ABSTRACTS

Assan, R.; Souchal, B.; Aubert, Ph.; Tchobroutsky, G.; and Derot, M. (Hotel-Dieu, Paris, France): NON-KETOTIC COMAS IN DIABETICS. La Presse Medicale 77:787-89, April 26, 1969.

Verbatim summary. Out of 184 metabolic comas occurring in diabetics, twenty-nine were not related with ketoacidosis; seventeen hyperosmolar nonketotic comas are analysed for etiologic circumstances, clinical and biological features.

Physiopathology, for a large part, remains unknown. Death occurred in more than 50 per cent of cases.

"Idiopathic" lactic acidosis (four patients), acidosis as a complication of acute ischemic condition (three patients), complex disorders such as ketosis+metabolic alcalosis, +hyponatremia (five patients) caused also metabolic comas in diabetics, and were characterized by extremely severe evolution.

Beigelman, Paul M.; Martin, Helen E.; Miller, Leona V.; and Grant, William J. (Los Angeles County-Univ. of Southern California Med. Center, & Dept. of Med., USC Sch. of Med., Los Angeles, Calif.): CRITICAL CARE MEDICINE. SEVERE DIABETIC KETOACIDOSIS. JAMA *210*:1082-86, Nov. 10, 1969.

The authors report on the methods of the results of treatment of fifty-one episodes of severe diabetic ketoacidosis in forty-six diabetic patients. Many had complications: seven shock, eight alcoholism, seventeen infection, two pregnancy, and five vascular disease. All recovered. The authors emphasized among their therapeutic technics the frequent chemical monitoring of the patients, the early use of large doses of insulin and the vigorous intravenous administration of potassium when indicated. S.B.B.

Bergström, Jonas; Hultman, Eric; and Roch-Norlund, Aasmund E. (Renal Clin. and Clin. Central Lab., St. Eriks Sjukhus, Stockholm, Sweden): LACTIC ACID ACCUMULATION IN CONNECTION WITH FRUCTOSE INFUSION. Acta Med. Scand. *184*: 359-64, November 1968.

Infusion of fructose in healthy experimental subjects and in patients with diabetes mellitus is found to cause an increase in the blood concentration of lactate that is in relation to the rate of infusion. At an infusion rate of 1 gm. per kilogram body weight per hour or above, the lactate concentration rises by 5 mEq. per liter. In healthy subjects infusion is generally associated with a relatively inappreciable rise in arterial glucose concentration. In diabetic patients, on the other hand, the rise is pronounced. Clinically significant acidosis is found to be exacerbated by rapid fructose infusion. It is therefore emphasized that this form of treatment is contraindicated in acidotic states. Administration of fructose has no beneficial effect on the metabolism in insulin-requiring diabetic patients whose insulin has been temporarily discontinued. On the contrary, it exacerbates their acidosis and produces a considerable rise in blood sugar. B.F.K.

Bocek, R. M.; and Beatty, C. H. (Depts. of Biochem., Oregon Regional Primate Res. Center, Beaverton, Ore.; and Univ. of Oregon Med. Sch., Portland, Ore.): EFFECT OF INSULIN ON THE CARBOHYDRATE METABOLISM OF FETAL RHESUS MONKEY MUSCLE. Endocrinology *85*:615-18, September 1969.

Muscle from rhesus fetuses, 125 days of gestational age and from adult monkeys were incubated with and without insulin in medium containing glucose-6-C-14. Insulin enhanced glucose uptake, lactate-C-14 and C-14-O_2 production equally in fetal and adult muscles. Glycogen concentration was unchanged with insulin but C-14 incorporation increased greatly with stimulation by insulin of the glucose to glycogen pathway manifested equally in fetal and adult muscles. Apparently the carbohydrate metabolism of muscle from the rhesus fetus at 125 days is responsive to insulin. C.R.S.

Brooks, Marion H.; Guha, Atin; Danforth, Elliot, Jr.; Weinstein, Jacob J.; and Barry, Kevin G. (Depts. of Clin. Renal Res. and Gen. Surg.; Washington Hospital Center, Washington, D.C.): PHEOCHROMOCYTOMA: OBSERVATIONS ON MECHANISM OF CARBOHYDRATE INTOLERANCE AND ABNORMALITIES ASSOCIATED WITH DEVELOPMENT OF GOLDBLATT KIDNEY FOLLOWING REMOVAL OF TUMOR. Metabolism *18*: 445-59, June 1969.

