

intestinal transport. J. F. DESJEU and C. L. MORIN. *Hôpital Sainte Justine, Montreal, P.Q., Canada.*

The purpose of this study is to know if saliva and serum of cystic fibrosis have a general activity on membrane transports and if there is a common abnormal factor in blood and saliva. The method measures the variations of rat intestinal uptake on alanine which is in relation with Na movements. Two groups of 10 children with cystic fibrosis were compared with a pool of normal children. The fresh saliva of the first group was in contact for 10 min with an everted ring of normal rat jejunum. The ring was then incubated 60 min in K.R.B. with 0.8 mm/liter  $^{14}\text{C}$ -alanine. The fresh serum of the second group was placed in the incubation medium for 60 min with  $^{14}\text{C}$ -alanine. The saliva of cystic fibrosis inhibits alanine uptake from 6 to 50% compared with normal pool saliva. These results seem constant with a dilution from  $\frac{1}{4}$  to  $\frac{1}{20}$ . No significant difference could be obtained with fresh or congealed serum with a dilution from  $\frac{1}{4}$  to  $\frac{1}{20}$ . Saliva (and, perhaps, other exocrine secretions) of cystic fibrosis has a general effect on cellular uptake (probably on Na uptake). But it seems that this factor is different from the abnormal factor of the serum of cystic fibrosis.

11. Fatal congenital lactic acidosis in two siblings. S. O. LIF, S. SKRIDE, and J. H. STRÖMME. *Univ. of Oslo, Norway.*

Chronic lactic acidosis has been described in children. We have studied two siblings who developed a severe metabolic acidosis during the 2nd day of life. Lactic acid levels of 88–108 mg/100 ml blood were found. The children were severely affected, and the disease showed a malignant course with death at the ages of 97 and 177 hr.

*In vivo* as well as *in vitro* studies were carried out in the second sibling in an attempt to localize the metabolic defect. Metabolism of lactate was determined by injecting lactate-2- $^{14}\text{C}$  intravenously. Postmortem examinations included determinations of liver and muscle glycogen, LDH-isoenzymes, the metabolism of radioactive lactate and pyruvate in liver and muscle slices and in isolated mitochondria. The studies indicated that the hyperlactatemia was due to an abnormally slow metabolism of lactate and not to a high production. The rate of oxidation was normal. Very low concentration of glycogen was found in liver and muscle. The incorporation of  $^{14}\text{C}$ -lactate into blood glucose and glycogen was insignificant *in vitro* as well as *in vivo*. These results are compatible with a reduced gluconeogenesis from lactate in our patient, resulting in a severe accumulation of lactate and a fatal acidosis.

12. Studies on thyroid proteins in congenital goiter. P. OLIN. *St Göran's Hosp. and Karolinska Hosp., Stockholm, Sweden.*

Congenital goitrous hypothyroidism may be caused by a metabolic bloc in the synthesis of the thyroid hormones or by an abnormal synthesis of iodinated proteins in the thyroid. Previously we have utilized labeling *in vitro* with  $^3\text{H}$ -leucine and  $\text{Na}^{125}\text{I}$  in the study of the normal synthesis of 17-19 S thyroglobulin in the human fetal thyroid gland (Olin, Vecchio, Ekholm, and Almqvist: *Endocrinology*, 86: 1011, 1970). This system has been applied to 2–10 mg specimens from congenital goiters obtained by percutaneous biopsy.

This report deals with two children with a pathological perchlorate-induced discharge of radioiodine. The first patient was an 18-day-old boy with diffuse goiter and hypothyroidism. The biochemical analysis revealed a normal uptake *in vitro* of  $^{125}\text{I}$ . No  $^{125}\text{I}$  was present in the crude extract after dialysis. Sucrose density gradient centrifugation of the soluble proteins, however, showed a distinct label of  $^3\text{H}$  in the 17-19 S region. The  $^3\text{H}$ -ra-

dioactivity was specifically precipitated by antiserum against human adult thyroglobulin.

The second patient was a 4-year-old girl with goiter and hypothyroidism since at least 1 year of age. At that time the perchlorate test was performed before treatment. The biochemical studies were performed while the patient was treated with thyroxine. Biopsies were obtained before and after stimulation with TSH (Actyron 1 IU/d for 5 days). Before TSH stimulation no iodide was accumulated *in vitro* and a slight  $^3\text{H}$ -peak was present in the 17-19 S region of the sucrose density gradient. After TSH stimulation the thyroid tissue did accumulate  $^{125}\text{I}$ , but only  $^3\text{H}$  was incorporated into the 17-19 S proteins.

The results indicate a normal synthesis of the protein moiety of thyroglobulin in these two congenital goiters with a defect in the organification of iodine. This is at variance with the current opinion that this type of goiter is caused by a deficient synthesis of thyroglobulin and a pathological formation of thyralbumin.

