ABSTRACTS

Amend, William J.C., Jr.; Steinberg, Steven M.; Lowrie, Edmund G.; Lazarus, J. Michael; Soeldner, J. Stuart; Hampers, C.L.; and Merrill, John P. (Renal Div. and E.P. Joslin Res. Lab., Dept. of Med., Harvard Med. Sch., Boston, Mass.): THE INFLUENCE OF SERUM CALCIUM AND PARATHYROID HORMONE UPON GLUCOSE METABOLISM IN UREMIA. J. Lab. Clin. Med. *86*:435-44, September 1975.

The uremic state is associated with impaired glucose tolerance, which may be associated with impaired peripheral glucose utilization and/or abnormal insulin secretion. Because insulin hyperresponsiveness without alteration in glucose disappearance has been described in hyperparathyroidism and since intravenous insulin administration is associated with a blunted glucose disappearance, both an increase in parathormone and changes in calcium ion concentration have been implicated as possible factors in the glucose intolerance of uremia. In this study, six normal-weight uremic women who were being treated by chronic dialysis were studied before and after parathyroidectomy and during states in which calcium was either elevated or depressed. Carbohydrate metabolism was assessed by intravenous glucose tolerance tests (IVGTT) and intravenous insulin tolerance tests (ITT). Parathyroidectomy per se had little effect on glucose disappearance or insulin responsiveness, but either an excess or a deficiency in serum calcium influenced insulin secretion and glucose disposal. Acute lowering of serum calcium produced a reduction in glucose disappearance and insulin responsiveness but not glucose lowering, as determined by insulin administration. Acute elevations of serum calcium also caused decreased glucose tolerance but little change in insulin secretion. The authors conclude that secondary hyperparathyroidism and parathyroid hormone levels per se are of little importance in the pathogenesis of the glucose intolerance of uremia. However, hypocalcemia may blunt insulin responsiveness and operate as a factor. T.G.S.

Brockman, Ronald P.; and Bergman, E.N. (Dept. of Physiol., Biochem., and Pharmacol., N.Y. State Veterinary Coll., Cornell Univ., Ithaca, New York): EFFECT OF GLUCAGON ON PLASMA ALANINE AND GLUTAMINE METABOLISM AND HEPATIC GLUCONEOGENESIS IN SHEEP. Am. J. Physiol. *228*:1627-33, June 1975.

Verbatim summary. Net hepatic uptakes of plasma alanine (Ala), glutamate (Glu), and glutamine (Gln) were measured before and during intraportal glucagon infusions in five normal and four insulin- and alloxan-treated (ITA), conscious, fed sheep. Since hyperinsulinemia is associated with glucagon administration, ITA sheep were used so that constant plasma insulin levels could be maintained. Glucose turnover was determined by a venacaval infusion of glucose-6-^{3}H. In addition, in ITA sheep, Ala-^{14}C was infused for measurement of plasma Ala turnover, its unidirectional organ metabolism, and contribution to glucose synthesis. During infusion of glucagon, the net hepatic uptake of Ala increased significantly ($p < 0.01$) from control values of 3.8 ± 0.5 and 2.7 ± 0.6 mmol/hr. to 5.9 ± 1.0 and 5.5 ± 0.8 mmol/hr. in normal and ITA sheep, respectively. Similarly, Gln uptake increased from 4.3 ± 1.4 and 1.6 ± 0.5 to 5.5 ± 1.6 and 3.7 ± 1.0 mmol/hr., respectively. The conversion of Ala to glucose increased from control values of 1.7 ± 0.5 to 3.0 ± 0.5 mmol/hr. Arterial plasma Ala and Gln concentrations decreased about 25 per cent during glucagon administration, presumably as a result of their increased hepatic uptakes. A decrease in utilization of plasma Ala, but no change in production, was calculated for the nonhepatic tissues, indicating that glucagon increased gluconeogenesis from Ala at the expense of muscle protein synthesis. Glucagon thus has a direct effect on the liver but only an indirect effect on other tissues.

Brodows, Robert G.; Pi-Sunyer, F. Xavier; and Campbell, Robert G. (Endo-Metab. Unit, Monroe Comm. Hosp., Dept. of Med., Univ. of Rochester Sch. of Med. & Dentistry, Roch., N.Y. & Med. Serv., St. Luke's Hosp. Center & Dept. of Med., Columbia Univ., N.Y., N.Y.): SYMPATHETIC CONTROL OF HEPATIC GLYCOGENOLYSIS DURING GLUCOPENIA IN MAN. Metabolism *24*:617-25, May 1975.

