ABSTRACTS

Arieff, Allen I.; and Carroll, Hugh J. (Dept. of Med., State Univ. of New York, Downstate Med. Center; and Med. Serv., Kings County Hosp., Brooklyn, N. Y.): HYPEROSMOLAR NONKETOTIC COMA WITH HYPERGLYCEMIA: ABNORMALITIES OF LIPID AND CARBOHYDRATE METABOLISM. Metabolism 20:529-38, June, 1971.

Measurements were made of plasma insulin (IRI), free fatty acids (FFA), and growth hormone (GH) in fifteen hyperglycemic comatose patients without ketosis. FFA levels were normal in these patients with nonketotic coma. Lack of mobilization of fats was not related to GH since plasma levels of this hormone ranged from low to high and displayed no correlation with the levels of plasma glucose or acetone. IRI levels were only slightly lower than fasting values found in normal or obese subjects; these levels were considered capable of suppressing lipolysis without preventing hyperglycemia. Dehydration and hyperglycemia may play a secondary role in prevention of fat mobilization and ketone production. C.R.S.

Bassett, J. M.; and Thorburn, G. D. (Div. of Animal Physiol., C.S.I.R.O., Ian Clunies Ross Animal Res. Lab., Prospect, N.S.W., Australia): THE REGULATION OF INSULIN SECRETION BY THE OVINE FETUS IN UTERO. J. Endocr. 50:59-74, May, 1971.

Verbatim summary. Fetal lambs (100 to 150 days' gestation) with indwelling vascular catheters were used to study the regulation of the insulin concentration in the plasma of fetal lambs in utero. Immediately after the implantation of the catheters the insulin concentration in fetal plasma was significantly correlated with the fetal glucose and fructose concentrations and with the maternal glucose concentration. On the next day the fetal insulin concentration was significantly correlated only with the maternal glucose concentration.

Both glucose and fructose, when infused intravenously, increased the insulin concentration in fetal plasma, but the increases were slow and far less than those observed in newborn lambs infused with glucose and fructose. Intravenous infusion of isoprenaline or glucagon did not alter the plasma insulin concentration of fetal lambs, but both caused a rapid increase in the insulin concentration of newborn lambs. Glucagon did not potentiate the insulin response to glucose. Addition of aminophylline to a glucagon infusion failed to cause insulin secretion in fetal lambs. The results suggested the cyclic-3′,5′-AMP dependent part of the insulin secretory mechanism does not develop fully before the last week of gestation.

Gel filtration of fetal plasma on Sephadex indicated that the immunoreactive material present was insulin. No significant amounts of proinsulin were found.

Bates, Robert W.; and Garrison, Mary M. (Sect. on Endocr., Lab. of Nutrition and Endocr., National Inst. of Arthritis and Metabolic Diseases, National Inst. of Health, Bethesda, Md.): STUDIES IN EIGHTY PER CENT PANCREATECTOMIZED RATS OF THE SYNERGISTIC INTERACTION OF GROWTH HORMONE, ACTH AND THE GLUCOCORTICOIDS (CORTICOSTERONE, CORTISOL, PREDNISONE AND DEXAMETHASONE) AS DIABETOGENIC AGENTS. Endocrinology 88:1429-36, June, 1971.

The diabetogenic effects of glucocorticoids given alone or in combination with ACTH or bovine growth hormone (BGH) were studied in pancreatectomized rats. The minimal effective dose producing glycosuria in five days was corticosterone, 10 mg.; cortisol, 3 mg.; prednisone acetate, 1 mg.; and dexamethasone, 50 mg. The two glucocorticoids, cortisol and dexamethasone, were synergistic when injected together. When each glucocorticoid was injected with ACTH or BGH, the effectiveness of cortisol was additive to that of BGH whereas the others showed partial synergism with BGH, with dexamethasone showing the greatest synergism. Dexamethasone synergized with ACTH as well as with BGH, whereas the other glucocorticoids gave partial synergism. These studies on the induction of glycosuria suggest that in the rat, adrenal steroids other than corticosterone are produced under the influence of ACTH stimulation and that they have a diabetogenic action differing from that of corticosterone. C.R.S.

Baum, David; and Porte, Daniel, Jr. (Depts. of Pediat. & Med., Univ. of Washington Sch. of Med., and Veterans Administration Hosp., Seattle, Wash.): ALPHA-ADRENERGIC INHIBITION OF IMMUNOREACTIVE INSULIN RELEASE DURING DEEP HYPOTHERMIA. Amer. J. Physiol. 221:303-11, July, 1971.