In a patient with pheochromocytoma the administration of glucose caused marked hyperglycemia with considerable impairment of insulin release. Arginine infusion was associated with a prompt rise in plasma insulin levels and a decrease in blood glucose concentration. These observations indicate that impairment of insulin release and not synthesis is primarily responsible for carbohydrate intolerance in pheochromocytoma. Normal 17-hydroxycorticoid, reduced growth hormone and rennin concentrations demonstrate that these factors are probably not related to carbohydrate intolerance. During the postoperative period insulin release in response to glucose improved markedly but did not return to normal. In the immediate postoperative period, left renal thrombosis with renovascular hypertension developed providing an opportunity to study the course and surgical correction of the Goldblatt kidney in man. C.R.S.

Brunfeldt, K.; Deckert, T.; and Thomsen, J. (Steno Memorial Hosp., Res. Lab., and The Danish Inst. of Protein Chem., Copenhagen, Denmark): HUMAN CRYSTALLINE INSULIN FROM NONDIABETIC AND DIABETIC PATIENTS. Acta Endocr. 60:543-49, March 1969.

Verbatim summary. Crystalline insulin was prepared from pooled pancreases from deceased maturity-onset diabetics and nondiabetics. A comparison was made of the amino acid composition, immunological reactivity and hypoglycemic activity. No differences could be demonstrated between the two preparations.

Burr, I. M.; Stauffacher, W.; Balant, L.; Renold, A. E.; and Grodsky, G. (Inst. of Clin. Biochem., Univ. of Geneva, Geneva, Switzerland): DYNAMIC ASPECTS OF PROINSULIN RELEASE FROM PERFUSED RAT PANCREAS. Lancet 2:882-83, October 25, 1969.

In an effort to understand better the role of insulin secretion, the authors analyzed the content of rat pancreas for insulin and proinsulin. They then stimulated pieces of pancreas isolated in a chamber by pumping a buffer containing 300 mg./100 ml. glucose through it. The effluent from the chamber was collected in sequential volumes and passed through a Sephadex column and various fractions derived from the column were assayed for immunoreactive insulin.

The percentage of immunoreactive (IRI) insulin extractable from the pancreas was 1 to 2 per cent. In the perfusion experiments proinsulin release became detectable after thirty to forty minutes of glucose stimulation. After fifty-five to sixty minutes, the percentage of immunoreactive insulin attributable to proinsulin rose to 17 per cent. The results are consistent with the hypothesis that there may be two compartments of stored insulin: one low in proinsulin which may be released first and another higher in proinsulin (more recently synthesized) which is released later. The physiological importance of these phenomena is not yet known. T.G.S.

Canivet, J.; Mantel, O.; Babinet, J. P.; and Lellouche, D. (Service de Nutrition-Endocr., Hôpital Saint-Louis, F-75-Paris (10E), France): HYPOPHYSECTOMY IN DIABETIC RETINOPATHY. Presse Med. 77:283-86, February 15, 1969.

Eight cases of proliferative diabetic retinopathy, representing the experience of the authors, were treated by yttrium or gold implantation, which induced only partial pituitary ablation. Seven patients showed improvement, which persisted in five for one to three years. M.C.B.

Chance, G. W.; Albutt, E. C.; and Edkins, S. M. (Inst. of Child Health and Birmingham Children's Hosp., Birmingham, England): SERUM LIPIDS AND LIPOPROTEINS IN UNTREATED DIABETIC CHILDREN. Lancet 1:1126-28, June 7, 1969.

Heretofore there has been no report describing serum lipid concentrations and patterns in untreated diabetic children. In this study serum lipid analyses were made in 135 newly diagnosed diabetic children aged ten months to thirteen-and-one-half years prior to any treatment. In 6 per cent of the cases the serum total lipids exceeded the normal upper limit of 750 mg./100 ml. and in 43 per cent the serum cholesterol was above the normal of 240 mg./100 ml. There was no relationship between lipid levels and blood sugar levels. Serum lipid electrophoretic patterns were done in 120 children. Only 23 per cent were normal. The most common abnormality was excessive pre-beta lipoproteinemia (43 per cent) while 18 per cent had beta plus pre-beta excess and 12 per cent had increased chylomicrons and pre-beta lipoproteins. Normal serum lipids were found in all children who were reinvestigated after control of diabetes had been achieved with insulin and a regulated carbohydrate diet. Diabetic children have a deficiency of insulin. This results in an inability of their muscle and adipose tissue to metabolize glucose and permits excessive mobilization of fatty acids from adipose tissue. This presents the liver with excessive quantities of fatty acid which is converted to triglyceride and released as pre-beta lipoprotein. T.G.S.

Chazan, Bernard I.; Rees, Searle B.; Balodimos, Marios C.; Younger, Donna; and Ferguson, B. Dan (Joslin Diabetes Foundation, New England Deaconess Hosp., Dept. of Med., Harvard Med. Sch., and Peter Bent Brigham Hosp., Boston, Mass.): DIALYSIS IN DIABETICS. A REVIEW OF FORTY-FOUR PATIENTS. JAMA 209:2026-30, Sept. 29, 1969.

