ABSTRACTS

Abramson, Eugene; and Arky, Ronald A. (Thorndike Memorial Lab., Harvard Med. Sch., Boston, Mass.): TREATMENT OF THE OBESE DIABETIC. A COMPARATIVE STUDY OF PLACEBO, SULFONYLUREA AND PHENFORMIN. Metabolism *16*:204-12, March 1967.

Three groups of obese diabetic out-patients were studied over a three-week period to compare the effects of diet and placebo, sulfonylurea, and phenformin on glucose tolerance, free fatty acids (FFA), insulin, cholesterol and body weight. Patients receiving diet and placebo manifested small increments in the immunoreactive insulin levels, transient fall in FFA, and no change in glucose tolerance. The phenformin-treated group exhibited reduced insulin output with decreased glucose and FFA levels. Sulfonylurea treatment resulted in a marked increase in insulin release with decrements in glucose and FFA comparable to the phenformin group. During the brief period of study no differences were observed in the mean loss of weight nor in the cholesterol-lowering influence of each regimen. Determination of the insulin/glucose ratios indicated a small increase in insulin production in the diet-placebo group, a direct hypoglycemic effect without insulin stimulation by phenformin, and a marked insulin-stimulatory action accompanied by decreased glucose levels in those treated with sulfonylurea. C.R.S.

Beaser, Samuel B. (Harvard Med. Sch., Boston, Mass.): LABORATORY PROCEDURES: THEIR CLINICAL SIGNIFICANCE. CLINICAL STATES WITH DECREASED GLUCOSE TOLERANCE. JAMA *199*:990-91, March 27, 1967.

The author discusses the technics of diagnosis of early diabetes mellitus by glucose tolerance tests in adults in the presence of pregnancy, obesity, hyperpituitarism, thyrotoxicosis, acute myocardial infarction, cirrhosis of the liver, and uremia. In addition, the adverse influence of age on the glucose tolerance test is described together with a compromise approach to diagnosis of diabetes in the elderly. The limited usefulness of ancillary blood insulin determination in these various conditions is mentioned. S.B.B.

Davies, D. M.; MacIntyre, A.; Millar, E. Joan; Bell, S. M.; and Mehra, S. K. (Shotley Bridge Gen. Hosp., Durham, England): NEED FOR GLUCAGON IN SEVERE HYPOGLYCAEMIA INDUCED BY SULPHONYLUREA DRUGS. Lancet *1*:363-64, Feb. 18, 1967.

Previous case reports have stressed that hypoglycemia secondary to overdosage of sulfonylurea drugs may be resistant to glucose infusion. This report describes a seventeen-year-old nondiabetic girl who took between 5.0 and 7.5 gm. of chlorpropamide seventeen hours before she was admitted to the hospital in coma. Her initial blood sugar was 35 mg. per 100 ml. and despite administration of 1 mg. of glucagon and 490 gm. of glucose over the next forty hours, her blood sugar fluctuated between 35 and 70 mg. per 100 ml. After forty hours, a regimen employing 1 mg. of glucagon intramuscularly every two hours was begun. The first glucagon injection was associated with a rise in blood sugar from 46 to 320 mg. per 100 ml. in thirty minutes. It was found that blood glucose could be maintained at hyperglycemic levels as long as glucagon was continued. Despite this response, the patient died on the eighth hospital day, and autopsy showed diffuse central nervous system changes. Prolonged hypoglycemia with sulfonylurea overdosage is believed to be due to sulfonylurea inhibition of hepatic glycogenolysis. Since this effect can be overcome by glucagon, it is suggested that this agent be used along with glucose in treatment of sulfonylurea-induced hypoglycemia. T.G.S.

Glover, J. S.; Salter, D. N.; and Shepherd, B. P. (The Radiochemical Centre, Amersham, Buckinghamshire, England): A STUDY OF SOME FACTORS THAT INFLUENCE THE IODINATION OF OX INSULIN. Biochem. J. *103*:120-28, April 1967.

The influences of carrier iodide, iodine monochloride and *p*H on the labeling of ox insulin with I-131 by the iodine monochloride method have been studied. The quantitative effect of the iodide in the radioactive iodine preparation was that predicted from a calculation of its specific activity. No other interfering factors were detected in the [I-131] iodide solutions used. Increasing the molar ratio of iodine monochloride to insulin resulted in an increase followed progressively by a decrease in the proportion of I-131 bound, while the total iodine bound increased to an amount characteristic of *p*H and thereafter remained constant. The influence of *p*H on the iodination of insulin with iodine monochloride was complex, and the *p*H curve showed two maxima, at *p*H 2.8 and 6.4. At *p*H 2.8, it was not possible to exceed 8 atoms of iodine bound per molecule by increasing the molar ratio of iodine monochloride. Similarly at *p*H 6.4, the substitution value of 11.5 atoms of iodine per molecule could not be exceeded. Iodinated insulins containing an average of 1.96, 2.74, 6.0 and 7.0 atoms of iodine per molecule fully retained the ability to bind guinea-pig anti-(ox insulin) serum, and the ability to compete with unlabeled insulin for antibody sites became significantly changed only in the most highly substituted preparations and in the presence of large concentrations of unlabeled insulin. The method for the iodination of insulin with 98 per cent incorporation of I-131 by using chloramine-T is described. I-131-iodinated insulin prepared with graded quantities of chloramine-T in excess of that required for efficient labeling was less efficiently bound by guinea pig anti- (ox insulin) serum than insulin labeled by the iodine monochloride method. P.H.W.