Spontaneous reversal of hypoglycemia dependent on mobilization of hepatic glycogen can be mediated by release of adrenomedullary catecholamines, enhanced glucagon secretion, or release of norepinephrine from sympathetic nerve endings. The role of these mechanisms was examined by infusing 2-deoxy-d-glucose (2-DG) intravenously into normal volunteers and adrenalectomized patients for 20 minutes to induce cellular glucopenia. In normals, the rise in FFA and growth hormone (HGH) corresponded with the rise in total catecholamines; lactate and cortisol rose more slowly, and no change in immunoreactive insulin was noted. Plasma glucose levels rose significantly and remained elevated. In adrenalectomized patients the plasma glucose rose also, despite no change in FFA, lactate, catecholamines, and glucagon; the HGH and IRI responses were similar to those of normals. These observations demonstrate that plasma glucose is raised during glucopenia despite unchanged adrenomedullary catecholamine and glucagon levels. The sympathetic neurotransmitter norepinephrine appears to contribute to the counterregulatory events during 2 DG-induced glucopenia, presumably because of its release from hepatic sympathetic nerve endings. C.R.S.

Day, J.L. (Ipswich Hosp., Anglesea Road Wing, Ipswich, England): PROGRESS IN ENDOCRINOLOGY AND METABOLISM—THE METABOLIC CONSEQUENCES OF ADRENERGIC BLOCKADE: A REVIEW. Metabolism *24*:987-96, August 1975.

In this review the metabolic actions of adrenergic blocking agents on plasma insulin, glucagon, HGH, and lipid metabolism are summarized. Basal insulin is slightly inhibited by beta- and enhanced by alpha-adrenergic blockade; more marked suppression is achieved under circumstances of high exogenous or endogenous catecholamine stimulation. Glucagon release is probably stimulated by beta- and inhibited by alpha-stimulation. Muscle glycogenolysis is inhibited by propranolol, and, under conditions of hepatic glycogen depletion, hypoglycemia may occur. HGH release is enhanced by beta-adrenergic blockade. FFA formation is inhibited by intravenous beta-blockade, but the effects of oral administration on TG and lipoprotein profiles remain uncertain. While interrelationships of adrenergic blockade at different sites

of hormone and substrate release are unclear, they appear to have important effects on carbohydrate and lipid metabolism. C.R.S.

DeFronzo, Ralph A.; Cooke, C. Robert; Andres, Reubin; Faloona, Gerald R.; and Davis, Paul J. (Clin. Phys. Br., GRC, NICH & HD, NIH, Baltimore, Md., Dept of Med., Johns Hopkins, Baltimore, Md.; V.A. Hosp., Dept. of Biochemistry, Univ. of Tex., Dallas; and Dept. of Med., Baltimore City Hosp., Baltimore Maryland): THE EFFECT OF INSULIN ON RENAL HANDLING OF SODIUM, POTASSIUM, CALCIUM, AND PHOSPHATE IN MAN. J. Clin. Invest. 55:845-55, April 1975.

A primary effect of insulin on the kidney is usually obscured by its systemic effects, which secondarily affect renal mechanisms. In an effort to study these effects, six normal subjects who were in a state of water diuresis were given a continuous intravenous infusion of insulin while blood glucose was maintained constant by a variable glucose infusion. In this manner, glomerular filtration rate, renal blood flow, filtered load of glucose, and plasma aldosterone were unchanged. With a rise in mean plasma insulin of 12 to 149 μU./ml., a significant fall in urinary sodium of 401 to 213 μEq./min. was observed while serum sodium remained constant; free water clearance increased significantly while osmolar clearance decreased and urine flow was constant. In addition, plasma and urine potassium and phosphorus decreased, and plasma calcium remained unchanged while urine calcium increased. Plasma glucagon decreased from 97 to 74 pg./ml. during insulin infusion. The demonstrated reduction in urinary sodium with insulin administration in the absence of changes in other known mediators of sodium excretion suggests an effect of insulin on the renal tubule, specifically the distal nephron, in view of the effect on free water clearance. These studies may help explain the sodium retention in patients after being placed on insulin or in fasted subjects during carbohydrate refeeding. R.R.

Feldman, Jerome M.; and Chapman, Barbara (Durham V.A. Hosp. & Div. of Endocr., Dept. of Med., Duke Univ. Med. Center, Durham, N.C.): CHARACTERIZATION OF PANCREATIC ISLET MONOAMINE OXIDASE. Metabolism *24*:581-88, May 1975.

Pancreatic islets of many species contain the monoamines dopamine, serotonin, and norepinephrine, which are capable of inhibiting insulin secretion. Islets of rabbits, golden hamsters, and rats were found to contain monoamine oxidase (MAO), the properties of which have been compared to those of hepatic MAO. Both liver and islet MAO have comparable sensitivity to MAO inhibitors, such as pargyline and tranylcypromine. The present studies suggest that islet MAO may modify insulin secretion. C.R.S.