This is an extensive account of the results of dialysis in forty-four diabetic patients, thirty-two for intractable anasarca (eight of whom had creatinine levels of less than 4 mg. per cent), eight for an acute exacerbation of chronic renal failure (six with diabetic glomerulosclerosis and two with chronic pylonephritis) and five with acute renal failure (three with acute tubular necrosis). The types of dialysis used were thirty-three peritoneal (mostly single), four hemodialysis and seven peritoneal followed by hemodialysis (five of the latter long term). The best results were in those with acute tubular necrosis without prior renal failure. The results in anasarca, admittedly used as a last resort, were least impressive, but could be used even in presence of ischemic heart disease or uremic pericarditis. The complication of hyperglycemia during dialysis could be obviated by monitored use of repeated injections of crystalline insulin. S.B.B.

Chimenes, H. (College de Medecine des Hopitaux de Paris, Hopital Beaujon, Paris, France): FALSE SUGAR DIABETES: FASTING DIABETES. La Presse Medicale 77:825-27, May 3, 1969.

Four cases are reported in which an abnormal glucose tolerance following dieting led to the diagnosis of diabetes. Dietary treatment brought loss of weight. A subsequent glucose tolerance test after high carbohydrate intake gave normal values in these patients and they were considered by the author as nondiabetic with an abnormal carbohydrate tolerance because of dieting. M.C.B.

Denis, Gustave; and Launay, Marc P. (Dept. of Physiol., Univ. of Montreal, Montreal, Canada): CARBOHYDRATE INTOLERANCE IN GOUT. Metabolism 18:770-75, September 1969.

Thirty patients with gouty arthritis were subjected to oral glucose tolerance tests. In none had diabetes been suspected previously. Depending upon criteria used for diagnosis from 7 to 55 per cent of the subjects were classified as diabetics. According to the most widely used criteria, the OGTT was borderline in two thirds of the subjects and strongly suggestive in one third. No correlation was found between the serum level of uric acid and the blood sugar concentration. The variability of the accepted criteria for the interpretation of the OGTT greatly affects the significance of studies such as this one and creates difficulty in determination of the prevalence of diabetes in any given group. From these data it is reaffirmed that there is a higher prevalence of diabetes among gouty patients than in the general population. C.R.S.

Fatourechi, Vahab; Molnar, George D.; Service, Frederick J.; Ackerman, Eugene; Rosevear, John W.; Moxness, Karen E.; and Taylor, William F. (Mayo Clin. and Mayo Foundation, Rochester, Minn.): GROWTH HORMONE AND GLUCOSE INTERRELATIONSHIPS IN DIABETES: STUDIES WITH INSULIN INFUSION DURING CONTINUOUS BLOOD GLUCOSE ANALYSIS. J. Clin. Endocr. 29:319-27, March 1969.

Verbatim summary. To examine changes in plasma levels of human growth hormone (HGH) in severe diabetics under conditions resembling hypoglycemic reactions, eight diabetic

and six normal subjects were given insulin infusions at a constant rate during continuous automated blood glucose (BG) analysis. HGH was determined by radioimmunoassay at frequent intervals. All subjects tested who reached a BG nadir of 35 mg./100 ml. had HGH increases. Other HGH increases occurred also during hyperglycemia in seven tests, but only in diabetics. Mean increases in plasma HGH were similar in normals and in diabetics, and whether during hyperglycemia or during hypoglycemia. No hyperglycemic or hypoglycemic effect of HGH increases was discernible. The method proved to be uniquely suited for exploring HGH and BG changes during the infusion of insulin. Diabetics differed from normals by augmenting circulating levels of HGH during hyperglycemia, whether or not BG was decreasing at the time the observations were made.

Floquet, J.; Laurent, J.; Florentin, P.; Rauber, G.; Grignon, G.; and Floquet, A. (Laboratoire D'Anatomie Pathologique, Faculte de Medecine, Nancy, France): ENDOCRINE TUMOURS OF THE PANCREAS. MORPHOLOGY AND HISTOGENESIS. La Presse Medicale 77:87-90, Jan. 18, 1969.

Verbatim summary. The histology of islet cell tumors is now fairly well known. Important progress was made following the discovery of ulcerogenic tumors, e.g., the cytology of the endocrine pancreas under the light and electronic microscopes, the role of gastrin. Some aspects are still not clear, for example, the malignant potential of these tumors.

A comparison of ulcerogenic and hypoglycemic tumors reveals surprising differences in behavior, e.g., numerous ectopic localizations and a quite definitely more frequent presence of malignancy in ulcerogenic tumors. The authors recall a few theories concerning the histogenesis of Zollinger tumors. The definition of a gastrin-secreting system and certain analogies with Feyrter's clear cell system or with carcinoid tumors may explain these differences.