13. Early postnatal weight gain of low weight newborns: Relationships with various diets and with intrauterine growth. E. REZZA, U. COLOMBO, G. BUCCI, M. MENDICINI, and S. UNGARI. *Univ. of Rome, Italy.*

From 10 to 34 days of age, the weight gain was studied in 134 low birth weight (LBW) infants (birth weight range 0.99–1.90 kg; gestational age range 28–38 weeks) on three different diets: (1) human milk; (2) a "humanized" milk formula; (3) a high protein, high GI, low fat cow's milk formula. The caloric intake (kcal/kg/24 hr) was always about 120 between 10 and 20 days, and about 140 thereafter. Six experimental groups were separated according to the three diets, and whether infants were "large for date" (LFD, *i.e.*, with birth weight > the 25th percentile for gestational age) or "small for date" (SFD, *i.e.*, with birth weight  $\leq$  the 25th percentile, and 50% of subjects  $\leq$  the 10th percentile). Weight gain curves were calculated by regression analysis using the least square method according to a polynomial model. In each group, an exponential relationship of weight gain with time was found. In SFD infants weight gain was slightly but significantly ( $P < 0.001$ ) faster than in LFD babies on *diet 3*, not on *diets 1* and *2*. Either in LFD or in SFD infants weight gain was markedly faster on *diet 3* as compared to *diet 1* or *2* ( $P < 0.001$ ), and slightly but significantly ( $P < 0.01$ ) faster on *diet 1* as compared to *diet 2*. Previous findings of a faster weight gain of LBW newborns on high protein formulas, as compared to human or "humanized" milk formulas, were therefore confirmed. The following main conclusions and speculations were also made: in studies on growth refeeding, LFD and SFD newborns should be discriminated, and statistical methods able to describe a possible nonlinearity of growth curves should be used; SFD babies presumably need more proteins than LFD infants for optimal weight gain in the early weeks of life.

14. Changes in the lipid pattern of human sera in the neonatal period. J. CLAUSEN and B. FRIS-HANSEN. *Rigshospitalet, Copenhagen, Denmark.*

The changes in serum  $\beta$ -lipoprotein and the relative distribution of lipoproteins as well as the pattern of fatty acids have been followed in infants during the neonatal period. The data obtained were correlated to the food intake as well as to the growth of the child. In infants living on human milk, the total content of  $\beta$ -lipoprotein increased from around 30% of the concentration in the mothers' serum at birth, to around 80% in the 2nd week of life. During the same period the lipoprotein pattern changed from a predominance of the pre- $\beta$ -lipoprotein band to a pattern

with the  $\beta$ -lipoprotein as a dominating fraction with contributions from other lipoprotein fractions seen in normal adult sera as elucidated by means of agar electrophoresis.

During the same period the fatty acid pattern also changed. At birth low values of oleic acid and linoleic acid and high values of palmitic acid and arachidonic acids were found in cord serum as compared to the corresponding values in the mothers' blood. During the 1st week the content of palmitic and arachidonic acids decreased slightly, whereas the oleic acid was found to increase.

Somewhat different values were found in infants of low birth weight, where the linoleic acid was found to be very low.

Related changes in serum levels of vitamin E will be discussed.

15. Intravenous fat loads in low birth weight infants. A. GUSTAFSON, I. KJELLMER, R. OLEGÅRD, and L. VICTORIN. *Univ. of Göteborg, Sweden.*

When the clinical course in low birth weight (LBW) infants is complicated by extreme immaturity, respiratory distress, or hyperbilirubinemia, the peroral route of feeding becomes difficult. In an attempt to investigate whether the caloric demands could be met by intravenous fat infusions, fat loads were performed in normal LBW infants. The fat was given as 20% Intralipid (a soybean oil emulsion) either in single injections or during extended infusions. The concentration of total lipids was followed in serum samples, and the distribution of the lipoproteins was evaluated by means of agar gel electrophoresis. In preterm infants the maximal removal capacity of fat from the intravascular compartment corresponded to some 6-8 g fat/kg in 24 hr. The fat particles injected had a half-life of 1-5 min. In small-for-date infants the initial maximal removal capacity was of the same order but the removal rate rapidly decreased concomitant with the appearance of a secondary generation of fat particles in the blood stream. These were identified as pre- $\beta$ -lipoproteins on the gel electrophoresis and were considered to originate in the liver. It is speculated that the slower removal of exogenous fat from the intravascular compartment of the small-for-date infants is due to a competition with the pre- $\beta$ -lipoproteins for the same elimination mechanisms.