Friedman, Sandor A.; Schulman, Robert H.; Weiss, Steven (Coney Island Hosp. Maimonides Med. Center; State Univ. of N.Y., Downstate Med. Center; & Albert Einstein Coll. of Med., Brooklyn, N.Y.): HEARING AND DIABETIC NEUROPATHY. Arch. Intern. Med. *135*:573-76, April 1975.

Twenty diabetic patients who had neither auditory symptoms nor histories of ear disease were studied. All 20 had symptomatic neuropathy. Thirty-two age-matched controls were also studied. Audiometry showed that 11 of the diabetics had symmetrical hearing loss of at least one frequency in the range from 125 to 8,000 cps. The impaired hearing of the diabetics was apparent even when the data were stratified to correct for age-related hearing loss. The deafness was of the sensorineural type, thought possibly related to dysfunction of the eighth nerve, although cochlear lesions could not be excluded. Both high and low frequencies were affected, in contrast to the pattern of presbycusis, which selectively affects high frequencies. The authors speculate that an eighth-nerve neuropathy may be part of the spectrum of diabetic neuropathy and might also account for otherwise unexplained vertigo in some diabetics.

Comment: As the authors recognize, it will be of interest to measure hearing in diabetics without severe symptomatic peripheral neuropathy. Such data would provide an index of the true prevalence of hearing loss among diabetics and would also provide a clue to the relationship between this disorder and neuropathy. V.R.L.

Greene, Douglas A.; De Jesus, Pacifico V., Jr.; and Winegrad, Albert I. (Geo. S. Cox Med. Res. Inst., Dept. of Med. and Dept. of Neurol., Univ. of Pa. Sch. of Med., Phila., Pa.): EFFECTS OF INSULIN AND DIETARY MYOINOSITOL ON IMPAIRED PERIPHERAL MOTOR NERVE CONDUCTION VELOCITY IN ACUTE STREPTOZOTOCIN DIABETES. J. Clin. Invest. *55*:1326-36, June 1975.

The effect of insulin and myoinositol on the impaired peripheral-motor-nerve conduction velocity (MNCV) in rats was studied 14 days after induction of diabetes with streptozotocin. Untreated diabetic rats with weight loss and hyperglycemia had a significantly decreased MNCV when compared with normal rats. Although all diabetic animals treated with insulin maintained a normal weight, those with inadequately controlled hyperglycemia showed no improvement in MNCV; however, in a group of animals in which hyperglycemia was prevented by frequent adjustment in the insulin dose based on blood sugar determinations, MNCV remained normal. Plasma free myoinositol was similar in all animals, but nerve free myoinositol content correlated with MNCV; adequately controlled diabetic animals with normal MNCV showed levels similar to those of controls, and inadequately controlled animals with impaired MNCV showed a decreased nerve free myoinositol. Control and untreated diabetic animals were given supplemental dietary myoinositol and were shown to have an elevated plasma and nerve myoinositol; in spite of uncontrolled diabetes with marked hyperglycemia and weight loss, the myoinositol-treated diabetic animals had a normal MNCV. Sorbitol and fructose concentrations of the nerve were elevated in the diabetic animals, and there was no change with myoinositol supplements. Thus, the development of impaired MNCV in rats with acute streptozotocin diabetes can be prevented by control of hyperglycemia and appears to be related to an alteration in nerve free myoinositol that can be modified by dietary factors. R.R.

Guisado, Raul; and Arieff, Allen I. (Depts. of Med. & Neurol. V.A. Hosp., San Francisco, Ca., & Depts. of Med. & Neurol., Univ. of California Sch. of Med., San Francisco, Calif.): NEUROLOGIC MANIFESTATIONS OF DIABETIC COMAS: CORRELATION WITH BIOCHEMICAL ALTERATIONS IN THE BRAIN. Metabolism *24*:665-79, May 1975.

Coma and other neurologic abnormalities observed in patients with either diabetic ketoacidosis (DKA) or nonketotic coma (NKC) may result from the interaction of a series of abnormalities.

In DKA, cerebral oxygen utilization is impaired; hyperviscosity and hyperosmolality are present; hyperketonemia may depress the sensorium; impairment of phosphofructokinase activity and pyruvate oxidation together with citrate accumulation have been demonstrated. Patients with NKC manifest a variety of neurologic disorders that revert to normal after correction of the hyperosmolality. Gamma amino butyric acid, which has been shown to elevate the seizure threshold, is normal in brains of ketoacidotic animals but may be low in nonketotic coma. Cerebral edema may complicate the treatment of either DKA or NKC. This condition may result from the direct action of insulin on the brain when plasma glucose decreases toward normal and may be avoided by stopping insulin therapy when plasma glucose lowering is progressing. C.R.S.