Similarly a statistical study of multiple pancreatic tumors (adenomatosis) associated with multiple tumors of other endocrine glands (multiple endocrine tumors) gives a certain weight to the findings of Wermer, who suggested a hereditary transmission of Langerhans tumors.

Frohman, Lawrence A.; Bernardis, Lee L.; Schnatz, J. David; and Burek, Lynne (Depts. of Med. and Path., and Neurosensory Lab., State Univ. of New York at Buffalo, N.Y.): PLASMA INSULIN AND TRIGLYCERIDE LEVELS AFTER HYPOTHALAMIC LESIONS IN WEANLING RATS. Amer. J. Physiol. 216:1496-1501, June 1969.

Verbatim summary. Weanling female rats with lesions in the ventromedial hypothalamic region and sham-operated controls were bled serially for a 2.5-week period to study the interrelationships between the previously reported hyperinsulinemia and hyperlipidemia. The following changes occurred in rats with hypothalamic lesions: (1) decreased food intake for eight days followed by a normal food intake; (2) hypoglycemia for five to seven days followed by normoglycemia; (3) hyperinsulinemia and hypertriglyceridemia occurring in a parallel manner by day 3 to 4; (4) increased carcass fat despite no increase in body weight. The plasma lipoprotein electrophoretic pattern suggested that the hypertriglyceridemia was due to endogenous synthesis. These results exclude hyperphagia and/or hyperglycemia as the etiology of hyperinsulinemia and hypertriglyceridemia. They are, however, compatible with a primary hyperinsulinemia accompanied by a partial growth hormone deficiency, which have previously been shown to occur after ventromedial hypothalamic destruction.

Hazzard, William R.; Spiger, Michael J.; Bagdade, John D.; and Bierman, Edwin L. (Dept. of Med., Univ. of Washington Sch. of Med., and Veterans Administration Hosp., Seattle, Wash.): STUDIES ON THE MECHANISM OF INCREASED PLASMA TRIGLYCERIDE LEVELS INDUCED BY ORAL CONTRACEPTIVES. New Eng. J. Med. 280:471-74, February 27, 1969.

Combined therapy of an estrogen, ethinyl estradiol, with a gestagen, medroxyprogesterone acetate, was studied in ten young women (mean age of twenty-five years, range of twenty to thirty-three years). None were obese or had family histories of vascular disease and only one had a positive family history of diabetes. All tests were conducted at bed rest after overnight fasting. Identical studies were performed before and after two weeks of daily treatment with ethinyl estradiol 0.05 mg., and medroxyprogesterone acetate, 10 mg. Before and during treatment, fasting plasma was analyzed for triglyceride (TG), basal serum immunoreactive insulin (IRI) and postheparin lipolytic activity (PHLA).

The combination of oral contraceptive drugs was associated with a rise in TG levels in all subjects. Estrogen alone appeared sufficient to cause the relative hypertriglyceridemia, since a rise in TG was associated with ethinyl estradiol alone in one subject studied. Hypertriglyceridemia during oral contraceptive therapy could result from increased plasma output, from dietary or endogenous sources or decreased plasma TG removal or a combination of the two. The exact mechanisms remain unknown; however, two significant findings in this report were considered relevant. First, a uniform decrease in PHLA was observed both with estrogen-gestagen and with estrogen alone. This relationship remains to be clarified. No circulating hypoprotein lipase inhibitor was demonstrated, nor was insulin insufficiency present. Basal IRI levels were elevated, and adequate postprandial insulin response was indicated by normal glucose tolerance observed in eight subjects tested.

The second observation, related to relative hypertriglyceridemia during oral contraceptive therapy, was increased basal IRI levels. A reasonable hypothesis may be that elevated IRI levels promote increased endogenous (hepatic) TG synthesis.

The relative importance of both decreased TG removal (suggested by decreased PHLA) or increased endogenous TG synthesis, or a combination of both factors must await further investigation. B.R.B.

Himal, H. S.; Goodhead, B.; Colle, E.; and MacLean, L. D. (Dept. of Surg., Royal Victoria Hosp., and Dept. of Pediat., McGill Univ., Montreal, Quebec, Canada): EXOCRINE AND ENDOCRINE FUNCTIONS OF THE ALLOGRAFTED PANCREAS. Canad. Med. Ass. J. 100:422-27, March 1, 1969.

Verbatim summary. Sixteen mongrel dogs, previously subjected to a total pancreatectomy, were recipients of a total pancreatic allograft. The donor celiac artery was anastomosed to the recipient proximal common iliac artery and the donor superior mesenteric vein to the recipient common iliac vein. Exocrine secretion of the allografted pancreas increased until the fourth postgraft day, then rapidly diminished and completely ceased after the seventh day. The allografted pancreas uniformly responded to intravenous secretin on the second posttransplant day but did not respond after the fifth day. Adequate endocrine function of the allograft was manifested by normal blood sugar and increased serum insulin levels. These

experiments demonstrate that: (1) blood glucose levels are more reliable than serum insulin levels in following the course of the allografted pancreas, and (2) failure of exocrine function precedes that of endocrine function in most animals.

