal sweat electrolyte changes.

Bicarbonate in final sweat approached asymptotically plasma concentrations (24 mEq/liter) thus providing no evidence for active secretion. Nevertheless, occurrence of sweat pH values (8.0–8.5) strongly alkaline to plasma were observed with increasing age. Simultaneous determination of CO_2 pressure revealed lower H_2CO_3 in sweat than in plasma, which means that with growing age an alkaline "disequilibrium pH" is established in sweat. These results can best be explained by assuming active reabsorption of H ions by the sweat gland duct.

74. Neonatal intrahepatic cholestasis and α_1-antitrypsin deficiency. Ø. AAGENÆS, M. FAGERHOI., and E. MUNTHE. *Rikshospitalet, Univ. of Oslo, Oslo, Norway.*

Five patients with α_1-antitrypsin deficiency and neonatal intrahepatic cholestasis are reported. A short summary of the clinical, light microscopic, and electron-microscopic findings is given. Immunohistologic studies on liver biopsies in one of these patients and in one patient with α_1-antitrypsin deficiency and emphysema but no liver disease are reported. Fluorescent-labeled antibody against α_1-antitrypsin was applied to the liver biopsies and showed strong fluorescence in the liver cell cytoplasm, both in the child with cholestasis and in the patient with emphysema. No fluorescence was found in the liver cells of normal children. This seems to indicate that the homozygote α_1-antitrypsin deficient state (Pi *type ZZ*), is a condition in which the release of α_1-antitrypsin from the liver is impaired. Why some of these persons with the *ZZ* type get liver cirrhosis, some get emphysema, and some are clinically well to old age is so far unsolved.

75. Fractionation of rat bone marrow cells. A study model for "stem cells." R. J. HAAS, T. M. FLIEDNER, and H. D. FLAD. *Ctr. for Basic Clin. Res., Univ. of Ulm, Ulm, Germany.*

Rats were labeled with ^{3}H-thymidine (^{3}H-TdR) *in utero* and for 6 weeks after birth in order to obtain 100% labeling of all bone marrow cells. Six weeks after the last ^{3}H-TdR injection only cytokinetically resting cells were still labeled. At this time the regenerative capacity of fractions obtained after centrifugation by means of a discontinuous albumin gradient was tested in 1200 *r* x-irradiated recipients and the results were compared with the effect observed after transplantation of identical amounts of unfractionated bone marrow cells. One of the fractions obtained produced a 10-fold increase in regeneratory capacity. This fraction was found to contain a concentration of undifferentiated blast cells and the highest amount of cytokinetically resting bone marrow lymphocytes as compared with all other fractions. In contrast, when the response to a phytohemagglutinin stimulation test was evaluted, this fraction showed a decreased incorporation of ^{14}C-TdR as compared with other fractions. The findings indicate a possible correlation between cytokinetically resting cells or blast cells, or both, and the regeneratory process after lethal x-irradiation.

76. Function of exocrine pancreas in newborns. G. ZOPPI, G. ANDREOTTI, F. PAJNO-FERRARA, and D. GABURRO. *Univ. of Verona, Verona, Italy.*

The function of exocrine pancreas has been studied in 34 newborns by means of a double balloon three-lumen polyvinyl-catheter tube and intravenous stimulation with pancreozymin and secretin. The patients of the first group (16 premature babies with a gestational age between 32 and 34 weeks and a weight at birth between 2.0 and 2.4 kg, and 8 full term newborns with a weight between 3.6 and 4.0 kg) were fed the same formula and the test was performed before the first feeding, 24 hr thereafter, at 1 week, and 1 month of life in order to state the influence of prematurity on pancreatic response to hormonal stimulations. Enzyme activities at birth were lower in premature than in full term newborns and became higher at 1 week of life. The patients of the second group (10 premature babies with a gestational age and a weight at birth similar to premature babies of the first group) were fed skimmed milk containing 2% soluble starch or 2% glucose. Induction of pancreatic α-amylase by starch was observed.