Hellman, Bo (Dept. of Histol., Univ. of Umeå, Umeå, Sweden): THE SIGNIFICANCE OF CALCIUM FOR GLUCOSE STIMULATION OF INSULIN RELEASE. Endocrinology *97*:392-98, 1975.

The effects of alterations in calcium concentration on glucose-stimulated insulin release and cyclic AMP levels in microdissected pancreatic islets from ob-ob mice were studied in vitro. In the absence of added extracellular calcium, glucose-stimulated insulin release was inhibited. Addition of extracellular calcium up to concentrations of 10 millimolar resulted in progressive increase in insulin responses to glucose. Beta-cell responses to glucose were inhibited with higher concentrations of calcium. Qualitatively similar results were obtained in studies performed after addition of 3-isobutyl-1-methylxanthine, a potent phosphodiesterase inhibitor. Alterations of calcium concentration did not change either islet or medium cyclic AMP content, although changes in insulin release were observed. In the presence of 3-isobutyl-1-methylxanthine, both cyclic AMP and insulin release were augmented; however, fluctuations in calcium concentration altered insulin release but not islet or medium cyclic AMP content. The effect of pH on insulin release at various concentrations of calcium was studied. Irrespective of the calcium concentration, basal insulin release increased with increasing pH. In additional studies, lanthanum, which has a high affinity for calcium-binding sites and is not known to penetrate intracellularly, was used to examine the interrelationship between calcium, cyclic AMP, and insulin secretion. Addition of lanthanum diminished both basal and glucose-stimulated insulin release even in the presence of 1-3-isobutyl-1-methylxanthine. The present studies support an important role of extracellular calcium in mediating glucose-induced insulin secretion. Since insulin secretion was inhibited in the absence of extracellular calcium and augmented with increasing pH, it was suggested that the hydrogen ion may compete for calcium-binding sites, thereby diminishing insulin secretion. Furthermore, the calcium effects on insulin secretion appear to be independent of an action on adenylate cyclase, since alterations in calcium concentration affected insulin release without changing intracellular cyclic AMP levels in control studies and in the presence of a potent phosphodiesterase inhibitor. J.E.G.

Henquin, Jean-Claude; and Lambert, André E. (Unité de Diabète et Croissance, Univ. of Louvain Sch. of Med., St. Pierre Hosp., Louvain, Belgium): COBALT INHIBITION OF INSULIN SECRETION AND CALCIUM UPTAKE BY ISOLATED RAT ISLETS. Am. J. Physiol. *228*:1669-77, June 1975.

Verbatim summary. Cobalt (Co^{++}) inhibited glucose-, leucine-, and K^{+}-induced immunoreactive insulin (IRI) release by isolated rat islets. This inhibition of the insulinotropic effect of glucose was dose-dependent, affected both phases of secretion, was very rapid, and was well reversible. It exhibited a kinetics similar to that of Ca^{++} omission, and the metal (2.5 mM) prevented Ca^{++} reintroduction from restoring a normal rate of IRI release. Theophylline (2 mM) partially overcame the inhibitory effect of 0.5 mM Co^{++} but not that of 2.5 mM. Glucose-induced secretion was less markedly reduced by 0.5 mM Co^{++} in the absence of Mg^{++} or in the presence of 7.5 mM Ca^{++}. Even at 12.5 mM, the metal did not alter glucose oxidation by the islets. By contrast, Ca uptake by islet cells was reversibly diminished (55 per cent) in the presence of 1.25 mM Co^{++}. Calcium influx (measured after 2.5 min.) was also reduced by Co^{++} to a degree that did not change after longer incubation periods. It is concluded that Co^{++} inhibits IRI release mainly through an antagonistic action on Ca entry in beta cells.

Joosten, Harrie F.P.; van der Kroon, Piet H.W.; and Buis, Anton J.M. (Dept. of Genetics, Univ. of Nijmegen, Nijmegen, The Netherlands): DEVELOPMENT OF THE OBESE-HYPERGLYCEMIC SYNDROME IN MICE WITH A GROWTH HORMONE DEFICIENCY. Metabolism *24*:573-79, May 1975.

By selective matings of mice heterozygous for the recessive gene obese with mice homozygous for the recessive gene dwarf and by subsequent matings of the offspring, mice homozygous for both obese and dwarf genes were obtained. The homozygous obese dwarf mice develop obesity and hyperinsulinemia with hyperglycemia not significantly different from that of nonobese dwarf mice. These observations demonstrate that obesity and hyperinsulinemia can develop under conditions of extreme growth-hormone deficiency. C.R.S.