16. Evolution of water and electrolyte content of muscle and skin tissues during growth. The concept of chemical maturity. J. DUBOIS and H. L. VIS. *Univ. Libre de Bruxelles, Brussels, Belgium.*

Variations in the hydroelectrolytic composition of skeletal muscle have been studied in 69 normal children aged 2 weeks to 18 months by neutron activation analysis of needle micro biopsies and in 41 adults by the analysis of surgical biopsies with classical chemical methods. The criteria of normality for age of the various elements measured (H, O, Na, K, Cl, P) were established by means of the statistical analysis of the results obtained. The same elements were also measured in the skin of 35 children. It was shown that hydroelectrolytic composition of muscle and skin tissues changes quite distinctly with age. During the first 6 months of life there is a relative diminution of water and extracellular electrolyte muscle values. This evolution is reversed in old age. In cutaneous tissue, during the first 18 months of life there is a gradual fall in the value of water, sodium, and chloride. There is no significant variation in muscle and skin potassium and phosphorus content in relation to age. On the basis of our results, the notion of chemical maturity as defined in the literature must be reconsidered as far as muscle tissue is concerned. In normal children, no correlation was found in the sum concentration of sodium and potassium in the plasma and in the

water of the two tissues investigated. This observation implies that the regulation of osmotic equilibrium between plasma and tissue does not depend exclusively on the water and electrolytes movements.

The role of amino acids in this regulation is illustrated by preliminary studies on the free amino acid content of muscle tissue in subjects of various ages.

17. Total body potassium, lean body mass and fat determination in children by  $^{40}\text{K}$  measurements with a liquid scintillation whole body counter. A. DONATH, G. PORETTI, and A. ZUPPINGER. *Univ. of Berne, Switzerland.*

Normal values of total body potassium are established by measuring 441 healthy children, expressing the results according to an obesity index ( $\text{O.I.} = W/10 \cdot H^3$ , where  $W$  = weight in kg and  $H$  = height in m) and classifying the children according to sex and age. While after puberty boys increase their K/kg and keep their O.I. constant, girls' O.I. goes up, but their total K/kg remains unchanged. Total potassium reflects the cellular mass and allows an objective evaluation of muscle waste in progressive muscular dystrophy. The calculation of the lean body mass and, by deduction, of the total fat shows extreme values of practically no fat in anorexia mentalis and 750 g/kg in obesitas permagnia. Total body water has been determined simultaneously in 62 children, and their lean body mass calculated and compared to the values obtained from K determination; the correlation between the two methods is satisfactory. Daily measurements of total body potassium and simultaneous potassium balance studies for 8 days in a case of newly diagnosed diabetes also correlated well.

18. Synthesis and release of plasma proteins by isolated perfused human fetal liver. M. KEKOMÄKI, M. SEPPÄLA and A. L. SCHWARTZ. *Children's Hosp., and Univ. of Helsinki, Finland.*

Plasma protein constituents are synthesized by explants of cultured human embryonic liver after the 5th week of gestation. To quantify the incorporation and release of protein in an abstracted physiological system, three human fetal livers of gestational ages of (a) 10, (b) 14, and (c) 20 weeks were perfused for 4 hr through the umbilical vein with an amino acid mixture and glucose in oxygenated Krebs-Ringer bicarbonate. L-Leucine- $^{14}\text{C}$  tracer was added to the medium at 60 min, when protein was released to the medium at constant rates of 0.45, 0.60, and 0.15  $\mu\text{g}/\text{min}/\text{mg}$  of liver protein in a, b, and c, respectively. The incorporation of  $^{14}\text{C}$  into the protein was characterized at 240 min by autoradiography of both (1) immunodiffusion in agar gel and (2) electrophoresis on cellulose acetate. (1)  $^{14}\text{C}$  was incorporated into albumin,  $\alpha$ -fetoprotein,  $\alpha$ - &  $\beta$ -lipoprotein, Gc-protein, and transferrin, but not into haptoglobin; (2a) a constant fraction (72%) of the label incorporated was found in (albumin +  $\alpha$ -fetoprotein) at all three gestational ages; (2b) the albumin/ $\alpha$ -fetoprotein incorporation of the label was 1.6, 2.3, and 4.4 for a, b, and c, respectively; these values related to each other like the albumin/ $\alpha$ -fetoprotein found in the plasma of corresponding fetuses: 2.9, 7.5, and 17; (2c) the (stored) protein released by the livers during the first 60 min was mainly albumin.

19. Studies of sulfur amino acids in the immature human: Is cyst(e)ine essential? G. E. GAULL, J. A. STURMAN, and N. C. R. RAIHA. *N.Y. State Inst. Basic Res. Mental Retard., Mt. Sinai Hosp. Sch. of Med., N.Y. and Univ. of Helsinki, Finland.*
- Cystathionase activity was not measurable in the liver or brain of 24 human fetuses and 3 prematures. Methionine-activating