Hoshi, Mitsuru; and Shreeve, Walton W. (Div. of Biochem., Med. Res. Center, Brookhaven National Labs., Upton, N.Y.): CHRONIC EFFECTS OF MANNOHEPTULOSE IN HYPERGLYCEMIC-OBESE MICE. Metabolism *18*:422-26, May 1969.

The effect of mannoheptulose upon plasma insulin concentrations, blood glucose and conversions of tagged glucose to fatty acids, body water and expired CO_2 was examined in the Bar Harbor strain of hyperglycemic-obese mice. The plasma immunoreactive insulin levels were 100 per cent higher in obese mice and 50 per cent higher in lean mice given mannoheptulose compared to untreated control groups. The fasting blood glucose and conversions of tagged glucose to fatty acids, CO_2 and water were unaffected in the treated groups. These findings differ from those described in other species which show inhibitory effects of mannoheptulose on the release of insulin. The effect may be one of intermittent suppression of insulin release with excessive discharge of accumulated insulin at other times. C.R.S.

Jakobson, Theodor; Kahanpää, Asko; and Mäenpää, Voitto J. (Fourth Dept. of Med., Univ. of Helsinki, and Dept. of Med., Maria Hosp., Helsinki, Finland): PREDNISONE-GLUCOSE TOLERANCE AND SERUM LIPIDS IN SURVIVORS OF MYOCARDIAL INFARCTION. Acta Med. Scand. *184*:451-57, November 1968.

Verbatim summary. Glucose tolerance has been examined by means of a prednisone-glucose tolerance (PGT) test in forty-one patients with clinically documented myocardial infarction three to four weeks after the attack and in age-matched control subjects without clinical evidence of cardiovascular disease. In addition serum cholesterol and triglyceride levels have been determined and free fatty acid (FFA) concentrations measured prior to the PGT test and after administration of the glucose load.

Abnormal glucose tolerance curves were obtained in 53.6 per cent of the patients three to four weeks after the infarction and in 25.8 per cent of the controls. Seventeen patients were retested approximately six months after the first test and glucose tolerance in seven patients with initially abnormal PGT curves were found to be within normal limits, while further impairment was observed in only four cases. A significant correlation between the PGT tests and serum cholesterol levels was found to exist only in patients over the age of sixty, while no correlation could be observed between prednisone-glucose tolerance and serum triglycerides or fasting levels of FFA. The mean decrease of FFA one hour after the administration of glucose was slightly less in the patients with myocardial infarction than in the controls, while a decrease of FFA to levels below 200 μEq./L. was observed in approximately one third of the patients one and/or three hours after the glucose load.

It is concluded that the impairment of glucose tolerance which frequently can be observed after recent myocardial infarction is probably due only in a minority of cases to a latent diabetic condition and that other factors which are known to influence carbohydrate metabolism must be taken into consideration in explaining the observed disturbances of glucose homeostasis.

Kaplan, Solomon A.; Frasier, S. Douglas; and Costin, Gertrude (Children's Hosp. of Los Angeles, Los Angeles County; Univ. of Southern California Med. Center; and Dept. of Pediat., Univ. of Southern California Sch. of Med., Los Angeles, Calif.): GROWTH HORMONE SECRETION IN IDIOPATHIC PRECOCIOUS PUBERTY: EFFECT OF MEDROXYPROGESTERONE. J. Pediat. *75*:133-38, July 1969.

Verbatim summary. Plasma growth hormone responses to insulin-induced hypoglycemia were measured in six girls and two boys with isosexual precocity. Resting levels of growth hormone in excess of 15 mμg. per ml. were found in five subjects; peak plasma concentrations after insulin-induced hypoglycemia were markedly higher than those seen in prepubertal children. Excitement and apprehension often resulted in release of significant quantities of growth hormone into the circulation in quantities in excess of those subsequently released following insulin-induced hypoglycemia. High resting levels and high peak plasma concentrations in response to hypoglycemia were also seen after administration of a single injection of 200 mg. medroxyprogesterone acetate (MPA) and long-term treatment with MPA for periods of twenty to sixty-six months. There was no evidence that MPA given in this dosage impairs the release of growth hormone. The high levels of plasma growth hormone found before and after insulin-induced hypoglycemia were in the range reported for adults and were probably associated with increased levels of circulating estrogens and androgens above the normal levels for prepubertal children.