Krotkiewski, Marcin; Sjostrom, Lars; Bjorntorp, Per; and Smith, Ulf (Clin. Metabolic Lab. of the Dept. of Med. I, Depts. of Medicine II, and Clncl. Rehab. I, Univ. of Goteborg, Sahlgren's Hosp., Gothenberg, Sweden): REGIONAL ADIPOSE TISSUE CELLULARITY IN RELATION TO METABOLISM IN YOUNG AND MIDDLE-AGED WOMEN. Metabolism *24*:703-10, June 1975.

Body composition and total number of fat cells were investigated in young and middle-aged women. Regional determinations of adipose-tissue thickness and fat-cell size and number were made, demonstrating the highest degrees of correlation in fat-cell sizes between epigastric and hypogastric regions and between femoral and gluteal regions. The plasma insulin levels correlated with the fat-cell sizes of the abdominal region but not with the femoral and gluteal regions. These data suggest that the fat cells of the abdominal region are more sensitive to nutritional and hormonal factors than those of other regions and imply the existence of different fat-cell populations. C.R.S.

Lamberts, S.W.J.; Timmermans, H.A.T.; Kramer-Blankestijn, M.; and Birkenhager, J.C. (Dept. of Int. Med. & Clinical Endocr.; Univ. Hosp. "Dijkzigt," Rotterdam, The Netherlands): THE MECHANISM OF THE POTENTIATING EFFECT OF GLUCOCORTICOIDS ON CATECHOLAMINE-INDUCED LIPOLYSIS. Metabolism *24*:681-89, June 1975.

Protein kinase activity was measured in homogenates of fat-cell suspensions after preincubation of rat epididymal fat with and without dexamethasone. Homogenates of epididymal fat-cell suspensions of control and cortisol-treated rats were studied simi-

larly. In both types of experiments, a higher cAMP-dependent protein kinase activity was observed after treatment with glucocorticoids. It was concluded that the induction of protein kinase by glucocorticoid hormone is responsible for the stimulatory action of this hormone upon lipolysis, augmenting both epinephrine and glucagon-induced lipolysis. C.R.S.

Lyall, Santokh S.; Marieb, Norman J.; Wise, Jonathan; Cornog, John L.; Neville, Edwin C.; and Felig, Philip (Hosp. of St. Raphael & Dept. of Intern. Med., Yale Univ. Sch. of Med., New Haven, Conn.): HYPERINSULINEMIC HYPOGLYCEMIA ASSOCIATED WITH A NEUROFIBROSARCOMA. Arch. Intern. Med. *135*:865-67, June 1975.

An 82-year-old woman had severe fasting hypoglycemia associated with a 680-gm. malignant neurofibrosarcoma in the left posterior mediastinum. Preoperatively, fasting plasma insulin was elevated despite hypoglycemia, and there was no increment of plasma immunoreactive glucagon following infusion of alanine. Following removal of the tumor, fasting glucose levels returned to normal, as did insulin levels. However, immunoreactive glucagon responses to alanine remained less than in normal young adults. No extractable immunoreactive insulin was detected in the tumor. The authors postulate that the tumor may have been producing a substance that stimulated pancreatic secretion of insulin and inhibited secretion of glucagon.

Comment: It should be remembered that this case is an exception—most cases of mesodermal tumors associated with hypoglycemia have not had elevated plasma insulin levels. V.R.L.

Ma, King W.; Masler, Donald S.; and Brown, David C. (Nephrol. Sec., Minneapolis V.A. Hospital, & Dept. of Med., Univ. of Minnesota, Minneapolis, Minn.): HEMODIALYSIS IN DIABETIC PATIENTS WITH CHRONIC RENAL FAILURE. Ann. Intern. Med. *83*:215-17, 1975.

Verbatim summary. Eighteen male diabetic patients with a mean age of 48.5 years and end-stage renal disease were maintained on chronic hemodialysis for a mean duration of 15.2 months. The cumulative survival rate for the first year was 86 per cent. Their diabetes was no more difficult to control after starting hemodialysis. Cardiovascular complications accounted for the two deaths and most of the management problems. Patient rehabilitation was considered to be satisfactory. It is concluded that chronic hemodialysis can be a suitable form of therapy in this group of patients.

