

and between IDM and controls. This report demonstrates that IDM are prone to NHC, are capable of conserving Ca and Mg, and have a positive calcemic response to PTE.

**Succinyl-CoA: 3-Ketoacid-CoA transferase (CoA transferase) deficiency, a new cause of keto-acidosis in infancy.** J. TYSON TILDON and MARVIN CORNBLATH. *Univ. of Maryland Sch. of Med., Baltimore, Md.*

In an infant with a unique form of persistent ketonemia and severe intermittent keto-acidosis, studies of post mortem brain, muscle and kidney tissue demonstrated the absence of CoA transferase, a critical enzyme in ketone metabolism. Other enzymes of glucose and ketone metabolism were present in both post mortem tissues and skin fibroblasts from this patient. The tissue culture fibroblasts in addition to having no CoA transferase activity, demonstrated an altered carbohydrate metabolism compared to that of normal cells. When initially harvested, these cells utilized glucose at a rate significantly less than that of controls (125 vs 680  $\mu\text{M}/\text{mg}/\text{hr}$ ). However, after incubation of 2.5 mM glucose for 18 hours, glucose uptake by patient's cells increased 20 fold (2560  $\mu\text{M}/\text{mg}/\text{hr}$ ) whereas, that by control cells remained constant (680  $\pm$  90). Concomitant with this increase, glucose-6- $^{14}\text{C}$  oxidation to  $^{14}\text{CO}_2$  in patient's fibroblasts rose from 8 to 2261  $\mu\text{M}/\text{mg}/\text{hr}$ , while that in control cells remained constant (485  $\pm$  175). This increase in glucose utilization was not due to new enzyme formation since incubation with puromycin had no effect. Mixing experiments demonstrated no transfer of permeable inhibitors or activating substances. These data indicate that the absence of CoA transferase was the probable cause of the keto-acidosis in this infant and of the abnormal glucose metabolism in the fibroblasts suggesting a regulatory role for this enzyme in peripheral tissue glycolysis.

**Complete ornithine transcarbamylase deficiency: A cause of lethal neonatal hyperammonemia.** ALEXANDER G. M. CAMPBELL, LEON E. ROSENBERG, PHILIP J. SNODGRASS, and CLAUDE T. NUZUM (Intr. by C. D. Cook). *Yale Univ. Sch. of Med., New Haven, Conn., and Peter Bent Brigham Hosp., Boston, Mass.*

Hyperammonemia secondary to deficiency of one of the enzymes of the urea cycle causes infantile somatic and mental retardation, but has not, hitherto, been noted to cause death in the newborn period. A term infant, born to healthy parents after an uneventful pregnancy and delivery, thrived for three days, then lapsed rapidly into deep coma. Because a previous sibling had died under identical circumstances, an inherited metabolic derangement was sought. The blood ammonia concentration was 1208  $\mu\text{g}\%$  (normal <150  $\mu\text{g}\%$ ). The blood urea nitrogen was 7 mg% and numerous other studies of plasma and urinary amino or organic acids were unrevealing. Despite a protein free diet, enemas, antibiotic therapy and an exchange transfusion, the blood ammonia remained about 1200  $\mu\text{g}\%$  and the child expired on the fifth day of life. Hepatic assays of the five enzymes of the urea cycle revealed absence of ornithine transcarbamylase (OCT) activity. No OCT activity was restored by changes in substrate concentration, enzyme concentration or pH, and mixing experiments excluded the presence of an inhibitor of OCT in the patient's cells. Activity of the other four urea cycle enzymes was in the range noted in other age-matched, autopsy-control livers. These findings document complete OCT deficiency for the first time and emphasize the lethality of this enzymatic defect. Hyper-

ammonemia must be considered in a newborn with coma, particularly if there is a family history of neonatal death. In such situations, unrestricted dietary protein ingestion will have disastrous consequences.

**$^{14}\text{C}$  Galactose incorporation into skin fibroblasts in glycolipid storage disorders (sulfatidosis, Fabry's, Gaucher's, and Hurler's disease).** MICHEL PHILIPPART. *Univ. of Calif. Sch. Med., Los Angeles, Calif.*

The turnover of (1- $^{14}\text{C}$ ) galactose was studied in fibroblast cultures, which were grown for 48 h. in a medium containing 5  $\mu\text{C}$  of label but without serum. Subsequently cultures were maintained for up to 5 weeks in a medium containing serum. Lipids were extracted from replicate cultures at various intervals between 2 and 35 d. Maximum incorporation of the label was usually observed at 2 d. It had decreased by about 65% 1 week later but in chronic Gaucher's disease 90% of the maximum activity was retained at 9 d. and 33% at 35 d. Labeled lipids were mixed with known carriers (lipids from spinal cord, neutral glycolipids from erythrocytes and hemoside from Gaucher spleen). Thin-layer chromatograms were run in a 2-dimensional system. Lipid spots were detected by exposure to iodine, scraped, eluted and read in a scintillation counter. About 35-62% of the lipid label was incorporated into trihexosyl ceramide but no degradation of this lipid was found in Fabry's cells. The label was not incorporated into sulfatides, even in sulfatidosis. This probably reflects the inability of fibroblasts to synthesize sulfatides. Increased incorporation of labeled galactose was found in cerebrosides from sulfatidosis but not from Gaucher cells. This may imply that galactose is not a good precursor of glucosyl ceramides.

These experiments suggest that significant portions of galactose may be incorporated as such into galactolipids, while other experiments with (1- $^{14}\text{C}$ ) acetate indicated that only a small fraction of this label is incorporated into glycolipids. The availability of galactose may represent a key factor in the rate of galactolipid synthesis. This hypothesis is presently being tested in patients with Fabry's disease, sulfatidosis and GM<sub>1</sub>-gangliosidosis.

**Detection of hyperlipoproteinemia: Family lipid studies in normal school children and children with diabetes mellitus.** ALLAN L. DRASH and FAY HENGSTENBERG. *Univ. of Pittsburgh Sch. of Med., Children's Hosp. of Pittsburgh, Pittsburgh, Pa.*

The possible relationship between hypercholesterolemia and the development of cardiovascular disease makes the early detection of lipid abnormalities of major importance. A screening technique [precipitable lipoprotein analysis (PLP)] for the detection of abnormalities of blood lipid and lipoprotein concentrations was carried out on 487 normal children in a public junior high school (80% of the school enrollment). Serum cholesterol (C) and lipoprotein electrophoresis (LPE) were obtained on all students with PLP values >40 units and on a comparable number with PLP values <40 units (total of 203 students studied). The corrected incidence of hypercholesterolemia (C > 200 mg%) was 8.6%. Abnormalities of LPE occurred in 25%. The parents and sibs of 26 children with hypercholesterolemia and, for comparison, the parents and sibs of 28 children with diabetes mellitus were studied for total lipid (TL), C, PLP, and LPE. The mean ages of the mothers, fathers, and sibs in the 2 groups are comparable. Unexpectedly TL and C concentrations were statistically higher in the families of hypercholesterolemic children than in the diabetic families. Abnormalities of LPE were also more com-