

ABSTRACTS

Berkowitz, Donald (Dept. of Med., Hahnemann Med. Coll. and Sidney Hillman Med. Center, Philadelphia, Pa.): GOUT, HYPERLIPIDEMIA, AND DIABETES INTERRELATIONSHIPS. *JAMA* 197:77-80, July 11, 1966.

The tolerance to 100 gm. of oral glucose was investigated in twenty-five patients with hypercholesterolemia (over 275 mg./100 ml.), and normal triglyceridemia (less than 150 mg./100 ml.), in twenty-five patients with elevations of both factions, and twenty-five patients with clinical gout. In the group with hypercholesterolemia alone 12 per cent had abnormal glucose tolerance and in the second group 72 per cent. In the patients with gout the results varied: of six patients with normal triglyceride levels only one had diminished glucose tolerance while it occurred in 74 per cent of those with hypertriglyceridemia. Thus abnormal glucose tolerance in gout seems to be more clearly related to the hypertriglyceridemia (as it does in the nongouty individuals) than to the gout. S.B.B.

Braun, Alan P. (Dept. of Med., Montefiore Hosp., New York, N.Y.): THE PREPARATION, POTENCY, AND SPECIFICITY OF GUINEA PIG ANTIGLUCAGON AND ITS EFFECT ON CARBOHYDRATES AND LIPID METABOLISM IN THE RAT. *Bull. N.Y. Acad. Med.* 42:251, March 1966.

Potent antiglucagon (AGS) was formed rapidly in guinea pigs utilizing "multiple portal" injections of crystalline beef-pork glucagon. The guinea pig serum was analyzed for antibody by the Unger modification of the Yalow-Berson technics of radiochromatoelectrophoresis and by radioimmuno-electrophoresis. The gamma-globulin thus produced was present in 92 per cent of the animals challenged and reacted with glucagon at a dilution up to 1,000. The pooled antiglucagon with a titer of 1:1,000 was maintained at a depressed blood sugar level for two hours in an intravenous glucose tolerance test in rats.

Acute hypoglucagonemia was induced in rats force-fed by stomach tube either with a controlled diet rich in lipid and carbohydrates but low in protein, or a diet rich in lipids and protein but low in carbohydrates. A seven-day study of hypoglucagonemia and its effect on the alpha cell was conducted utilizing the low protein, high carbohydrate diet. At the conclusion of the experiment, the animals were killed and histological study of pancreas, liver, heart, and kidney performed. The results indicated that immunological hypoglucagonemia was associated with a consistent trend toward hypoglycemia and hyperlipidemia first noticeable less than five hours after antiglucagon administration. Noted histologically were definite degranulation, coarse smudging of the cytoplasmic granules, and focal death of the alpha cells with nuclear debris at sixteen hours after a single injection of AGS. Following repeated administration of AGS, a reactive hyperplasia of alpha cells was present. No evidence of beta cell damage or pathologic change in liver, kidney, or heart was found. Interpretation was that antiglucagon serum bound circulating glucagon, resulting in alpha cell stimulation to produce more at increased rates with eventual exhaustion and necrosis of some

cells, accompanied by a reactive hyperplasia of other cells. R.F.B.

Camerini-Davalos, Rafael A. (New York Med. Coll., New York, N.Y., and Health Research Council of the City of New York): SYMPOSIUM: TOTAL CARE OF DIABETIC PATIENT FROM PHYSIATRIST'S POINT OF VIEW. DIAGNOSIS OF EARLY ASYMPTOMATIC DIABETES. *N.Y. J. Med.* 66:1636-42, June 15, 1966.

The concept of prediabetes is presented. The findings on ear lobe biopsy, renal biopsy, as well as serum insulin, mean blood glucose, free fatty acid and sialic acid levels are compared with those found in normal and overtly diabetic patients. P.S.E.

Denton, R. M.; Yorke, R. E.; and Randle, P. J. (Dept. Biochem., Univ. of Bristol, Bristol, England): MEASUREMENT OF CONCENTRATIONS OF METABOLITES IN ADIPOSE TISSUE AND EFFECTS OF INSULIN, ALLOXAN-DIABETES AND ADRENALINE. *Biochem. J.* 100:407-19, August 1966.

