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## A B S T R A C T S

*Alp, Haluk; and Recant, Lillian* (Nutrition Research Lab. of the Dept. of Preventive Med. and the Dept. of Medicine, Washington Univ. Sch. of Med., St. Louis, Mo.): STUDIES OF THE INSULIN-INHIBITORY EFFECT OF HUMAN ALBUMIN FRACTIONS. *J. Clin. Invest.* 44:870-83, May 1965.

The authors report findings that confirm the basic observations of Vallance-Owen that there is an inhibitor of insulin associated with the plasma albumin fraction. Fractions of human plasma albumin were prepared by both the Debro procedure and the method 6 of Conn. Both of these preparations demonstrated significant insulin-inhibitory activity when tested in vitro with rat diaphragm muscle. Albumin preparations were made from normal subjects, diabetic patients, and pregnant nondiabetic women in the third trimester of pregnancy. Albumin prepared from normal subjects and used in a concentration of 3 to 3.5 per cent demonstrated significant inhibition of insulin action. In concentrations of 2 per cent or less no significant degree of insulin inhibition was observed. Albumin preparations from diabetic patients were used in a concentration of 1.25 per cent to 2.5 per cent. Throughout this range of concentration there was highly significant inhibition of insulin action. Albumin prepared from pregnant nondiabetic women and used in a concentration of 2.5 per cent or less also demonstrated significant insulin inhibition. The mechanism of insulin inhibition appeared to be competitive. At higher concentrations of insulin, the inhibitory effect of the same concentration of albumin was decreased. The competition of inhibitor with insulin did not appear to be manifested by an impairment of binding of insulin to the diaphragm. Studies were done that demonstrate that the inhibition is not quantitatively related to free fatty acid content of the albumin. The authors point out that it is not possible to say whether the inhibitor is albumin itself or some molecule associated with the albumin. J.D.B.

*Antoniades, Harry N.; Huber, Agnes M.; Bosbell, Boris R.; Saravis, Calvin A.; and Gershoff, Stanley N.* (Protein Foundation Labs., Jamaica Plain, Mass.; Dept. of Med., Harvard Med. Sch., Dept. of Nutrition, Sch. of Public Health, Harvard Univ. Boston, Mass.; the Dept. of Med., Univ. of Alabama Med. Center, Birmingham, Ala.): STUDIES ON THE STATE OF INSULIN IN BLOOD: PROPERTIES OF CIRCULATING "FREE" AND "BOUND" INSULIN. *Endocrinology* 76:709-21, April 1965.

The immunologic reactivity of "free" and "bound" insulins with guinea pig anti-insulin antisera, their electrophoretic mobilities on Pevikon block and their chromatographic behavior on Sephadex were examined. Bound insulin was obtained from pooled sera on Dowex resin columns; acid ethanol extracts of this insulin were prepared. The "free" insulin was found to correspond to Crystalline Insulin in its physicochemical, immunologic and biological properties. The "bound" form of insulin exhibited a higher molecular weight, slower electrophoretic mobility and was unreactive to insulin antisera. The acid ethanol extraction procedure increased the reactivity of "bound" insulin with insulin antisera as demonstrated by the inhibition of the biological activity of the extracts of "bound" insulin on epididymal adipose tissue by antisera. Identification of the chemical nature of "bound" insulin remains to be elucidated. C.R.S.

*Aronson, Stanley M.; and Aronson, Betty E.* (Dept. of Path., State University of New York, Downstate Med. Center; and the Inst. of Path., Kings County Hosp. Center, Brooklyn, N.Y.): *Arch. Neurol.* 12:390-98, April 1965.

From the autopsy records of 9,223 cases studied at Kings County Hospital Center from 1953 to 1963, the incidences of certain types of brain tumors found in diabetic patients were compared with those found in the nondiabetic population. There was a notable decrease in the frequency of gliomas and metastatic cancers in the 1,011 cases designated as diabetic. The frequencies of meningioma, neurinomas and pituitary

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tumors did not differ appreciably between the two autopsy populations. Sample surveys of the pathology records of another hospital were corroborative. C.R.S.

*Beardwood, Donald M.; Alden, James S.; Graham, Charles A.; Beardwood, Joseph T., Jr.; and Marble, Alexander* (The Joslin Clinic, Boston, Mass., and the Abington Memorial Hosp., Abington, Pa.): EVIDENCE FOR A PERIPHERAL ACTION OF CHLOROTHIAZIDE IN NORMAL MAN. *Metabolism* 14:561-67, May 1965.