Maruhama, Yoshisuke; Ohneda, Akira; Tadaki, Hiroshi; Ohtsuki, Masao; Yanbe, Akira; Abe, Ryuzo; and Yamagata, Shoici (Third Dept. of Intern. Med., Tohoku Univ. Sch. of Med., Seiryocho, Sendai, Japan): HEPATIC STEATOSIS AND THE ELEVATED PLASMA INSULIN LEVEL IN PATIENTS WITH ENDOGENOUS HYPERTRIGLYCERIDEMIA. Metabolism *24*:653-64, May 1975.

In patients with hypertriglyceridemia, hepatic steatosis was demonstrated in over 50 per cent on histologic examination of biopsied specimens. All patients showed increased responses in both immunoreactive insulin and plasma glucose to an oral glucose load over that of control subjects. These responses were more exaggerated in the patients with steatosis than in the group without steatosis. Analysis of variables in these patients, with liver triglyceride as the dependent variable, revealed that plasma insulin was the most closely related variable and the blood glucose level the next. The decay of injected insulin in plasma was not delayed in patients with steatosis, but insulin sensitivity following intravenous administration of insulin was significantly decreased in all hypertriglyceridemic patients. Thus, the hyperinsulinemia was considered to be due to increased insulin secretion associated with decreased insulin sensitivity. It is likely that elevated plasma insulin and blood glucose levels are essential abnormalities in patients with endogenous hypertriglyceridemia, which, in extreme cases, might lead to massive triglyceride accumulation in the liver. C.R.S.

McMonagle, James; and Felig, Philip (Dept. of Intern. Med., Yale Univ. Sch. of Med., New Haven, Conn.): EFFECTS OF ETHANOL INGESTION ON GLUCOSE TOLERANCE AND INSULIN SECRETION IN NORMAL AND DIABETIC SUBJECTS. Metabolism *24*:625-32, May 1975.

Ethanol administered hourly prior to the ingestion of a glucose load in a group of normal subjects and mild diabetic patients resulted in a fall in blood glucose and a rise in the early insulin-secretory response. Ethanol intake had no effect on the glucagon response to glucose ingestion. These data suggest that ethanol enhances glucose-stimulated insulin secretion; the suppressed blood glucose rise may be related to the augmented insulin response or to reduced gastrointestinal absorption of glucose. In mild diabetes, moderate intake of ethanol is without acute deleterious effects on carbohydrate homeostasis and may in some instances improve the blood glucose response to ingested carbohydrate. C.R.S.

Nicholson, John F. (Babies' Hosp., The Children's Med. & Surg. Ctr. of N.Y., Columbia-Presbyterian Med. Ctr., N.Y., N.Y.): METABOLIC DISEASE: BEHAVIORAL ASPECTS. N.Y. State J. Med. *75*:1044-46, June 1975.

The initial manifestations of certain metabolic disorders may be behavioral disturbances, such as infantile autism, schizophrenia, or learning disability. Examples of diseases in which behavioral manifestations may predominate: Lesch-Nyhan disease, Hartnup disease, Wilson's disease, acute intermittent porphyria, late-onset metachromatic leukodystrophy, phenylketonuria, and galactosemia. Contrarily, in histidinemia the possibility of a causal relationship to mental retardation and/or language disorder remains questionable. Two illustrative case histories are given. V.R.L.

Nuttall, F.Q.; Gannon, M.C.; and Bergstrom, W.J. (Dept. of Med., Endocr., and Metab., V.A. Hosp., Dept. of Med., Univ. of Minn. Sch. of Med., Minneapolis, Minn.): INSULIN AND EPINEPHRINE EFFECTS ON HEART GLYCOGEN SYNTHETASE AND PHOSPHORYLASE ACTIVITY. Am. J. Physiol. *228*:1815-20, June 1975.

Verbatim summary. The effect of intravenous epinephrine on heart glycogen synthetase and phosphorylase systems in control and insulin-pretreated rats was studied. The per cent of synthetase in the I form decreased rapidly after epinephrine treatment but the change was small and sometimes not significant. In insulin-pretreated rats in which the per cent synthetase I was increased, epinephrine produced a definite and highly significant decrease. There was a simultaneous increase in per cent phosphorylase *a* in both groups. The synthetase and phosphorylase responses were statistically significant at 2.5 μg. epinephrine/kg. or more. These

data are compatible with a mechanism in which protein kinase is activated by an increased cAMP concentration and affects both the synthetase and phosphorylase systems simultaneously. Propranolol blocked the epinephrine effects on cAMP, synthetase I, and phosphorylase *a*. Although insulin had little effect on the response of the synthetase and phosphorylase systems to epinephrine, it nearly completely blocked glycogen degradation. The mechanism is unknown, but it appears to be due to an inhibition of phosphorylase *a* catalytic activity in vivo. Acetylcholine had no effect on synthetase I, phosphorylase *a*, or cAMP in control or insulin-pretreated animals.