Kobberling, J.; Appels, A.; Kobberling, G.; and Creutzfeldt, W. (Gastroenterological and Metabolic Unit of the Dept. of Med. and the Inst. of Human Genetics, Univ. of Gottingen, Gottingen, Germany): GLUCOSE TOLERANCE TESTS IN 727 FIRST-DEGREE RELATIVES OF MATURITY-ONSET DIABETICS. Germ. Med. Mth. *14*:290-94, June 1969.

Seven hundred and twenty-seven first-degree relatives of maturity-onset diabetics received 75 gm. of glucose as an oral glucose tolerance test. The glucose tolerance curves were assessed according to the following criteria: Levels of 200 mg. per 100 ml. at one hour or of 150 mg. per 100 ml. at two hours were regarded as indicative of latent diabetes. Levels of 170 mg. per 100 ml. at one hour and of 130 mg. per 100 ml. at two hours were described as suspicious. 30.8 per cent were found to have a definitely diabetic metabolic state; 4.1 per cent had overt diabetes. The incidence of newly discovered latent or overt diabetes increased with age and overweight of the person studied. This disturbance in carbohydrate metabolism was discovered in a greater proportion of men (35.6 per cent) than women (22.7 per cent). The incidence of latent or overt diabetes among the siblings was 38.9 per cent and among children was 22.7 per cent. This might be accounted for by the greater age of the former group. D.R.C.

Kuo, Peter T. (Cardiac Sect., Dept. of Med., Robinette Foundation for Cardiovascular Res., and George S. Klump Lab., Univ. of Pennsylvania Hosp., Philadelphia, Pa.): METABOLIC BASIS OF HUMAN ATHEROSCLEROSIS. Metabolism *18*:631-34, August 1969.

Among the important risk factors in atherosclerosis is hyperglycemia. Intensive research has advanced the understanding of interrelationships between atherosclerosis and abnormal lipid-carbohydrate-insulin metabolism. The role of insulin in the

synthesis of endogenous lipogenesis from carbohydrate is well-known, and investigators have demonstrated a significant correlation between hypertriglyceridemia (hyperprebetalipoproteinemia) and serum IRI levels in both fasting and carbohydrate-fed states. Such increases in endogenous lipoprotein, rich in cholesterol and triglyceride, account for the rise in these lipids observed in patients with coronary heart disease. Individuals with mild degrees of endogenous hyperlipemia exhibiting glucose intolerance and hyperinsulinism appear predisposed to premature atherosclerosis. The author has demonstrated capillary abnormalities similar to diabetic microangiopathy in a high proportion of patients with endogenous hyperlipoproteinemia using a method of reflected light manifold capillaroscopy. Subsidence of these capillary abnormalities following successful control of endogenous lipogenic activity offers hope of prevention of atherosclerotic complications by appropriate therapeutic measures. C.R.S.

London, D. R.; and Prenton, M. A. (Dept. of Chem. Path., St. Thomas's Hosp. Med. Sch., and Dept. of Metabolic Diseases, St. Thomas's Hosp., London, England): BETA-ADRENERGIC RECEPTORS AND THE PLASMA AMINO ACID RESPONSE TO INSULIN IN MAN. Clin. Sci. *35*:55-61, August 1968.

Verbatim summary. 1. Plasma amino-nitrogen and glucose levels following insulin administration have been measured. 2. The fall in amino nitrogen induced by insulin is reduced when propranolol is given. However, the glucose rebound is not significantly altered by the drug. 3. Intravenous isoprenaline produces a fall in animo-nitrogen levels. 4. It is concluded that the beta action of adrenaline released as a result of insulin hypoglycemia may produce a lowering of plasma amino acid levels and that this action can be blocked by propranolol.

Lotz, Myron; and Geraghty, Michael (District of Columbia Gen. Hosp., Washington, D.C.): HYPERGLYCEMIC, HYPEROSMOLAR, NONKETOTIC COMA IN A KETOSIS-PRONE JUVENILE DIABETIC. Ann. Intern. Med. *69*:1245-46, December 1968.

This is a case report of a twenty-four-year-old juvenile diabetic with many episodes of diabetic ketoacidosis presented with hyperglycemic, hyperosmolar, nonketotic coma that progressed rapidly to death despite vigorous conventional therapy with hypotonic fluids, insulin, and potassium.

This report was made because at that time the syndrome had not been previously described in a patient with ketosis-prone diabetes mellitus. However, at the end of the report the authors call attention to a somewhat similar case in which the patient survived. It was reported by H. D. Kolodny, and L. Sherman in JAMA *203*:461, 1968. B.F.K.

McFadzean, A. J. S.; and Yeung, R. T. T. (Dept. of Med., Univ. of Hong Kong, Hong Kong): FURTHER OBSERVATIONS ON HYPOGLYCAEMIA IN HEPATOCELLULAR CARCINOMA. Amer. J. Med. *47*:220-35, August 1969.