The inhibitory effect of deep hypothermia on immunoreactive insulin (IRI) release was investigated in puppies. Despite marked hyperglycemia, plasma IRI remained at baseline levels in hypothermic puppies given glucose infusions. Plasma IRI elevation following glucagon administration was less during hypothermia than with euthermia although plasma glucose increases were similar in both circumstances. Phentolamine-induced *a*-adrenergic blockade resulted in pronounced plasma IRI rises in hypothermic animals with or without concomitant glucose infusion. In contrast, glucose infusion in euthermic puppies resulted in substantive plasma IRI increases, while phentolamine produced little or no change in IRI. Propranolol-induced *B*-adrenergic blockade at low body temperature did not evoke IRI release. When given with phentolamine, propranolol did not alter IRI release associated with *a*-adrenergic blockade. Although producing hypotension and probable vasodilation similar to phentolamine, neither diazoxide nor hydra-

lazine reversed inhibition of IRI release in hypothermic animals. Observations are interpreted to demonstrate that IRI release is inhibited in deeply hypothermic puppies by *a*-adrenergic receptor stimulation and suggest intrinsic adrenergic regulation of plasma insulin. J.D.G.

Calvayrac, Regis; Van Lente, Fred; and Butow, Ronald A. (Dept. of Biochem. Sciences, Frick Chem. Lab., Princeton Univ., Princeton, N. J.): EUGLENA GRACILIS: FORMATION OF GIANT MITOCHONDRIA. Science 173:252-54, July 16, 1971.

The addition of antimycin A to cultures of a bleached strain of Euglena gracilis in the logarithmic phase of growth on succinate as a carbon source results in interruption of growth for twenty-four hours, an increase in whole-cell respiration, and the emergence of a novel succinoxidase activity within two to four hours. After three to five hours, mitochondria enlarge, fuse, and form a sheathlike structure situated close to the periphery of the cell. J.D.G.

Chalkley, Sylvia R.; and Tanner, J. M. (Dept. of Chem. Path. and Growth and Development, Inst. of Child Health and The Hosp. for Sick Children, London, England): INCIDENCE AND EFFECTS ON GROWTH OF ANTIBODIES TO HUMAN GROWTH HORMONE. Arch. Dis. Child. 46:160-66, April, 1971.

An immunochemical method for the detection of growth hormone antibodies in sera was employed in this study. Serum samples were obtained from ninety-eight children who had received parenteral human growth hormone for growth retardation for periods of six months to seven years. Thirty-eight patients had isolated growth hormone deficiency and the remainder was comprised of twenty-one children with acquired pituitary lesions and thirty-nine with short stature probably not due to growth hormone privation. Antibody titers in these sera were quantitated against reference standards and the results were compared to analyses of sera from fifty-one children who had never received the hormone.

Antibodies were not present in sera of any patients before treatment, nor were they detected in untreated control subjects. Of the ninety-eight subjects receiving growth hormone, four developed significantly elevated antibody titers. All were in the group with isolated growth-hormone deficiency. Two children had permanent resistance to the growth-promoting effects of the hormone. The other two had evanescent resistance which spontaneously disappeared within a few months despite continuation of parenteral injections. The improved response was associated with a fall of antibody titers to lower levels.

The authors conclude that pediatric patients with isolated growth-hormone deficiency may have a greater predilection to develop antibody-induced growth hormone resistance. They also point out that such resistance is by no means permanent in all cases. R.K.K.

Despopoulos, Agamemnon (With the Technical Assistance of April Kopp and Quita Simms) (Dept. of Physiol., Sch. of Med., Univ. of New Mexico, Albuquerque, N. Mex.): CONGRUENCE OF RENAL AND HEPATIC EXCRETORY FUNCTIONS: SULFONIC ACID DYES. Amer. J. Physiol. 220:1755-58, June, 1971.

Hepatic excretion of sulfonic acid dyes was examined in isolated perfused rat liver. Slices of rabbit kidney cortex were used as an experimental model of renal tubular excretory transport process in intact kidney. In kidney, dyes showed the same pattern of transport as 4-aminohippurate: slice-to-medium concentration ratios were greater than unity in control experiments, were increased in presence of acetate, and were decreased in presence of probenecid or in anoxia. The process in liver demonstrated concentration of the same dyes in bile several times above concentrations in perfusion fluid. Administration of probenecid was followed by a prompt fall in bile to perfusion fluid concentration ratios and in rates of excretion. These parallelisms contribute to the concept that kidney and liver share a common transport process for organic acids. J.D.G.