Simultaneous determinations of blood glucose and serum inorganic phosphorus were performed in groups of normal subjects with blood samples obtained serially after intravenous administration of sodium tolbutamide. The subjects were divided into three groups: controls, those pretreated with chlorothiazide, and those pretreated with chlorothiazide and potassium chloride. The rate of fall of blood glucose in three groups was nearly identical. There was a significant difference at the forty-five and sixty-minute intervals in the per cent of phosphorus fall in the thiazide-treated groups compared to the control group. The addition of potassium chloride did not influence the decrease in serum phosphorus. An alteration in cellular permeability to phosphorus may have been produced by the action of chlorothiazide. C.R.S.

*Bernard, A. G.; and Ginsburg, Jean* (Dept. of Obstet. and Gynec., Charing Cross Hosp. Med. Sch., London, England): GLUCOSE CONTENT OF NORMAL URINE. *Brit. Med. J.* 1:1437, May 29, 1965.

A method for estimating glucose in urine using a glucose-oxidase method differing from that reported by J. Fine (*Brit. Med. J.* 1:1209, 1965) is reported to yield 100 per cent of glucose recovery as compared to only 80 per cent by the method of Fine. The authors also have found over 90 per cent of apparently normal adults with a mean urinary glucose content of 7 mg. per 100 ml. and that urinary glucose content invariably increases after a carbohydrate load. R.F.B.

*Crombie, D. L.; FitzGerald, M. G.; and Wall, Mary* (Birmingham, England): THE FAMILY HISTORY OF DIABETES. REPORT OF A WORKING PARTY APPOINTED BY THE COLLEGE OF GENERAL PRACTITIONERS. *Brit. Med. J.* 1:960-62, April 10, 1965.

During 1961-1962, 1,307 patients with clinical diabetes confirmed by capillary blood glucose in excess of 180 mg. per 100 ml. two hours after a meal were compared with a nondiabetic control group of 859 persons taken at random as to the known family history of diabetes in the parents, siblings and offspring alive or dead. Asymptomatic cases where a glucose tolerance test was required for diagnosis were excluded if fasting blood glucose was less than 130 mg. per 100 ml. The control group was defined as nondiabetic based upon the absence of glycosuria using Clinistix. For comparison the prevalence rates for known diabetes at different ages were estimated from 18,532 people who constituted a population in or around Birmingham.

In the nondiabetic controls, the proportion of those with known diabetic relatives rose from 2.9 per cent under thirty years of age to 11.4 per cent at seventy years and over. In the diabetic population, the proportion of those under thirty years of age with a diabetic first degree relative was 21.4 per cent, and remained constant for all other age groups. The diabetics under thirty years of age at diagnosis were, therefore, seven times as likely to have at least one first degree diabetic

relative as those in the general population of the same age, whereas those diagnosed at seventy years of age and over had equivalent rates only twice as great.

For siblings of diabetics a high but steady rate of diabetes at all ages was noted, whereas in the control group the much lower rate rose with age and confirmed the general trend noted in all first degree relatives of the control series.

On comparison of the control group with the large general population, the rate of known diabetes was in general agreement and again showed a trend of steady increase with increasing age.

Under thirty years of age when compared with the non-diabetic control, a diabetic at diagnosis was between twelve and twenty-four times as likely to have a similarly affected sibling. The corresponding rate at seventy years or over is only 1.5 times. The results suggest that only diabetes of early onset has a strong genetic background. R.F.B.

*Dannenburg, Warren N.; and Burt, Richard L.* (Dept. of Obstet. and Gynec. Bowman Gray Sch. of Med. and North Carolina Baptist Hosp., Winston-Salem, N.C.): THE EFFECT OF INSULIN AND GLUCOSE ON PLASMA LIPIDS DURING PREGNANCY AND THE PUERPERIUM. *Amer. J. Obstet. Gynec.* 92:195-201, May 15, 1965.

*Verbatim Summary:* (1) Evidence was presented that confirmed the hyperlipidemia of pregnancy and showed that with the exception of esterified cholesterol, significant decrements occurred in the fasting levels of plasma lipids by the fourth postpartum day. (2) The mean changes in plasma levels of triglycerides, free cholesterol, and lipid phosphorus in non-pregnant, pregnant, and puerperal subjects differed significantly in their responses to insulin and/or glucose. (3) Mean changes in cholesterol ester were not attributed to the differential response of the three groups to insulin and glucose, but appeared to be related to the free cholesterol levels. (4) Analysis of variance revealed that with the exception of lipid phosphorus levels, the mean changes in the plasma lipids were attributable to factors other than the group x treatment interaction. (5) Glucose metabolism during pregnancy was altered in favor of cholesterologenesis, and it was indicated this difference was due to impaired carbohydrate metabolism through the dissociation of the effect of insulin on extra-hepatic tissue. (6) The relative amounts of insulin and glucose were reflected in the plasma levels of free cholesterol in pregnant and puerperal subjects. E.A.W.