The authors studied both in vivo and in vitro the incidence and mechanism of hypoglycemia in 142 patients with massive hepatocellular carcinoma of the liver (all superimposed on postnecrotic cirrhosis of the liver). Their 142 patients could be divided into two clinical types: 124 or 87 per cent of type A with only a 1/6th incidence of hypoglycemia which was usually terminal. The tumor was rapidly growing and the patients suffered weight loss and muscle weakness but the hypoglycemia was controlled readily by oral feeding. In the second, type B, the tumor was slow growing but the hypoglycemia was difficult to control, especially in the fasting state, without use of intravenous feeding and occurred months before death.

Oral glucose tolerance tests combined with blood insulin studies showed results consistent with the underlying cirrhotic state. From their enzyme and other studies they concluded that the hypoglycemia was attributed to excess use by a diversion to the tumor cells of glucose in both types of tumor. However, in the patients with type B tumor there was the added feature of glycogenosis and difficulty with glycogenolysis of the adequate glycogen stores of B tumor and surrounding liver tissue. S.B.B.

Milner, A. D. (Hosp. for Sick Children, London, England): BLOOD GLUCOSE AND SERUM INSULIN LEVELS IN CHILDREN WITH CYSTIC FIBROSIS. Arch. Dis. Child. *44*:351-55, June 1969.

Verbatim summary. The results of glucose and insulin levels after oral glucose and intravenous glucose, glucagon, and tolbutamide in sixty-one children with cystic fibrosis are presented. The results suggest that the increased incidence of impaired glucose tolerance found in them is due to a defect in the release of a glucagon-like substance from the alimentary system, in addition to defective islet cell function.

Montes, Leopoldo F.; Dobson, Harold; Dodge, Billy G.; and Knowles, W. R. (Depts. of Dermatology and Intern. Med., Baylor Univ. Coll. of Med., Houston, Tex.): ERYTHRASMA AND DIABETES MELLITUS. Arch. Derm. 99:674-80, June 1969.

Erythrasma is a superficial bacterial infection caused by *Corynebactrium minutissimum.* In patients with extensive erythrasma diabetes occurs with sufficient frequency to warrant the routine performance of studies of carbohydrate metabolism. Nine of nineteen patients with extensive erythrasma of the groins, axillae and/or trunk, proven by culture, and by coral-red fluorescence under a powerful Wood's light, were diabetics. Eight of the nine diabetics with erythrasma were obese. Six other patients had clinical evidence suggesting the presence of diabetes mellitus. These findings strongly suggest that diabetes mellitus may be a predisposing factor in the development of erythrasma.

The authors point out the analogy with candidiasis as a herald of diabetes. D.R.C.

Pi-Sunyer, F. Xavier; Van Itallie, Theodore B.; and Zintel, Harold A. (Depts. of Med. and Surg., St. Luke's Hosp. Center, New York, N.Y.): INSULIN STIMULATORY TESTS IN A PATIENT WITH ISLET CELL ADENOMA. Amer. J. Surg. *118*: 95-99, July 1969.

A sixty-eight-year-old female developed hypoglycemic convulsions and electroencephalographic abnormalities improved by eating. Elevated fasting serum insulin and decreased glucose indicated the correct diagnosis, but seemed to prevent the characteristic insulin responses to glucose, tolbutamide, leucine and glucagon. These tests were either normal, borderline (tolbutamide) or misleading. Insulin content of the excised islet adenoma was markedly elevated despite the minimal response to tolbutamide. Elevated insulin concentration of normal pancreatic tissue removed from the tail indicated that the glucose-induced hyperglycemia postoperatively was not caused by suppression of normal islet secretion but by coexistent, unrelated diabetes mellitus. A.R.C., JR.

Samaan, Naguib A.; Stone, Daniel B.; and Eckhardt, Richard D. (Dept. of Intern. Med., Univ. of Iowa Coll. of Med., Iowa City, Ia.): SERUM GLUCOSE INSULIN, AND GROWTH HORMONE IN CHRONIC HEPATIC CIRRHOSIS. Arch. Intern. Med. *124*:149-52, August 1969.

Verbatim summary. Plasma glucose, radioimmunoassayable insulin, and growth hormone (HGH) concentrations were measured during oral glucose tolerance tests (GTT) in twenty-two patients with chronic hepatic cirrhosis and in fifteen normal subjects. Of the cirrhotics, fifty per cent had normal results and fifty per cent showed impaired glucose tolerance. Cirrhotic patients with normal results showed hyperinsulinism. Abnormal results for GTT were associated with hypoinsulinism compared with normal subjects. Fasting levels of HGH were higher than in normal subjects. During GTT, HGH levels in eighteen cirrhotics were either not suppressed or showed paradoxical rise but normal subjects had complete suppression. Patients with hepatic cirrhosis and abnormal GTT results had higher HGH levels at 60, 90, and 120 minutes compared with patients with normal GTT results. High HGH levels may be responsible for the high incidence of abnormal glucose tolerance in hepatic cirrhosis and hyperinsulinism preceding hypoinsulinism.