Leemann, W.; Almary, F.; and Constam, G. R. (Zürich, Switzerland): DISTURBANCE OF ZINC METABOLISM IN A DIABETIC HORSE AND A DOG MADE DIABETIC WITH ALLOXAN. Zbl. Veterinarmed. *13*:392-404, 1966.

In the diabetic man, horse, and dog, the authors have observed an increase in zinc excretion in the urine. In one alloxan diabetic dog, the rise in zinc excretion did not occur until after four months. This excretion was higher in the presence of poor diabetic control. However, the excretion of zinc did not correlate closely with diabetes control. In a diabetic female dog the plasma zinc level was 135 μg. per cent before insulin therapy, falling to a range of 74 to 110 μg. per cent when insulin therapy was initiated, with sporadic

rises to 121 to 143 μg. per cent. Daily doses of 25 to 28 U. of long-acting insulin produced in the first six to ten hours a fall in plasma zinc to 80 μg. per cent, followed by a rise up to a mean of 104 μg. per cent towards the end of the day. The blood-sugar level fell in the first ten hours to about 40 mg. per 100 ml. and rose in the following thirteen to fourteen hours to a mean of 325 mg. per 100 ml. In this dog the course of the zinc level in plasma and urine was studied after injecting 1 mg. zinc per kilogram body weight in the form of 1:2 zinc-histidine complex. In twenty-two days 30 to 49 per cent of the injected zinc had been excreted in the urine. The level of plasma zinc fell in the first four hours from a very high initial value of about 190 μg. per cent, representing the distribution of the injected zinc throughout the body, and descended in the following four days to 102 μg. per cent as a result of the excretion of zinc. Assay of the autopsy specimen five years after the production of alloxan diabetes revealed the zinc content of the pancreas to be 4.5 mg. per cent and that of the tapetum nigrum 102.6 mg. per cent, while the dry matter of the retina contained 7.4 mg. per cent of zinc. The glycogen content of the liver (4.51 per cent) was normal. **J.A.G.**

Lubos, Manuel C.; Gerrard, John W.; and Buchan, Douglas J. (Dept. of Pediat. and Dept. of Med., Univ. of Saskatchewan, Saskatoon, Sask., Canada): DISACCHARIDASE ACTIVITIES IN MILK-SENSITIVE AND CELIAC PATIENTS. J. Pediat. 70:325-31, March 1967.

Oral lactose tolerance as well as disaccharidase activity and mucosal histology in jejunal biopsies were assessed in three groups of patients and compared to a control group. Eighteen subjects (Group I) with diarrhea in association with sensitivity to cow's milk had normal intestinal mucosal morphology and enzyme activities despite the presence of a flat lactose tolerance curve in six subjects. Diarrhea was induced evanescantly in only one. Thirteen patients with celiac disease treated with gluten-free diets (Group II) and nine untreated patients with celiac disease (Group III) had abnormal morphology and significantly decreased disaccharidase activities. Oral lactose tolerance curves were flat in five patients tested in Group III. No diarrhea or abdominal discomfort was elicited, however. The authors conclude that milk intolerance observed in milk-sensitive and celiac disease patients does not correlate well with intestinal enzyme deficiencies. R.K.K.

Malaisse, Willy; Malaisse-Lagae, Francine; and Wright, Peter H. (Dept. of Pharmacol., Indiana Univ. Med. Center, Indianapolis, Ind.): A NEW METHOD FOR THE MEASUREMENT IN VITRO OF PANCREATIC INSULIN SECRETION. Endocrinology 80:99-108, January 1967.