*Dürr, F.* (Medizinische Universitätsklinik, Tübingen, Germany): A CASE OF HYPEROSMOLAR NON-ACIDOTIC DIABETIC COMA. *German Med. Month.* 9:58-63, February 1964.

A fifty-year-old woman was admitted to the hospital in a coma. She had no history of diabetes, but for the past few weeks had complained of polydipsia and polyuria. For two weeks prior to admission, she had been very tired and weak. Urine contained sugar (7 per cent); blood sugar was 1,200 mg./100 ml. There was no acidosis or ketosis. Fluid was administered in the form of 5 per cent levulose or 5 per cent glucose together with electrolytes. The blood sugar returned to normal within fourteen hours after administration of a total of 894 units of soluble insulin. Consciousness returned to normal only after both fluid balance and serum osmolarity had returned to normal. Eventually, her diabetes was controlled on 100 mg. of n-butyl-biguamide daily. J.A.G.

*Editorial.* INHERITANCE OF DIABETES MELLITUS. Brit. Med. J. 1:940-41, April 10, 1965.

The concept that inheritance of diabetes is a Mendelian recessive is questioned in view of the fact that only about 20 per cent of those genetically prone to develop it are subsequently shown to have diabetes. Efforts to define the question of single or multiple genes in the inheritance of diabetes are clouded by the difficulty in dividing clearly the nondiabetic and the diabetic on the basis of blood sugar values or other metabolic criteria. It is stated that it would not be illogical for a single gene and a multifactorial system of genes to be responsible for the inherited aspects of diabetes. This possibility is compatible with the clinical concept that the syndrome is a result of an imbalance between insulin antagonistic activity and insulin sensitivity into which are interwoven certain environmental factors. R.F.B.

*Ernesti, Manfred; Mitchell, M. L.; Raben, M. S.; and Gilboa, Ygal* (Medical Service, Lemuel Shattuck Hospital, Boston, Mass.): CONTROL OF HYPOGLYCEMIA WITH DIAZOXIDE AND HUMAN GROWTH HORMONE. Lancet 1:628-30, March 20, 1965.

Intractable hypoglycemia is often the most distressing manifestation of metastatic islet-cell carcinoma of the pancreas. Its control with human growth hormone (HGH) is possible but not practical. This report describes the management of hypoglycemia with benzothiadiazines in a seventy-six-year-old woman with an inoperable tumor. Severe hypoglycemia could not be controlled with dietary measures. It could be ameliorated with daily injections of 5 mg. of HGH. When diazoxide was used alone in a dose of 300 mg./day, marked increases of free fatty acids (FFA) occurred and blood sugar values rose to normal. However, nausea and vomiting made this dose impractical. When diazoxide in a dose of 150 mg./day and bendroflumethiazide 10 mg./day were given, effective control of hypoglycemia was possible. When 5 mg./day of HGH was added a chemical diabetes developed. None of these treatments exercised an effect on serum insulin. It is possible therefore, that one action of the thiazides may be to increase levels of FFA sparing glucose oxidation and increasing fat oxidation. T.G.S.

*Hadden, David R.; and Prout, Thaddeus E.* (Dept. of Med., The Johns Hopkins Univ. Sch. of Med., Baltimore, Md.): STUDIES ON HUMAN GROWTH HORMONE: I. RADIOIODINATION. Bull. Hopkins Hosp. 116:110-21, February 1965.

Human growth hormone preparations (Raben or Wilhelm) following iodination with I-131 were tested for homogeneity by Sephadex gel filtration, immunoelectrophoresis in agar gel and polyacrylamide gel electrophoresis. Radioactive growth hormone of low specific activity (average 17.6  $\mu\text{C}/\mu\text{g}$ ) was found to be a stable preparation, but it was rapidly degraded when the specific activity was high (average 138  $\mu\text{C}/\mu\text{g}$ ). O.V.S.

*Hadden, David R.; and Prout, Thaddeus E.* (Dept. of Med., The Johns Hopkins Univ. Sch. of Med., Baltimore, Md.): STUDIES ON HUMAN GROWTH HORMONE: II. THE EFFECT OF HUMAN SERUM ON GROWTH HORMONE LABELED WITH RADIOACTIVE IODINE. Bull. Hopkins Hosp. 116:122-31, February 1965.