Olefsky, Jerrold M.; Johnson, Jennifer; Liu, Francis; Jen, Phyllis; and Reaven, Gerald (Dept. of Med., Stanford Univ. Sch. of Med., & Veterans Hosp., Palo Alto, Ca.): THE EFFECTS OF ACUTE AND CHRONIC DEXAMETHASONE ADMINISTRATION ON INSULIN BINDING TO ISOLATED RAT HEPATOCYTES AND ADIPOCYTES. Metabolism *24*:517-27, April 1975.

The relationship between insulin-receptor binding and glucocorticoid-induced insulin resistance was examined by determining insulin binding to specific receptors located on isolated adipocytes and hepatocytes obtained from dexamethasone (D)-treated rats. Three dosage schedules were studied: acute high dose, acute low dose, and chronic low dose. In isolated hepatocytes the insulin binding was only 30-50 per cent of control values when cells from D-treated animals were used. The decrease was greatest for cells from the acute high dose and least for the chronic group, indicating both a dose-response effect and a tendency to return to insulin-receptor binding during chronic treatment. Isolated adipocytes displayed binding of 50-60 per cent of control values when D-treated cells were used. Although the magnitude of decrease was less than that seen with hepatocytes, the decrease was greatest for the acute-high-dose group. However, with chronic D-treatment, insulin binding to adipocytes returned to near-normal levels, while a 55 per cent decrease in binding to hepatocytes persisted. These observations may explain the amelioration in the glucocorticoid-induced insulin-resistant state seen after chronic administration of these steroids to humans. These results demonstrate (a) a decrease in insulin binding associated with corticosteroid excess, (b) a return toward normal of insulin binding after chronic D-treatment, and (c) a difference in effects of chronic D-treatment on insulin binding to hepatocytes versus adipocytes, indicating that changes in insulin binding may be tissue-specific. C.R.S.

Pessacq, Maria Teresa; and Gagliardino, Juan José (Catedra de Fisiologia con Biofisica, Instituto de Fisiologia, Facult. de Ciencias Medicas, Universidad Nac. de La Plata, La Plata, Argentina): GLYCOGEN METABOLISM IN MUSCLE: ITS CIRCADIAN AND SEASONAL VARIATIONS. Metabolism *24*:737-43, June 1975.

The glycogen content and the rate of labeled glucose incorporation into glycogen were studied in mouse diaphragms. The authors observed a circadian rhythm in glycogen content with a peak value at four hours and a similar rhythm for glucose incorporation. During fasting, the glycogen variations remained present, with absolute glycogen content of about one-third as high as those obtained in control animals. The results suggest that the rhythm in glycogen content is due, in part, to the circadian variation in its synthesis and that food intake is not the major factor responsible for the circadian rhythm. C.R.S.

Raichle, M.E.; Larson, K.B.; Phelps, M.E.; Grubb, R.L., Jr.; Welch, M.J.; and Ter-Pogossian, M.M. (Div. of Rad. Sci., Edward Mallinckrodt Inst. of Radiol., Dept. of Neurol., Biomedical Computer Lab., Wash. Univ. Sch. of Med., St. Louis, Mo.): IN VIVO MEASUREMENT OF BRAIN GLUCOSE TRANSPORT AND METABOLISM EMPLOYING GLUCOSE-^{11}C. Am. J. Physiol. *228*:1936-48, June 1975.

Verbatim summary. The radiopharmaceutical glucose-^{11}C was used for in-vivo measurement of brain-glucose transport kinetics and metabolism in the rhesus monkey. Radio-tracer was injected intravenously as a bolus. Radioactivity was continuously recorded from the head and from the arterial blood via an indwelling peripheral artery catheter for a collection period of two to three minutes. To correct the reading obtained from the head for radioactivity contained in blood, a second intravenous injection of the vascular tracer ^{15}O-labeled carboxyhemoglobin was used. The method was tested in nine phencyclidine-anesthetized monkeys in which cerebral glucose metabolism (CMR_{Glc}) was simultaneously measured by our method and by a standard method employing the Fick principle. A highly significant correlation was found between the two methods of measuring CMR_{Glc} ($r = 0.929$). In addition, our model predicted a ratio of forward-to-reverse glucose flux across the blood-brain barrier (BBB) (1.37 ± 0.23 S.D.), the brain-to-blood glucose concentration ratio across the BBB (0.633 ± 0.14), the relative tissue free-glucose space (17 ± 7 per cent), the brain free-glucose concentration (13.6 ± 8.5 mg./100 gm. of tissue), and the brain free-glucose turnover time (2.96 ± 1.98 min.).