Pancreatic tissue incubated in a buffered medium with insulin rapidly destroys the hormone through the action of a lytic factor released into the medium. Insulin which is bound by antibodies in guinea pig anti-insulin serum (GPAIS) is not affected by the lytic substance. When GPAIS is added to the medium, it traps insulin secreted by the pancreas before lysis occurs. The secretion of pancreatic insulin in vitro can be measured from the fall in insulin binding capacity of known amounts of GPAIS added to the medium at the beginning of incubation. Insulin secretion occurs at a constant rate for the first two hours of incubation and is directly related to the weight and size of incubated tissue. Glucose and mannose stimulate insulin secretion in normal pancreas; no neutralization of GPAIS occurs using pancreatic tissue from the alloxan-diabetic rat or in normal tissue incubated in the presence of mannoheptulose. The stimulant effect of glucose is abolished by anoxia, 2, 4, dinitrophenol and cyanide; it is competitively inhibited by 2-deoxyglucose. The method of estimating pancreatic insulin secretion is simple and reproducible and offers opportunity for studies of the mechanisms of insulin secretion and factors influencing it. C.R.S.

Moorhouse, J. A.; Smithen, C. S.; and Houston, E. S. (Metabolic Lab., Winnipeg Gen. Hosp., and the Dept. of Physiol., Univ. of Manitoba, Winnipeg, Manitoba, Canada): A STUDY OF GLUCOSE TRANSPORT KINETICS IN MAN BY MEANS OF CONTINUOUS GLUCOSE INFUSIONS. J. Clin. Endocr. 27: 256-64, February 1967.

Verbatim Summary. Continuous glucose infusions were given to ten healthy subjects, ten subjects with nonketotic diabetes of varying severity and four ketosis-prone diabetic subjects. The diabetic subjects were treated with insulin so that the fasting blood glucose level at the beginning of their tests would be within or near the normal range. The infusions were continued until a constant blood glucose level was reached. At equilibrium the rate of glucose uptake by the tissues was presumed to be equal to the glucose infusion rate minus the rate of glucose loss in the urine. The rate of glucose uptake at equilibrium was plotted against the increment in the blood glucose concentration produced by the infusion. The rate-concentration relationship for each group of subjects conformed to a hyperbola which fits the Michaelis-Menten equation. This is consistent with the presence throughout the body of saturable cell-membrane glucose transport systems. The values calculated for maximal transport velocity (V) were 59, 22 and 5 gm./hr./m^2 and for the blood glucose increment at half-maximal velocity (K_m) and 62, 152 and 133 mg. per 100 ml. in the healthy and in the nonketotic and ketosis-prone diabetic subjects, respectively. Serum insulin levels during the glucose infusions rose less in the diabetic than in the healthy subjects and did not correlate significantly with the infusion rate. The results suggest that disorders of cellular glucose transport in diabetes can be studied in man; that the abnormality of glucose transport persists in diabetic subjects carefully treated with depot insulin; that glucose transport kinetics are quantitatively similar in nonketotic diabetes of varying clinical severity; and that during prolonged glucose infusions the rate-limiting factor for insulin activity may be the capacity of the islet cells to synthesize new insulin.

Özen, Muhlis A.; Sandalci, Özkan; and Berker, Ferhan (Cape Intern. Diseases Clinic, Topkapi, Istanbul, Turkey): ETHACRYNIC ACID AND CARBOHYDRATE METABOLISM. Amer. J. Med. Sci. 252:558-63, November 1966.

The authors studied the carbohydrate metabolism after the intermittent administration of 2,3-dichloro-4-(2-methylene butyryl) phenoxyacetic (ethacrynic acid) to six patients who were edematous, nondiabetic, nonhypertensive and without a positive family history of diabetes mellitus. Three patients had nephrosis, one decompensated arteriosclerotic heart disease and two cor pulmonale. They were all males and their ages ranged from twenty-nine to sixty-six years. The drug was administered for four weeks on a set schedule. After an initial

four days of increasing dosage from 50 to 200 mg. daily, the drug was administered at a dose of 200 mg. per day for three days alternating with drug-free intervals of four days each up to thirty days, a total of 2,300 mg. per patient for the month. Carbohydrate metabolism was tested by intravenous glucose tolerance test (0.5 gm. per kg. ideal body weight), intravenous insulin tolerance test (0.05 U. per kg.) and intravenous sodium tolbutamide test (1.0 gm. intravenously) before and after the month of therapy. No change in the carbohydrate metabolism as measured by these tests was noted in all of the patients. S.B.B.

Pell, Sidney; D'Alonzo, C. Anthony (Med. Div., E. I. du Pont de Nemours and Co., Wilmington, Del.): SICKNESS ABSENTEEISM IN EMPLOYED DIABETICS. Amer. J. Public Health '57:253-60, February 1967.