Efendic, S.; Cerasi, E.; and Luft, R. (Dept. of Endocr. and Metabolism, Karolinska Hosp., Stockholm, Sweden): ROLE OF GLUCOSE IN ARGININE-INDUCED INSULIN RELEASE IN MAN. Metabolism 20:568-79, June, 1971.

The plasma IRI response in five healthy subjects to intravenous arginine is markedly diminished during insulin-induced hypoglycemia. This effect is not due to catecholamine secretion during hypoglycemia since infusions of epinephrine fail to suppress the IRI response to arginine. Thus, the insulinogenic action of arginine requires a normal blood glucose concentration. The relationship between glucose and arginine was manifested by a marked enhancement of insulin secretion when the intravenous glucose infusion was preceded by administration of arginine. When hyperglycemia was produced by epinephrine infusion, no synergism could be demonstrated between arginine and elevated blood glucose on insulin secretion. When the epinephrine infusion was stopped an immediate, marked insulin peak was obtained. These findings indicate that synergism between glucose and arginine occurs only when glucose is able to elicit insulin release. The mechanism by which arginine stimulates insulin release appears to operate through the insulinogenic signal evoked by glucose and not through a direct effect on insulin secretion. C.R.S.

Elkeles, R. S.; Lowy, C.; Wyllie, A. D. H.; Young, J. L.; and Fraser, T. Russell (Endocrine Unit, Dept. of Med., Royal Postgrad. Med. Sch., London, England): SERUM INSULIN, GLUCOSE, AND LIPID LEVELS AMONG MILD DIABETICS IN RELATION TO INCIDENCE OF VASCULAR COMPLICATIONS. Lancet 1:880-83, May 1, 1971.

This study was done to determine if a correlation between vascular complications (such as retinopathy, neuropathy and peripheral arterial insufficiency) and chemical findings (such as fasting and sixty-minute blood glucose and insulin and fasting triglyceride and cholesterol levels) could be found in maturity-onset noninsulin-requiring diabetics. When the log of the concentration of serum insulin sixty minutes after a 50 gm. glucose load was plotted against the concentration of blood sugar the regression line of insulin on glucose showed an inverse correlation. This line was used to separate the 117 diabetics into groups having a "moderate insulin response" and a poor insulin response. It was found that the vascular complications were not necessarily associated with either raised levels of triglyceride or cholesterol and that there were more complications in subjects with a poor insulin response than in those with a moderate insulin response. The poor response group had lower triglyceride levels than the moderate response group. The data suggest that poor insulin response could be related to shunting of glucose to noninsulin-dependent pathways leading to increased production of glycoprotein, which in turn could lead to the basement membrane proliferation seen in diabetic microangiopathy. T.G.S.

Gagliardino, Juan José; and Hernández, Rodolfo Eduardo (Laboratorio de Endocrinología Experimental, Inst. de Fisiología, Facultad de Ciencias Médicas, Universidad Nacional de La Plata, Buenos Aires, Argentina): CIRCADIAN VARIATION OF THE SERUM GLUCOSE AND IMMUNOREACTIVE INSULIN LEVELS. Endocrinology *88*:1529-31, June, 1971.

Serum glucose and IRI levels in mice display a clear circadian rhythm having their highest and lowest values located in the resting (light) and activity (darkness) period respectively. The levels are not hourly coincident since the glucose peak preceded the insulin peak by four hours. This fact is explained on the basis of hormonal interaction during the day and indicates the importance of chronobiology in endocrine studies. C.R.S.

Hockaday, Judith M.; Williamson, D. H.; and Whitty, C. W. M. (Dept. of Neurol., United Oxford Hosp. and Metabolic Res. Lab., Radcliffe Infirmary, Oxford, England): BLOOD GLUCOSE LEVELS AND FATTY ACID METABOLISM IN MIGRAINE RELATED TO FASTING. Lancet *1*:1153-56, June 5, 1971.

In susceptible individuals fasting precipitates an attack of migraine and either a low blood sugar or a fall in blood sugar have been proposed as trigger factors. Ten patients were selected either because they related their migraine attacks to fasting or the symptom of undue hunger. Each was fasted overnight and at 8 a.m. was given 50 gm. of glucose orally. Blood was collected at half-hour intervals for four hours. Measurements of glucose, FFA, ketone bodies and glycerol were also made. In six patients a migraine attack occurred between one and three-and-one-half hours after the oral glucose. There was no difference in glucose levels between those with and without headache either during or subsequent to the GTT. In the headache group, FFA levels and ketone rose to higher levels after the initial fall. Glycerol concentrations did not differ between groups. The data suggest that rising FFA levels may be either an associated or causative factor in the genesis of this variety of migraine. T.G.S.