Radioactive human growth hormone of low specific activity (average 17.6  $\mu\text{C}/\mu\text{g}$ ) was shown by immunoelectrophoresis to be exclusively bound to serum alpha-2-macroglobulin. The binding was reversible in that the label was removed upon addition of antigrowth hormone immune serum. Similar experiments with growth hormone of high specific activity (average 138  $\mu\text{C}/\mu\text{g}$ ) showed irreversible binding to occur to a number of serum proteins. The latter results were considered to be a product of damaged growth hormone, but the former results were not, and it was therefore concluded that binding of growth hormone to serum alpha-2-macroglobulin may be a factor responsible for the nonspecific inhibition found in some assay systems. O.V.S.

*Haines, Howard; Hackel, D. B.; and Schmidt-Nelson, Knut* (Depts. of Zoology and Path., Duke Univ., Durham, N. C.): EXPERIMENTAL DIABETES MELLITUS INDUCED BY DIET IN THE SAND RAT. Amer. J. Physiol. 208:297-300, February 1965.

The sand rat (*Psammodmys obesus*), a rodent from the Near East and North Africa, becomes diabetic when raised on standard laboratory feeds. Animals collected in their natural habitat, on the other hand, show no signs of diabetes mellitus. Twelve animals were raised in the laboratory on Purina laboratory chow supplemented with fresh vegetables. Most of these animals developed severe diabetes mellitus as indicated by hyperglycemia, glycosuria, and pathological lesions including cataracts, obesity, and B-cell degranulation and vacuolization of the pancreatic islet tissue. Obesity preceded the onset of overt diabetes in the laboratory chow-fed animals. Ten animals raised entirely on fresh vegetables remained healthy without signs of diabetes or obesity. This species offers a fascinating opportunity for the study of the prediabetic state and factors that influence the appearance of overt, chemical diabetes mellitus. M.G.B.

*Heald, Felix P.; Mueller, Peter S.; and Dangel, Mary Z.* (Div. of Adolescent Med., Children's Hosp., Dist. of Columbia; Dept. of Pediatrics, Georgetown Univ. Sch. of Med.; and Lab. of Clinical Science, National Institutes of Health, Bethesda, Md.): GLUCOSE AND FREE FATTY ACID METABOLISM IN OBESE ADOLESCENTS. Amer. J. Clin. Nutr. 16:256-64, February 1965.

Using a study group of twelve obese adolescents and a control group of fourteen adolescents, the effect of a twenty-four hour fast as well as the intravenous administration of glucose, epinephrine and insulin on plasma free fatty acids and blood glucose levels was studied. Initial mean fasting concentrations of free fatty acids for obese normal adolescent subjects were significantly higher than the mean for normal adults. However, initial mean fasting serum concentrations of free fatty acids and glucose did not differ significantly between obese and control adolescent subjects. Four hours after glucose infusion, the blood glucose level was significantly lower in the obese subjects than in the control adolescent subjects. The obese subjects developed less hyperglycemia and had a delay in rise of free fatty acids following epinephrine injection as compared to the controls. Free fatty acids response to insulin infusion was diminished in the obese subjects; however, there was no difference in the glucose response to insulin between the groups.

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*Editorial comment:* The initial free fatty acid concentration was abnormally high in the obese subjects which may have affected the insulin sensitivity of these individuals to some degree. B.R.B.

*Herman, Michael V.; and Gorlin, Richard* (Peter Bent Brigham Hosp. and Harvard Med. School, Boston, Mass.): EDITORIAL. PREMATURE CORONARY ARTERY DISEASE AND THE PRECLINICAL DIABETIC STATE. *Amer. J. Med.* 38:481-83, April 1965.

A review of the concept that diabetic vascular disease may occur prior to the symptoms or diagnosis of diabetes. A study of seventy-nine patients with coronary artery disease manifested at an early age (thirteen below forty years and thirty-seven below fifty years of age) by angina pectoris and confirmed by cinearteriography. Blood sugar levels were studied in the fasting state in fifty-five by intravenous glucose tolerance test. Studies of blood lipids were performed in all seventy-seven. The prevalence of unsuspected diabetic glucose tolerance tests was 62 per cent. Hyperlipidemia was present in 57 per cent of the entire group and 62 per cent of those with abnormality of carbohydrate metabolism. S.B.B.