A study of diabetics employed by the DuPont Company was begun in 1963 to investigate certain epidemiologic aspects of disease and to determine what effect, if any, the disease had on the working life of the diabetic. Six hundred and twenty-two diabetics were studied, and they were matched against a control group. The study indicated that 72 per cent of the diabetics had either no absences or only one absence during the year, and six per cent had more than three absences. As a group, however, the diabetics had more bouts of illness, almost twice as many days of disability and, when ill, were disabled for a longer period of time. Those with severe diabetes requiring insulin had slightly more absenteeism than the milder cases. Digestive disorders were significantly more frequent among the diabetics, who also had notably more absence for heart disease and neurologic disorders. The number of cases in these categories, however, was too small to be statistically significant. Respiratory infections occurred with about the same frequency in both groups, but prolonged disability for these illnesses was more common among the diabetics. About seven per cent of the diabetics had at least one absence during the year because of the diabetes. The need to assess the risk in hiring each diabetic on an individual basis was emphasized. P.S.E.

Pollack, Albert A.; McGurl, Thomas J.; Macintyre, Neil (Mutual Life Insurance Co., New York, N.Y.): DIABETES MELLITUS. A REVIEW OF MORTALITY EXPERIENCE. Arch. Intern. Med. 119:161-63, February 1967.

A study was done of the mortality experience of those diabetics who purchased life insurance from Mutual of New York. The study corroborated the findings of similar studies which indicated that the longer the duration of diabetes and the younger the age at diagnosis the higher is the mortality ratio. Of great clinical interest was the favorable mortality of those diabetics treated with diet alone, with oral hypoglycemic agents alone and those receiving small amounts of insulin. The incidence of heart disease and cerebrovascular disease as a cause of death was found to be very high. P.S.E.

Posner, Norman A.; Silverstone, Felix A.; Pomerance, William; and Singer, Nechama (Depts. of Obstet. and Gynec. and Med., Maimonides Med. Center; Dept. of Obstet. and Gynec., State Univ. of New York, Downstate Med. Center, Brooklyn, N.Y.): ORAL CONTRACEPTIVES AND INTRAVENOUS GLUCOSE TOLERANCE. II. LONG-TERM EFFECT. Obstet. Gynec. 29:87-92, January 1967.

Verbatim Summary. Forty women attending a Family Planning Clinic received an intravenous glucose tolerance test before, two to four months after, and four to six months after beginning Enovid for contraceptive purposes. After six months a significant decline was noted in K, the measure of carbohydrate tolerance, when compared with pretreatment values. This decline was not present in a control group of seven women using an intrauterine contraceptive device. Diabetes suspects showed an earlier decrease in glucose tolerance than nondiabetic subjects. There was a distinct tapering in the rate of decline in K during the second fifteen weeks as compared with the first nine weeks. In ten subjects observed for eighteen months with five tests, there was a tendency toward reversal of the previous decline in tolerance. No subject developed an elevated fasting blood sugar or overt diabetes. Although several abnormally low K values were recorded, this pattern of change was not consistent. The evidence is insufficient to warrant indiscriminate elimination of oral contraceptives. It is suggested that, at least in diabetes suspects, repeated observations of glucose tolerance be carried out during therapy with oral contraceptives.

Rabinowitz, D.; Merimee, T. J.; Burgess, J. A.; and Riggs, L. (The Johns Hopkins Univ. Sch. of Med., Baltimore, Md.): GROWTH HORMONE AND INSULIN RELEASE AFTER ARGININE: INDIFFERENCE TO HYPERGLYCEMIA AND EPINEPHRINE. J. Clin. Endocr. 26:1170-72, October 1966.

Plasma insulin and growth hormone levels were studied by immunoassay following an arginine load (30 gm.) in twelve healthy female subjects. During the experiment blood sugar was kept at hyperglycemic levels (above 150 mg. per 100 ml.) by constant infusion of either epinephrine or glucose. When arginine was infused, plasma insulin concentrations promptly rose from normal to some 80 mU./ml., and growth hormone concentrations rose to some 25 mμg./ml. These results indicate that the release of the two hormones can be effectively influenced by signals other than changes of blood sugar levels. O.V.S.

Root, Allen W.; Oski, Frank A.; Bongiovanni, Alfred M.; and Eberlein, Walter R. (Dept. of Pediat., Univ. of Pennsylvania Sch. of Med., Children's Hosp. of Philadelphia, and Hosp. of the Univ. of Pennsylvania, Philadelphia, Pa.): ERYTHROCYTE GLUCOSE-6-PHOSPHATE DEHYDROGENASE ACTIVITY IN CHILDREN WITH HYPOTHYROIDISM AND HYPOPITUITARISM. J. Pediat. 70:369-75, March 1967.

Verbatim Summary. Erythrocyte glucose-6-phosphate dehydrogenase activity was measured in nine children with hypothyroidism, and in seven children with hypopituitarism. Pretreatment enzyme activities were well below normal in all children with hypothyroidism, and in six children with hypopituitarism. The administration of thyroid hormone was followed by increased enzyme activity in five of five subjects studied. The administration of human growth hormone was associated with increased enzyme activity in four of six patients after short-term administration, and in two of two subjects after long-term administration. Red cell G-6-PD activity was a sensitive index of the metabolic status of the patient.