Kaplan, B. S.; Gale, Diana; and Ipp, Tania (Dept. of Pediat., Univ. of the Witwatersrand, Johannesburg, South Africa; and Sch. of Path., South African Inst. for Med. Res., Univ. of the Witwatersrand, Johannesburg, South Africa): HYPERLIPIDEMIA IN THE HEMOLYTIC-UREMIC SYNDROME. Pediatrics *47*:776-79, April, 1971.

Other laboratories have described the existence of hypertriglyceridemia in nonnephrotic chronic renal disease. In the present study, six pediatric patients, aged eight to twenty-four months, who presented with the hemolytic-uremic syndrome, were evaluated for lipid disturbances. All of the six children had elevated serum triglyceride, cholesterol and phospholipid concentrations at some time during the course of their disease. It was concluded that this syndrome, like certain other forms of renal disease, is associated with marked abnormalities in lipid metabolism. R.K.K.

Lubchenco, Lula O., and Bard, Harry (Newborn and Premature Center, Div. of Perinatal Med., Univ. of Colorado Med. Center, Denver, Colo.): INCIDENCE OF HYPOGLYCEMIA IN NEWBORN INFANTS CLASSIFIED BY BIRTH WEIGHT AND GESTATIONAL AGE. Pediatrics *47*:831-38, May, 1971.

Blood glucose levels were measured in 374 newborn infants three to six hours after birth before their first feeding and again at three to four days of age after short-term fasting. All neonates were placed in one of three classes: (1) small for gestational age (SGA), (2) appropriate size for gestational age (AGA) and (3) large for gestational age (LGA). The three classes were further subdivided into preterm, term and postterm parturitions. Hypoglycemia was defined as a blood glucose below 30 mg./100 ml.

In each of the three classes the highest incidence of hypoglycemia was in the preterm groups with gestational ages under thirty-eight weeks. SGA infants also had significantly greater frequencies of hypoglycemia regardless of gestational age, than did AGA or LGA neonates. Infants of diabetic mothers were predominantly in the LGA group. Among infants with neonatal hypoglycemia there was also greater incidence of perinatal distress including hypoxia, as well as evidence of malnutrition.

The authors suggest that SGA infant hypoglycemia is related to inadequate carbohydrate reserves that are necessary for the maintenance of euglycemia early in life. The added stress of hypoxia may accelerate glucose utilization and compound the problem. R.K.K.

Mudd, S. Harvey (Lab. of Gen. and Comparative Biochem., National Inst. of Mental Health, Bethesda, Md.): PYRIDOXINE-RESPONSIVE GENETIC DISEASE. Fed. Proc. 30:970-76, June, 1971.

Clinical or chemical abnormalities characteristic of certain genetic diseases respond to amounts of B_6 many times the normal recommended intake. The biochemical mechanisms underlying such responsiveness are reviewed. The diseases are more specific than would be expected were they due to failure to convert dietary forms of B_6 to coenzymatically active forms. Three B_6-responsive genetic diseases in which enzyme deficiency is known can be largely overcome by elevated concentrations of the cofactor. In contrast, the B_6 response in patients with homocystinuria due to cystathionine synthase deficiency is usually not due to restoration of a close-to-normal activity of the affected enzyme, but may be due to a small enhancement of the residual enzyme activity. The B_6-responsive diseases suggest that enhancement of residual enzyme activities may be an effective means of treating inborn metabolic errors. J.D.G.

Rizza, R. A.; Crass, M. F., III; and Shipp, J. C. (Dept. of Med., Univ. of Florida Coll. of Med., Gainesville, Fla.): EFFECT OF INSULIN TREATMENT IN VIVO ON HEART GLYCERIDES AND GLYCOGEN OF ALLOXAN-DIABETIC RATS. Metabolism 20:539-43, June, 1971.

Alloxan-diabetic rats were found to have a two- to threefold increase in glyceride and glycogen content of heart muscle. The rise in heart glycerides and glycogen and the concentrations of serum FFA were maximal at thirty-six hours while serum glucose continued to rise. Insulin given at twenty-four hours after alloxan restored heart glycerides to normal in twenty-four hours and reduced heart glycogen, FFA, and serum glucose concentrations. Heart glycogen and serum FFA were normal twenty-four hours after insulin treatment. C.R.S.