*Issekutz, B., Jr.; Miller, H. I.; Paul, P.; and Rodahl, K.* (Div. Res., Lankenau Hosp., Philadelphia, Pa.): AEROBIC WORK CAPACITY AND PLASMA FFA TURNOVER. *J. Appl. Physiol.* 20:293-96, March 1965.

Palmitate-1-C-14 was given by continuous intravenous infusion to dogs during a period of standardized exercise on a treadmill. The oxygen uptake was approximately the same in all animals, but they could be divided into two groups according to the changes observed in blood lactate. Dogs that exhibited a large rise in blood lactate during exercise were classified as "untrained," and those showing little rise in blood lactate were called "trained." In trained dogs there was a moderate rise in plasma free fatty acid concentration and turnover rate, whereas in the untrained group the free fatty acid concentration and turnover fell during exercise. It is known that infusion of lactate can decrease the mobilization of free fatty acids from adipose tissue. Therefore, it is concluded that if exercise is relatively severe enough to cause a rise in blood lactate, this increase in lactate can in turn decrease the release and turnover of free fatty acids. H.T.N.

*Kane, John P.; Longcope, Christopher; Pavlatos, Fotios Ch.; and Grodsky, Gerold M.* (Metabolic Res. Unit and the Dept. of Med. of the Univ. of California Sch. of Med.; and the Heart Disease Control Program, Field and Training Station, U.S. Public Health Service, San Francisco, Calif.): STUDIES OF CARBOHYDRATE METABOLISM IN IDIOPATHIC HYPERTRIGLYCERIDEMIA. *Metabolism* 14:471-86, April 1965.

Studies were conducted of carbohydrate metabolism in fourteen subjects with idiopathic hypertriglyceridemia characterized by mild hyperglycemia after a glucose load, absence of ketosis, and lipemia with normal levels of lipoprotein lipase activity in postheparin blood plasma. The response of these patients to insulin, glucagon and tolbutamide injections with respect to glucose and free fatty acid (FFA) levels were compared with those obtained in twelve control subjects. Serum insulin levels were estimated by fat pad bioassay and radioimmunoassay technics during the oral glucose tolerance test. The hypertriglyceridemic patients exhibited a decreased sensi-

tivity to insulin during glucose loading and had impaired blood glucose responses to tolbutamide. The fasting levels of FFA were higher in plasma and did not decline as rapidly or to as low levels as in control subjects during glucose loading or after intravenous insulin, glucagon or tolbutamide. Serum insulin levels were generally within the normal ranges during glucose loading. These findings suggest a relatively reduced responsiveness to insulin in tissues of these patients. C.R.S.

*Lerman, Sidney* (Depts. Surg. and Biochem., Univ. of Rochester Sch. Med. and Dentistry, Rochester, N.Y.): METABOLIC PATHWAYS IN EXPERIMENTAL SUGAR AND RADIATION CATARACT. *Physiol. Rev.* 45:98-122, January 1965.

The histologic and biochemical changes that are observed in the lens of experimental animals given large amounts of galactose or xylose are compared with the findings in diabetic cataracts. Alterations that occur in lenses after exposure to X rays are also reviewed. H.T.N.

*MacGregor, Malcolm; and Robinson, Ronald* (Warwick Hosp., Warwick, England): RAPID ESTIMATION OF BLOOD GLUCOSE (Correspondence). *Brit. M. J.* 1:587, Feb. 27, 1965.

The reliability of Dextrostix in rapid estimation of blood glucose in diabetic children is confirmed except for an experience cited by the authors in a female infant forty-eight hours after birth. In the latter instance, blood sugar estimation using a heel-prick sample by the Dextrostix method yielded no color change, indicating a blood glucose of less than 40 mg. per 100 ml. An umbilical vein venous sample revealed a glucose concentration of 80 mg. per 100 ml. After intravenous dextrose solution, the estimation of blood glucose by Dextrostix on a sample obtained by heel prick again revealed no color change, but immediately afterwards a repeat umbilical vein sample yielded a value of 800 mg. per 100 ml. In view of the fact that these blood glucose levels were determined because of a sudden, prolonged episode of cyanosis in the infant, it was presumed that stagnation of peripheral circulation had caused the extremely low glucose level obtained by Dextrostix, and that heel-prick samples for diagnosis of hypoglycemia in neonates may be misleading. R.F.B.

*Marubama, Yosbisuke* (Med. Dept. of Prof. Shoichi Yamagata, Tohoku Univ. Sch. of Med., Sendai, Japan): DIET AND BLOOD LIPIDS IN NORMAL AND DIABETIC RATS. *Metabolism* 14:78-87, January 1965.

