leukopenia, thrombopenia, and failure to thrive had the biochemical abnormalities of ketotic hyperglycinemia: metabolic acidosis (pH 7.2; HCO_3^- 7 mEq/liter); hyperglycinemia (8.2 mg/100 ml); increased serum levels of glutamine, glutamic acid, and the ketogenic amino acids as well as a positive urinary Acetest and diphenylhydrazine reaction. Gas chromatography of the serum volatile fatty acids (VFA) showed a considerable increase of propionic acid up to 70% of the total VFA content (normal value 3.2%) and a concomitant decrease of acetic acid to 24% (normal value 88%).

The results indicate that the acidosis of ketotic hyperglycinemia is accompanied by increased propionic acidemia and allow some speculation on the metabolic block of the disorder.

5. β -Hydroxyisovaleric aciduria and β -methylcrotonylglycinuria in a newborn child, caused by a new inborn defect in the leucine degradation pathway. O. STOKKE, E. JELUM, and L. ELDJARN. *Rikshospitalet, Oslo, Norway*.

The patient was a 4.5-month-old girl, whose parents are related. She suffered from neurological symptoms similar to those of Werdnig-Hoffmann's disease. Clinical data are presented in the abstract of H. Pande *et al.* In periods the urine had a peculiar odor, like that of cat's urine. Urine and serum samples were sent to us for further examination. Several screening procedures for abnormal metabolites were used. Analyses of urinary extracts by gas-liquid chromatography, using polar columns, showed large quantities of two components normally not present. Mass spectrometric analyses revealed spectra compatible with β -hydroxyisovaleric acid (β -OH-IV) and β -methylcrotonylglycine (β -MCG). Analyses of synthesized authentic compounds verified these structures. Daily amounts excreted were about 400 mg β -OH-IV and 100 mg β -MCG. Neither the metabolites nor any short chain fatty acids, including isovaleric acid, could be demonstrated in the serum, the levels of these compounds must therefore be below 0.5 mg/100 ml. Both the mother, father, and the two elder brothers, all healthy, excreted 15–40 mg β -MCG daily in the urine, indicating that the condition is genetically determined. Both β -OH-IV and β -MCG stem from the leucine degradation pathway, and the accumulation is probably due to a defective β -methylcrotonyl-CoA carboxylase. Biochemically, as well as clinically, our findings are distinctly different from previously described errors in the leucine metabolism.

6. Symptoms of infantile spinal muscular atrophy combined with a hitherto not described error in leucine metabolism. H. PANDE, P. E. WAALER, O. STOKKE, E. JELUM, and L. ELDJARN. *Univ. of Bergen, and Rikshospitalet, Univ. of Oslo, Norway*.
A 4½-month-old girl with clinical signs of Werdnig-Hoffmann's disease (infantile spinal muscular atrophy) had in addition a peculiar smell from her urine. Large amounts of two abnormal metabolites were found: β -methylcrotonylglycine (β -MCG) and β -OH-isovaleric acid. (See separate paper by Stokke, Jellum and Eldjarn.) The urinary smell resembled that of cat's urine or black currant leaves. The metabolites were not found in the blood. She had no episodes of acidosis. By giving a diet low in leucine the urinary excretion of β -OH-isovaleric acid dropped from 400 mg to about 50 mg/24 hr, and β -MCG from 100 mg to about 50 mg/24 hr. The clinical course however, did not change during 3 months on diet, and it is doubtful whether her clinical condition was due to the error in leucine metabolism. She died when 9½ months old from pneumonia.

7. Celiac disease sans diarrhea. B. McNICHOLL and B. EGAN-

MITCHELL. *Regional Hosp. and University College, Galway, Ireland*.

