jected to a continuous water loading test initiated by giving 25 cc/kg of water while on chlorpropamide in a dose sufficient to cause antidiuresis without hypoglycemia. Water excretion was impaired in all patients. Serum Na fell at least 10 mEq/L in each patient. Serum osmolality fell 25 mosm/kg in 2 patients and fell 20 mosm/kg and 15 mosm/kg in the other 2 patients. All patients gained weight. Chloride spaces increased from 3% to 5% after the water load. CH_2O remained negative throughout the entire test in 2 patients. A third patient developed a CH_2O of +0.9 cc/min/1.73 m^2. This maximum CH_2O occurred 6½ hours after the water load. A fourth patient developed a CH_2O of +2.5 cc/min/1.73 m^2. This maximum CH_2O occurred 2 hours after the water load, subsequently fell to .6 cc/min/1.73 m^2 and never again exceeded +2.1 cc/min. Since published evidence indicates that chlorpropamide acts by potentiating ADH, our data suggests that the subthreshold circulating ADH presumed to be present in our patients is not further suppressed by water loading. Therefore, a potential danger exists for anyone taking chlorpropamide who either requires intravenous therapy, or who may drink a large amount of fluid.

"Transient acetylcholinosis": Cause of Chinese Restaurant syndrome. H. GHADIMI, F. ABAGI, M. RATHI and S. KUMAR. *Downstate Med. Ctr., S.U.N.Y., and Methodist Hosp. of Brooklyn, N. Y.*

Both clinical data and biochemical findings in our studies suggest that the signs and symptoms following monosodium glutamate (MSG) ingestion represent "transient acetylcholinosis." Dose-related reactions occurred in 14 volunteers after MSG ingestion on empty stomach, including numbness of neck, heaviness of eyelids and legs, lacrimation, headache, nausea, urgency of urination and defecation, drowsiness, substernal pressure, abdominal discomfort, palpitations and colicky pain. The protean nature of the symptoms, the mode of appearance and recovery, variations in severity, all were remarkably similar to the diffuse, evanescent action of acetylcholine (ACh). In 4 subjects primed with atropine, there was blockage of symptoms even though MSG dose was doubled. On the other hand, prostigmine (⅓ usual dose) given with MSG markedly exacerbated symptoms in 4 subjects tested. Others have shown that glutamate is a suitable substrate for ACh synthesis. In 10 subjects receiving 150 MSG/kg body wt., cholinesterase (ChE) was measured at 0, 20, 40, 60, 90, 150, and 180 minutes. At 60 min., there was a drop of 30% below baseline. A significantly sharper drop was observed when prostigmine was administered simultaneously with MSG. On the other hand, control tests with histidine showed no fluctuation beyond 5%. Following infusion of ACh into a dog, the pattern of ChE activity was strikingly similar to that observed in man following MSG ingestion. Clinical response to ACh also paralleled human symptoms, except for severity. In 2 infants with Down's Syndrome, ChE changes after MSG also followed the pattern seen in adult volunteers. Judging by this criterion infants do develop Chinese Restaurant Syndrome following MSG ingestion.

Incorporation of heparin-S^{35} by cultured leucocytes as a diagnostic tool in cystic fibrosis (CF). MARK W. STEELE and JOAN B. RODNAN (Intr. by Richard Michaels). *Univ. of Pittsburgh Sch. of Med., Children's Hosp., Pittsburgh, Pa.*

By culturing leucocytes for 5 days in media with Heparin-S^{35} and PHG and then assaying for cellular incorporation of S^{35}, we were able to distinguish homozygous CF from: heterozygous CF and Hurler's; and homozygous normal and Hurler's. We also noted that cells after incorporating higher levels of Heparin-S^{35} disrupted when fixed in Carnoy's mixture; so that after staining with Toluidine Blue O, the slide was covered with heavy amorphous metochromatic debris.

	S*	N†	Mean S.A.‡	Range (S.A.)	Cell Disruption§
Presumed Normals	6	11	27	9–45	2/11
Heterozygous CF	8	15	41	19–83	3/15
Homozygous CF	6	12	129	47–349	12/12
Heterozygous Hurler's	1	2	48	41–55	0/2
Homozygous Hurler's	1	2	39	36–41	0/2

* # of Subjects.
† # of Assays.
‡ DPM/mg. protein.
§ # positive instances/N.

The mean S.A. for homozygous CF was significantly ($p < 0.01$) greater than that for all other subjects. The mean S.A. for heterozygous CF, heterozygous and homozygous Hurler's were all the same and different ($p < 0.01$) from the S.A. for homozygous normal. There was a significant positive ($r = 0.65$, $p < 0.001$) correlation between cell disruption and S.A. We suggest that these two complimentary assay systems could be useful in confirming the diagnosis of CF in questionable cases. Furthermore, contrary to metochromasia, cellular Heparin-S^{35} uptake might differentiate homozygous from heterozygous CF. Hence, if applicable to cultured amniotic fluid cells, the technique could allow detection of homozygous CF in utero.

The response to parathyroid extract (PTE) in infants of diabetic mothers (IDM). REGINALD C. TSANG, LEONARD I. KLEINMAN, IRWIN J. LIGHT, and JAMES M. SUTHERLAND. *Univ. of Cincinnati, Cincinnati, Ohio.*

Neonatal hypocalcemia (NHC) in infants of diabetic mothers (IDM) has been thought to be related to transient hypoparathyroidism or lack of responsiveness to parathyroid hormone. Previous reports of NHC in IDM have not documented its existence when compared to gestation matched infants. A previous study of low birth weight infants demonstrated the importance of early gestation on the incidence of NHC. In the present study 28 IDM were matched with infants of similar age, sex, gestation and perinatal complications. Seven IDM developed NHC compared with one in controls ($p < 0.025$). In IDM mean calcium levels were lower at 12, 24, 48, 60 and 72 hours of age. One IDM (maternal class D) developed temporary hypomagnesemia with NHC. During the first 3 days of life, in all infants tubular reabsorption of P (TRP) fell (93% to 87%), urinary P excretion rose (5 to 40 mg/24 hour) and urinary Ca and Mg remained low (<1 and <0.5 mg/24 hr respectively). In 6 IDM who were given PTE (5 units/kg) at 24 hours and 48 hours of age, 5 responded with temporary elevations of Ca at 12 hours post-injection compared with untreated IDM ($p < 0.05$). There was no significant difference in serum Mg and P levels, TRP and urinary P, Ca and Mg between treated and untreated IDM

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 mμM/mg/hr). However, after incubation of 2.5 mM glucose for 18 hours, glucose uptake by patient's cells increased 20 fold (2560 mμM/mg/hr) whereas, that by control cells remained constant (680 ± 90). Concomitant with this increase, glucose-6-^{14}C oxidation to $^{14}CO_2$ in patient's fibroblasts rose from 8 to 2261 μμM/mg/hr, while that in control cells remained constant (485 ± 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 μg% (normal <150 μg%). 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 μg% 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. Hyperammonemia 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}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}C) galactose was studied in fibroblast cultures, which were grown for 48 h. in a medium containing 5 μc 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 hematoside 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}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_1-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-