The effects of six kinds of test diets upon the blood lipid levels in normal and diabetic (alloxan) rats were observed. Saturated fat diets produced hypercholesterolemia in both groups of animals. High cholesterol diets produced hypercholesterolemia in diabetic rats but not in normal rats. Unsaturated fat diets caused a fall of plasma total cholesterol in both groups. Unsaturated fat diets rich in cholesterol produced a rise of plasma cholesterol in normal rats and a fall in diabetic rats. High carbohydrate diets caused a rise in plasma triglyceride in both groups. The unsaturated fat diets, with or without cholesterol, raised the plasma triglyceride in the diabetic animals and lowered the level in the normal group. Cholesterol-rich diets alone did not affect triglycerides in either group. The diet which lowered the level of plasma cholesterol had an effect of increasing the triglyceride in the diabetic rat. The glucose tolerance in the diabetic animals was adversely affected by carbohydrate feeding. C.R.S.

ABSTRACTS

*Medley, D. R. K.* (Manchester Royal Infirmary, Manchester, England): THE RELATIONSHIP BETWEEN DIABETES AND OBESITY: A STUDY OF SUSCEPTIBILITY TO DIABETES IN OBESE PEOPLE. *Quart. J. Med.* 34:111-32, January 1965.

Results of prednisolone-stressed intravenous glucose tolerance tests were reported in a series of 134 obese, but otherwise normal, men and women. The amount of prednisolone was 0.4 mg. per kilogram body weight equally divided into two doses, administered to fasting patients eight and one-half hours and two hours prior to an intravenous glucose tolerance test. Special mathematical treatment was used to validate the following results: A group of normal, nonobese people showed no impairment of glucose tolerance while obese patients did. This was particularly significant for those who had a family history of diabetes and gave birth to heavy children. The author inferred from these results that the frequent association of obesity and diabetes may mean that either the former is a precipitating factor for the latter, or obesity is a consequence of the prediabetic state. O.V.S.

*Merimee, Thomas J.* (Dept. of Med., Johns Hopkins Univ. School of Med., Baltimore, Md.): INSULIN RESISTANCE, STUDY OF EFFECT OF 6-MERCAPTOPYRINE. *Lancet* 1:69-71, Jan. 9, 1965.

A comparison of the effects of 6-mercaptopyrine and prednisone on amelioration of insulin resistance is reported. In one instance, a fifty-two-year-old woman displayed a daily insulin requirement of 2,400-2,700 U. This was not reduced by use of pork insulin or 6-M.P. When she was given 30 U. of prednisone daily, the insulin requirement promptly fell to 140 U. None of the agents influenced the insulin binding capacity of her plasma. A second patient had an average daily insulin requirement of 3,400 U. Again, neither substitution of pork insulin or 175 mg. daily of 6-M.P. changed the insulin need. Prednisone administration not only reduced the insulin requirement to less than 100 U. but the insulin binding capacity fell from 980-1,250 to 85-125 milliunits per ml. T.G.S.

*Nydicke, Martin; Samols, Ellis; Kuzuya, Takeshi; and Williams, Robert H.* (Dept. of Med., Univ. of Washington, Seattle, Wash.): A DIFFICULT DIAGNOSTIC PROBLEM IN SPONTANEOUS HYPOGLYCEMIA: REACTIVE HYPOGLYCEMIA IN MILD DIABETES MELLITUS. *Ann. Intern. Med.* 61:1122-27, December 1964.

A fifty-three-year-old female patient who was thought to have an insulinoma was studied with serum insulin responses during the following tests: oral glucose tolerance, intravenous sodium tolbutamide, intravenous glucose tolerance, oral L-leucine tolerance and intravenous glucagon. The results disclosed mild diabetes mellitus and reactive hypoglycemia. The differential diagnosis and several possible explanations of the cause of this syndrome are discussed. This is apparently the first reported case of mild diabetes with hypoglycemia in which serum-insulin responses have been studied. B.F.K.

*Pengelly, C. R.* (Altrincham, Cheshire, Eng.): DIABETES MELLITUS AND CYCLOPHOSPHAMIDE. *Brit. Med. J.* 1:1312-13, May 15, 1965. (Correspondence)

The development of diabetes mellitus in three female patients, two with carcinoma of the breast and metastases and one with carcinoma of the lung with pleural metastases, occurred after treatment with cyclophosphamide 100 to 200 mg.

daily. Control of diabetes was obtained with diet and/or sulfonylureas. No blood glucose or glucose tolerance data were obtained prior to treatment with cyclophosphamide. Two patients succumbed and at postmortem examination no definite metastases in the pancreas were found. R.F.B.