Three infants presented around 1 year of age with failure to thrive, vomiting, and anorexia and were shown to have severe jejunal mucosal lesions characteristic of celiac disease before or at the time of onset of mild diarrhea. Two infants had fecal retention, none had steatorrhea, and all have thrived on gluten-free, milk-containing diets. Other investigations were confirmatory, including some sugar tolerance tests, and assays of mucosal lactase, glutamyl-tyrosine, γ -glutamyl- β -naphthylamide, and glycyl-leucine; the dipeptidase assays were by a zymographic technique. Immunoglobulins were measured by single radial diffusion and showed high IgA in each child, low IgM in one, and variable IgG levels. The mucosal lesion of gluten-induced celiac disease can be demonstrated before diarrhea or steatorrhea occur.

8. Studies of intestinal fructose absorption in the rat. M. GRACEY, V. BURKE, and A. OSHIN. *Univ. of Birmingham, England*.

Fructose is an important dietary sugar, and its intake is increasing. However, the mechanism of its absorption is unknown. It is generally accepted that active transport does not occur and it is thought that transport is either passive or facilitated. We studied fructose uptake by the small intestine using rat jejunal segments 1.5 cm long, fixed in Plexiglas chambers [1] and incubated in Krebs-Henseleit buffer containing C^{14} fructose. A double incubation technique was used [2]. A base line tissue concentration is thus achieved during the first incubation, and subsequent absorption of the sugar from the second medium can then be studied. This method consistently showed accumulation of the sugar against a concentration gradient. This effect is more easily demonstrated and more marked in young rats, just after weaning. We have therefore shown active transport of fructose in the small intestine of the rat. This process is disrupted by lithium and so is sodium-dependent; it is also depressed by dinitrophenol. Moderate inhibition occurs with galactose, lysine, and proline. These findings suggest that active transport of fructose occurs via a sodium-dependent, energy-dependent mechanism which may be shared by other small, water-soluble molecules. These findings are relevant to clinical situations seen in childhood, particularly temporary monosaccharide malabsorption and glucose-galactose malabsorption.

1. SIMENZA G.: *Biochim. Biophys. Acta*, **173**: 101 (1969).
2. ALVARADO F.: *Biochim. Biophys. Acta*, **112**: 292 (1966).

9. Peptidase activities of brush border membrane of rat intestine. S. ACRICCHIO, M. PIERRO, and M. ORSATTI. *Univ. of Naples, Italy*.

A new method for the assay of peptidase activities is developed based on the oxidative deamination of L-amino acids with L-amino acid oxidase. This method measures the products of the enzymatic hydrolysis, without any interference from the peptides.

Brush border membrane hydrolyzes very rapidly tri- and tetra-L-alanine, L-leucyl-glycyl-glycine, L-leucyl-glycine, L-phenylalanyl-L-alanine, and L-leucine amide.

The enzymatic activities of the brush border membrane hydrolyzing L-phenylalanyl-L-alanine and L-leucine amide were characterized with regard to pH-activity curves, ion activation, and intracellular distribution.

The results suggest that intrinsic enzymes of the brush border membrane play a role in the terminal digestion of proteins.

10. Effect of saliva and serum of cystic fibrosis on alanine *in vitro*

intestinal transport. J. F. DESJEUX 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}C -alanine. The fresh serum of the second group was placed in the incubation medium for 60 min with ^{14}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. LIE, S. SKRIDE, and J. H. STRØMME. *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}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}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 ^3H -leucine and Na^{125}I in the study of the normal synthesis of 17-19 S thyroglobulin in the human fetal thyroid gland (Olin, Vecchio, Ekholm, and Ahnqvist: *Endocrinology*, 86: 1041, 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}I . No ^{125}I was present in the crude extract after dialysis. Sucrose density gradient centrifugation of the soluble proteins, however, showed a distinct label of ^3H in the 17-19 S region. The ^3H -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 ^3H -peak was present in the 17-19 S region of the sucrose density gradient. After TSH stimulation the thyroid tissue did accumulate ^{125}I , but only ^3H 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. BUGGI, 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 ≤ the 25th percentile, and 50% of subjects ≤ 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. FRUS-HANSEN. *Rigshospitalet, Copenhagen, Denmark.*

The changes in serum β -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 β -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- β -lipoprotein band to a pattern