77. Transport of amino acid residues of peptides across the intestinal brush border. A. RUBINO and M. FIELD. *Harvard Med. Sch., Children's Hosp. Med. Ctr., and Beth Israel Hosp., Boston, Massachusetts, USA.*

To understand better the pathophysiology of protein malabsorption, more knowledge of the digestive-absorptive process for peptides is required. All glycine (Gly) which is accumulated in rabbit ileum incubated with glycyl-L-proline (Gly-Pro) is in the free form, but this Gly enters the cell by a saturable system unshared by Gly free in the lumen (Rubino *et al.*: Pediat. Res., *4*: 477, 1970). The transport of the Pro residue of Gly-Pro is now studied by measuring uptake of (^{3}H-Pro) Gly-Pro by rabbit ileum. This process follows saturation kinetics and has a low affinity for free Pro: percentage of control influx (±1 SE) of 0.5 mM (^{3}H-Pro) Gly-Pro in presence of 20 mM Pro is 92.4 ± 7.1; influx of 1 mM ^{3}H-Pro is unaffected by 20 mM Gly-Pro. To study where hydrolysis occurs, tissue uptakes of ^{3}H and ^{14}C are simultaneously measured after brief exposure to (^{3}H-Pro)- and (^{14}C-Gly)Gly-Pro. ^{14}C uptake/^{3}H uptake ratios at 0.5, 2, and 4 mM Gly-Pro concentrations are 1.4 ± 0.04, 1.4 ± 0.05, and 1.3 ± 0.04, respectively, indicating that a back flux of Pro, without a corresponding Gly efflux, is rapidly initiated. It is concluded that hydrolysis occurs, at least in part, in the brush border and the released Gly and Pro are then translocated by way of systems unshared by Gly and Pro free in the lumen.

78. *Vitamin E absorption in children.* J. T. HARRIES, D. P. R. MULLER, and J. K. LLOYD. *Inst. of Child Hlth., London, England.*

The intestinal absorption of vitamin E (α-tocopheryl acetate) has been studied in 86 children: cystic fibrosis of the pancreas (47), obstructive jaundice (17), celiac disease (10), abetalipoproteinemia (7), and intestinal lymphangiectasia (5). Each group represents an experimental model in which one or more of the known absorptive steps for vitamin E absorption are absent or defective. The vitamin E status of the patients was assessed by estimating serum concentration of vitamin E and peroxide hemolysis. Before vitamin E administration the mean serum levels of vitamin E and peroxide hemolysis in the 86 children with malabsorption were 0.23 mg/100 ml ± 0.16 (1 SD) and 35.8% ± 28.5 (1 SD), respectively, compared with 21 children without malabsorption who had mean levels of 0.80 mg/100 ml ± 0.18 and 1.89% ± 2.15. Deficiency was greatest in obstructive jaundice and abetalipoproteinemia. Absorption was further investigated by assessing the response to short and long term administration of differing doses of fat-soluble and water-miscible preparations of vitamin E, and the results suggest that the following factors are important for absorption. (*1*). Bile is of major importance. (*2*). Within the intestine, both bile and pancreatic lipase are necessary for solubilization of the vitamin. (*3*). The jejunum is an important site for vitamin E absorption. (*4*). The majority of vitamin E is probably transported from enterocytes via lymphatic channels in association with chylomicrons. (*5*). Chylomicron formation is not obligatory for absorption, and in conditions where chylomicrons cannot be formed (abetalipoproteinemia) absorption can occur by way of the portal vein.

79. Chemical changes in a patient with Gm_1 gangliosidosis *type I*. C. BORRONE and B. BERRA. *G. Gaslini Inst., Genoa-Quarto, and Inst. of Biol. Chem., Univ. of Milan, Milan, Italy.*

A case of Gm_1 gangliosidosis *type I* has been studied from clinical, radiologic, histologic, histochemical, and chemical points of view.

Hurler-like morphologic and radiologic features, early appearence and rapid course, and presence of a cherry-red spot at fundus oculi suggested a generalized gangliosidosis. β-Galactosidasic activity seemed to be absent in liver. A careful study of gangliosides isolated from different cerebral districts and different organs (liver, spleen, lung, kidney, myocardium, thyroid, and mediastinic lymph node) showed an increase of gangliosides content, and, on thin layer chromatography, an increase in Gm_1 ganglioside percentage, especially evident in encephalon (89.9% in the bridge).