*Schlichtkrull, J.; Munck, O.; and Jersild, M.* (Hvidovre Hosp., and Novo Terapeutisk Laboratorium A/S, Copenhagen, Denmark): THE M-VALUE, AN INDEX OF BLOOD SUGAR CONTROL IN DIABETICS. *Acta Med. Scand.* 177:95-102, January 1965.

Based upon multiple blood sugar estimations daily for a six-day period, a formula was worked out called the M-value. It may be used for assessing various hypoglycemic treatments and for characterizing the lability of diabetes. B.F.K.

*Schwartz, Philip; Kurucz, J.; and Kurucz, A.* (Dept. of Path., Warren State Hosp., Warren, Pa.; Dept. Exper. Path. of Korányi Res. Instit., and Clin. of Pediat. of the Hosp. for Infect. Dis., Budapest, Hungary): FLUORESCENCE MICROSCOPY DEMONSTRATION OF CEREBROVASCULAR AND PANCREATIC INSULAR AMYLOID IN PRESENILE AND SENILE STATES. *J. Amer. Geriat. Soc.* 13:199-205, March 1965.

The authors did fluorescence microscopy on material from 111 autopsies of patients in the fifty to ninety-one-year age group. Cerebral and cerebral vascular amyloidosis was present in 82 per cent, pancreatic-islet amyloidosis was present in 75 per cent; both cerebral and pancreatic-islet tissues were affected in 50 per cent of thirty autopsies that were examined for both. Generalized amyloidosis was observed in only two of these patients. One had syphilis and the other was suffering from chronic purulent bronchitis. No amyloidosis was observed in a group of six younger persons whose ages ranged from thirty to forty-five years.

*Editorial Comment:* Is it possible that amyloid deposits in the islets may account for carbohydrate intolerance in the elderly? B.R.B.

*Weller, John M.; and Borondy, Paul E.* (Dept. of Intern. Med., Univ. of Mich., Ann Arbor, Mich.): EFFECTS OF BENZOTHIADIAZINE DRUGS ON CARBOHYDRATE METABOLISM. *Metabolism* 14:708-14, June 1965.

The administration of chlorothiazide both to man and to rats resulted in hyperglycemia following a glucose load. Glucose tolerance tests done on patients revealed that long-term chlorothiazide therapy resulted in a decreased rate of glucose utilization despite potassium chloride supplementation. Experiments with the rat epididymal fat pad demonstrated both in vivo and in vitro effects of the drug. The fat pad of animals receiving chlorothiazide showed a reduced rate of glucose disappearance from the medium whether or not insulin is added to the medium. Adding chlorothiazide to the medium further depressed the utilization of glucose by the fat pads of the chlorothiazide-treated animals. This effect was observed also in the fat pad of the untreated rat when chlorothiazide was added to the medium. These effects of chlorothiazide may be due to a decrease in serum insulin-like activity which would lower the availability of insulin-dependent intracellular enzymes as well as to a direct effect of the drug upon the tissues. The latter action was demonstrated by the addition of the drug directly to the incubating medium resulting in a decrease in glucose uptake by the fat pad. C.R.S.

ABSTRACTS

Whaley, William H.; Zuspan, Frederick P.; and Nelson, George H. (Dept. of Obstet. and Gynec., Med. Coll. of Georgia, Augusta, Ga.): GLUCOSE AND NONESTERIFIED FATTY ACID LEVELS IN MATERNAL AND CORD PLASMA. *Amer. J. Obstet. Gynec.* 92:264-66, May 15, 1965.

*Verbatim Conclusion:* (1) Simultaneous maternal and newborn plasma glucose and NEFA levels were determined at the time of delivery in forty-four patients. (2) Maternal NEFA and glucose levels were higher than newborn levels. (3) The maternal: newborn NEFA ratio was 1.7:1. The maternal: newborn glucose ratio was 1.3:1. (4) The glucose: NEFA ratio was significantly different in the mother and newborn. E.A.W.

Whitfield, A. G. W.; Crane, C. W.; French, J. M.; and Bayley, T. J. (United Birmingham Hospitals, Birmingham, England): LIFE WITHOUT A PANCREAS. *Lancet* 1:675-77, March 27, 1965.

A review of the literature shows few reports of long-term observations made on patients who have survived total pancreatectomy. The authors describe the course of a man who had this operation when fifty-five years of age and remains alive fifteen years later. For twelve of the fifteen years, this patient has taken a "free diet" and his diabetes has been treated with 18 to 22 units of Regular Insulin plus 4 to 8 units of Protamine Zinc Insulin daily. His optic fundi are normal, there is no evidence of coronary or peripheral arteriosclerosis and his urine is free of protein. The only neurological defect is absence of the knee and ankle jerks. The longest observations made by other authors are up to twelve years. T.G.S.