Searle, G. L.; Gulli, R.; and Cavalieri, R. R. (V.A. Hosp. and Univ. of California Med. Center, San Francisco, Calif.): EFFECT OF PHENFORMIN IN NONDIABETIC HUMANS. ESTIMATION OF GLUCOSE TURNOVER RATE AND CORI CYCLE ACTIVITY. Metabolism *18*:148-54, February 1969.

Using C-6 labeled C-14 glucose, the glucose turnover and rate of recycling of glucose carbon into glucose was estimated in nondiabetic subjects before and after administration of phenformin. While glucose concentrations were not affected, glucose turnover rates increased by 20 per cent, glucose recycling rates were increased by 50 per cent, and the rate of glucose oxidation tended to increase. The enhanced recycling and turnover of glucose provide evidence of stimulation of gluconeogenesis as well as increased activity of the Cori cycle. Estimates of expired C-14-O_2 indicate a slight stimulation of glucose oxidation by the drug, a finding which fails to support the previous hypothesis of decreased aerobic metabolism as a mechanism for its blood sugar-lowering action. C.R.S.

Sutton, P. M.; and Taghizadeh, A. (Dept. of Morbid Anat., Univ. Coll. Hosp., Med. Sch., London, England): A NEW PANCREATIC HORMONE AND THE ETIOLOGY OF DIABETES MELLITUS. Lancet *2*:935-37, Nov. 1, 1969.

Diabetes is not always the result of simple insulin deficiency. The obese maturity onset diabetic may be resistant to insulin therapy and may display a high insulin concentration after oral glucose. Since the authors performed a study in rats in which they removed the entire pancreas and two thirds of the liver and found that the animals became profoundly hypoglycemic some hours later, they speculate that the pancreas may secrete a hormone which causes hepatic gluconeogenesis. They propose that maturity onset diabetes may result from an initial overproduction of pancreatic gluconeogenic hormone. Early, the beta cells respond by increased insulin secretion. Later, a relative insulin deficiency but not ketosis occurs. In contrast, juvenile diabetes is caused by primary beta cell failure. T.G.S.

Verdy, Maurice; Cholette, Jean-Paul; Nadeau, Pierre; Fauteux, Jean-Panet; and Demay, Francois (Hôtel-Dieu de Montréal, and Univ. de Montreal, Montreal, Quebec, Canada): HYPOGLYCEMIE ET TUMEURS MESENCHYMATEUSES. Canad. Med. Ass. J. *100*:470-74, March 8, 1969.

Verbatim summary. Two cases are reported of hypoglycemia secondary to mesenchymatous tumors, one a retroperitoneal and the other a pleural fibrous mesothelioma. In the latter patient the insulin levels were estimated, by both radioimmunological and biological methods, in the peripheral blood, in the blood draining from the tumor and in extracts of the tumor itself. All the values so measured were normal. The release by the tumor of one or several substances which either produce hypoglycemia or else potentiate the action of insulin, is likely but has not been completely proved.

Weintraub, B.; Sarcione, E. J.; and Sokal, J. E. (Div. of Med., Roswell Park Memorial Inst., New York State Dept. of Health, Buffalo, N.Y.): EFFECT OF GLUCAGON ON PHOSPHORYLASE ACTIVITY OF THE ISOLATED PERFUSED LIVER. Amer. J. Physiol. *216*:521-26, March 1969.

Verbatim summary. Exposure of the isolated perfused rat liver to concentrations of glucagon as low as 0.14 mμg./ml. plasma results in measurable activation of phosphorylase. Maximal activation was observed at glucagon concentrations of 1.4-4.0 mμg./ml. When glycogen-containing livers were used, the increases in phosphorylase activity were accompanied by increases in hepatic glucose release, and there was a quantitative correlation between these two effects over a thirty-fold concentration range. Phosphorylase activation was detectable within one minute of exposure of the liver to glucagon and was not blocked by puromycin. Both phosphorylase activity and hepatic glucose output were uniformly high at initiation of perfusion; this may be the result of secretion of glucagon during surgical preparation of liver donor rats. It is concluded that activation of phosphorylase is a very rapid and consistent result of glucagon action on the liver, that it can be observed at all concentrations of glucagon which cause glycogenolysis, and that it is not dependent on glycogenolysis or protein synthesis. The effects of glucagon were sufficiently reproducible in these experiments to recommend the isolated perfused rat liver as a semiquantitative bioassay system for glucagon.