Reichle, Frederick A.; Shuman, Charles R.; and Tyson, R. Robert (Depts. of Surg. & Int. Med., Temple Univ. Health Sciences Center, Philadelphia, Pa.): FEMOROTIBIAL BYPASS IN THE DIABETIC PATIENT FOR SALVAGE OF THE ISCHEMIC LOWER EXTREMITY. Am. J. Surg. *129*:603-05, 1975.

Verbatim summary. Severe ischemia of the lower extremity in diabetic patients without runoff in the popliteal artery should not deter an aggressive diagnostic and therapeutic approach. Femorotibial or femoroperoneal bypass can affect limb salvage and avoid primary amputation if distal small-vessel patency can be demonstrated by arteriography.

Schwartz, Peter L.; and Turfus, Ian M. (Dept. of Clin. Biochemistry, Univ. of Otago Med. School, Dunedin, New Zealand): INHIBITION OF GLYCERALDEHYDE 3-PHOSPHATE DEHYDROGENASE BY PLASMA AND SERUM: ULTRAFILTRATES DUE IN PART TO A LOW-MOLECULAR-WEIGHT, NONPEPTIDE MATERIAL. Metabolism *24*:569-72, May 1975.

Ultrafiltrates of plasma or serum from normals and diabetics were freeze-dried, yielding a residue that inhibited glyceraldehyde 3-phosphate dehydrogenase (G3PDH). The inhibitory material on gel filtration appeared to have a molecular weight below 700; it was not significantly affected by acid hydrolysis and did not absorb on cation-exchange resin. This material differs from the growth-hormone-derived polypeptide somantin, which is described by other workers as being elevated in plasma of diabetic patients and determined by the same enzyme-inhibition test. It appears that inhibition of G3PDH cannot be employed as a definitive measure of somantin levels in ultrafiltrates of plasma or serum. C.R.S.

Shima, Kenji; Sawazaki, Norio; Tanaka, Ryochi; Tarui, Seiichiro; and Nishikawa, Mitsuo (Central Lab. for Clin. Investigation, Osaka Univ. Hosp., Osaka, & Second Dept. of Int. Med., Osaka Univ. Med. Sch., Osaka, Japan): EFFECT OF AN EXPOSURE TO CHLORAMINE-T ON THE IMMUNOREACTIVITY OF GLUCAGON. Endocrinology *96*:1254-60, 1975.

The effect of chloramine-T on the immunoreactivity of glucagon was studied. Preparations exposed to chloramine-T for different periods reacted identically with a nonspecific antibody whether the glucagon was used as tracer or standard. However, exposure to chloramine-T under severe conditions reduced immunoreactivity of glucagon to a specific antibody. Amino acid analysis of hormone exposed to chloramine-T indicated that methionine at position 21 in the glucagon molecule had been oxidized to methionine sulfoxide. Addition of dimethyl sulfoxide (DMSO) protected the glucagon molecule from the damaging effects of chloramine-T. Because damage due to exposure to chloramine-T altered reactivity of glucagon against the specific antibody (30K) but not against a nonspecific antibody, it was concluded that specificity on the antiserum may involve amino acid residues near the carboxyl end of the molecule. J.E.G.

Tiengo, Antonio; Muggeo, Michele; Assan, Roger; Fedele, Domenico; and Crepaldi, Gaetano (Dept. of Int. Med., Div. of Gerontol. and Metab. Diseases, Univ. di Padova, Italy, and Clinique Médicosociale du Diabète et des Maladies de la Nutrition, Hôtel-Dieu, Paris, France): GLUCAGON SECRETION IN PRIMARY ENDOGENOUS HYPERTRIGLYCERIDEMIA BEFORE AND AFTER CLOFIBRATE TREATMENT. Metabolism *24*:901-14, August 1975.

Endogenous hypertriglyceridemia (types IV and V) is frequently associated with diabetes or with impaired glucose tolerance. In 13 type-IV patients, a positive correlation was demonstrated between fasting insulin and triglyceride (TG) levels and between fasting insulin/glucagon (I/G) molar ratio and triglyceride levels. These patients manifested a significantly increased glucagon response to arginine infusion over that of control subjects. No correlation was found between glucagon and TG or FFA levels; nor was a correlation noted in normal subjects rendered hyperlipidemic by means of Intralipid infusion that did not modify the glucagon response to arginine. Clofibrate treatment caused a reduction in plasma TG that was correlated with a reduction in the I/G molar ratio. After clofibrate treatment, there was a reduction in fasting glucagon immunoreactivity and in the insulin response to arginine as well as an increase in the glucagon response. These results suggest that clofibrate may exert a hypolipidemic effect by modifying the insulin/glucagon bihormonal pattern. C.R.S.

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