Wilber, John F.; and Odell, William D. (Endocr. Branch, National Cancer Inst., National Insts. of Health, Bethesda, Md.): HYPOGLYCEMIA AND DWARFISM ASSOCIATED WITH THE ISOLATED DEFICIENCY OF GROWTH HORMONE. *Metabolism* 14:590-97, May 1965.

A seven-year-old dwarfed boy with a history of severe, recurrent hypoglycemic episodes since age one year and retarded bone age was studied with respect to carbohydrate metabolism before and during human growth hormone administration. Hepatic, thyroid and adrenal functions were normal. Fasting hypoglycemia with blood sugars of 30 to 40 mg. per 100 ml. was noted. He was not sensitive to L-leucine but showed insulin sensitivity and hypoglycemic unresponsiveness. Normal responses in glycogenolysis occurred following administration of epinephrine and glucagon. Fasting growth hormone levels were abnormally low and did not rise during insulin-induced hypoglycemia or after a glucose tolerance test. It appeared that the patient had an isolated deficiency of growth hormone associated with alterations in carbohydrate metabolism which were corrected by administration of growth hormone. The failure to observe similar relationships between isolated growth hormone deficiency and abnormalities in carbohydrate metab-

olism in other patients described in the literature remains unanswered. C.R.S.

Wybregt, Susan H.; Reisner, Solomon H.; Patel, Roda K.; Nellhaus, Gerhard; and Cornblath, Marvin (Depts. Pediat. and Neuro.—Neuro. Surg., Univ. Ill. Coll. Med., Chicago, Ill.): THE INCIDENCE OF NEONATAL HYPOGLYCEMIA IN A NURSERY FOR PREMATURE INFANTS. *J. Pediat.* 64:796-802, June 1964.

An attempt to correlate hypoglycemia in newborns admitted to a premature nursery unit with the infant's later physical, neurological and mental development. The study group consists of all infants admitted to the premature nursery during the year 1963. Two or more blood glucose measurements were made during the first five days of life and the infants were classified according to the presence and severity of hypoglycemia. The infants will be followed for five years, during which annual examinations will be performed by neurology, psychology, and social service.

Eight of 128 infants had symptomatic hypoglycemia in the nursery. The incidence of hypoglycemia is approximately 15 per cent in all symptomatic infants whose birth weights are less than the fiftieth percentile for gestational age. J.M.P.

Yeager, Vernon L.; Picchioni, Janice A.; Sether, Lowell A.; and Severson, Arlen R. (Dept. of Anat., Univ. of N.D., Sch. of Med., Grand Forks, N.D.): LATHYRISM IN DIABETIC RATS. *Arch. Path.* 79:206-12, February 1965.

The adductor longus-pectineus exostoses were measured in lathyric, diabetic-lathyric, and weight-paired-lathyric rats following two weeks on beta-aminopropionitrile (BAPN) treatment. The diabetic-lathyric rats had larger exostoses than other groups of animals despite factors of age, weight gain, possible adrenal hyperplasia and muscle atrophy, each operating in opposition to this observed effect in the diabetic animals compared to other groups. Rats receiving limited food intake did not develop typical exostoses. C.R.S.

Young, R. B.; Bongiovanni, Alfred M.; Kaye, Robert; and Smolens, Joseph (The Children's Hosp. of Philadelphia and Dept. of Pediatrics, University of Pennsylvania, Philadelphia, Pa.): HYPERGLYCEMIC FACTOR IN DIABETIC PLASMA: RESPONSE IN IDIOPATHIC HYPOGLYCEMIA. *Amer. J. Med. Sci.* 249:499-505, May 1965.

Two infants (ages thirty and twenty-five months) with idiopathic hypoglycemia (not due to leucine sensitivity) were treated with intravenous injections of 10 to 50 ml. of plasma from known, insulin-treated diabetic patients. Plasma from three adult (maturity-onset) diabetic patients had no effect whereas a hyperglycemic response of up to four days duration resulted from plasma obtained from juvenile diabetic patients during insulin withdrawal (NPH twenty-four hours and Crystalline for sixteen hours). There was no correlation between the hyperglycemic effect and the presence of antibodies to commercial (beef-pork) insulin in the blood of donors, nor could the results with whole plasma be duplicated by use of various separated protein fractions of the same plasma. S.B.B.