An acid mucopolysaccharide isolated from liver, whose features are not yet defined, is now under study.

80. Pathogenetic studies in leukodystrophy. N. HERSCHKOWITZ and A. KOHLSCHÜTTER. *Univ. of Berne, Berne, Switzerland.*

"Jimpy" is a genetically determined leukodystrophy in the mouse, in which the nervous system is practically devoid of myelin. This disorder can serve as a model for human leukodystrophies of a similar type.

Our investigations show that in the "jimpy" mouse myelin is lacking in the central but not in the peripheral nervous system. Neither ultrastructural nor biochemical evidence (cholesterol ester) for increased myelin breakdown could be observed. However, enzymatic activities for the synthesis of myelin compounds such as sulfatide was significantly reduced *in vitro* and *in vivo* in the central nervous system. Inhibition of enzyme activity could be excluded by *in vitro* mixing experiments. Normal enzyme activities were found in the peripheral nervous system and in the kidney. The postnatal development of myelin was studied by separating several myelin-like fractions by density gradient ultracentrifugation. In the normal mouse, around the 11th day, myelin-like fractions disappear and true myelin with the characteristic physical and chemical qualities appears. In the "jimpy" mouse no such development could be observed. With an adaptation of method for neuron and glia separation by Norton (Science, *167:* 1144, 1970), we found that ^{35}S-sulfatide synthesis was impaired in both cell fractions. The fact that the activity of several enzymes is decreased in the "jimpy" brain but K_m and electrophoretic pattern is normal, makes it possible that the primary defect is a mutation in the operator gene.

81. Mucolipidosis *I* and *II:* Evidence for different biochemical lesions. U. WIESMANN and N. HERSCHKOWITZ. *Univ. of Berne, Berne, Switzerland.*

Mucolipidosis *I* (MLp) is a genetic disease with severe progressive mental retardation and skeletal abnormalities, resembling a mucopolysaccharidosis but with normal amounts of urinary mucopolysaccharides (MPS). MLp *II* is a similar genetic disorder but with milder clinical manifestations. Cultured fibroblasts from *type I* show enlarged cells with granular material (I-cell phenomenon). Metachromasia is found after lipid extraction and intracellular MPS is increased. We report on our results on fibroblasts of a patient with MLp *II*. The I-cell phenomenon and metachromasia could be demonstrated. A significant decrease in the activities of seven lysosomal enzymes but normal values for mitochondrial and cytoplasmic enzymes were found in the cells. In fibroblasts from the parents, intermediate values were found. The degradation of $^{35}SO_4$ MPS and of $^{35}SO_4$-sulfatide was greatly impaired. In the media in which the cells had been grown for 3 days, the activities of five lysosomal enzymes were increased as compared with media from normal cells. Increased cellular death and reduced enzymatic inactivation in the media, causing the elevated enzyme activities, could be excluded and leakage of lysosomal enzymes has to be considered as the most possible cause of the multiple enzyme deficiency. Fibroblasts from *type I* also showed decreased lysosomal activities, but no leakage of enzymes into the media was observed. Thus two different etiologies for these disorders are to be assumed.

82. Hereditary galactokinase deficiency. J. G. H. COOK, N. A. DON, and T. P. MANN. *Royal Alexandra Hosp. for Sick Children, Brighton, England.*

A baby with galactokinase deficiency, a recessive inborn error of galactose metabolism, is described. The case is exceptional in that there was no evidence of gypsy blood in the family concerned. The investigation of neonatal hyperbilirubinemia led to the discovery of galactosuria. As noted by others, the paucity of presenting features makes early diagnosis difficult, and detection by biochemical screening seems desirable. Cataract formation, of early onset, seems to be the only severe persisting complication and may be due to the biosynthesis and accumulation of galactitol in the lens. The paucity of manifestations in the few cases so far identified in the newborn period throws some light on the symptom complex of the allied transferase defect (congenital galactosemia). Ophthalmic surgeons need to be aware of this enzyme defect, because with early diagnosis and dietary treatment these lens changes should be reversible.