Methods for the extraction and assay of certain metabolites in the rat epididymal fat pad after incubation *in vitro* are described. The intracellular water volume was unaffected by insulin, alloxan diabetes or adrenalin. The intracellular ATP content was lower than in cardiac or diaphragm muscle; concentrations of ADP and AMP were greater. None of the adenine nucleotides were affected by insulin, alloxan diabetes or adrenalin. The concentration of glucose-6-phosphate was raised by insulin and lowered by alloxan diabetes and adrenalin. L-glycerol 3-phosphate was increased by insulin and lowered by adrenalin but was not affected by alloxan diabetes. Citrate concentration was increased by both adrenalin and alloxan diabetes but was unchanged by insulin. Insulin raised and alloxan diabetes reduced V_{max} of glucose uptake but neither affected K_m . P.H.W.

Di Girolamo, M. (Dept. Med., Columbia Univ. Coll. Phys. and Surg., Columbia Univ. Res. Serv., Goldwater Mem. Hosp., New York, N.Y.): DIFFERENCES AMONG MAMMALS IN THE CARBOHYDRATE METABOLISM AND INSULIN RESPONSIVENESS OF ADIPOSE TISSUE. *Bull. N.Y. Acad. Med.* 42:250, March 1966.

Metabolism of C-14-U-glucose by epididymal and perirenal adipose tissue slices of rat, hamster, guinea pig, and rabbit was prepared: (1) Krebs-Ringer-phosphate (KRP) solution with 3 per cent albumin and 0.25 or 2.5 mg./ml. glucose, under air; (2) Krebs-Ringer-bicarbonate (KRB) with same additions, under 95 per cent O_2 -5 per cent CO_2 ; and (3) these solutions with 0.1 U./ml. bovine insulin. Glucose uptake and transformation of glucose into CO_2 , glyceride-glycerol, and glyceride-fatty acids were measured. The total quantity of glucose metabolized, the quantity of glucose converted to glyceride-fatty acids, and the degree of stimulation of glucose metabolism by insulin, varied markedly with species in the order: rat > guinea pig > rabbit > hamster. The failure of adipose tissue from hamster and rat and of rabbit to respond to bovine insulin was also found with porcine and ovine in-

sulins. The data showed that the responsiveness of rat adipose tissue is limited in magnitude for rabbit and virtually absent for hamster adipose tissue. R.F.B.

Dougherty, Jocelyn (Univ. Kansas Sch. of Med., Kansas City, Kan.): HYPOGLYCEMIC STUPOR CAUSED BY ACETOHEXAMIDE. *New Eng. J. Med.* 274:1256-57, June 2, 1966.

The author reports the case of a garbage collector who found acetohexamide pills while at his work and took them for headaches. He had taken several tablets a day and arrived in the emergency room with a convulsive seizure and a blood sugar of 36 mg. per 100 ml. The article emphasizes the importance of considering hypoglycemia secondary to drug ingestion in all patients who enter the emergency room with coma and/or convulsions of unknown etiology. B.R.B.

Ellenberg, Max (Mount Sinai Hosp. and Mount Sinai Sch. of Med., New York, N.Y.): SYMPOSIUM: TOTAL CARE OF DIABETIC PATIENT FROM PHYSIATRIST'S POINT OF VIEW. NEUROLOGIC COMPLICATIONS AND FUNCTIONAL ABNORMALITIES IN DIABETES. *N.Y. J. Med.* 66:1642-48, June 15, 1966.

The general problem of diabetic neuropathy is discussed with emphasis on neurotrophic arthropathy, neurotrophic ulcer and orthostatic hypotension: the three main challenges to the physiatrist. Neurotrophic ulcer must be differentiated from ulcer secondary to occlusive vascular disease since the treatment and prognosis are entirely different. P.S.E.

Friedman, Gerald J. (Beth Israel Hosp. and New York Univ. Coll. of Med., New York, N.Y.): SYMPOSIUM: TOTAL CARE OF DIABETIC PATIENT FROM PHYSIATRIST'S POINT OF VIEW. EMPLOYABILITY OF DIABETIC PERSONS. *N.Y. J. Med.* 66:1662-69, June 15, 1966.

The recommendations for evaluating the employability of job applicants with diabetes made by the Committee on Employment and Insurance of the New York Diabetes Association are discussed. The actual forms devised by the Committee are reproduced.

1. Discrimination against diabetic persons based solely on diagnostic grounds is unwarranted. Emphasis should be placed on the individual's attitude, aptitude, experience, education, the severity of his diabetes, the degree of its control, his emotional adjustment, and the demands of the job.
2. Well-controlled, cooperative, closely supervised diabetic patients are good-risk employees. Because they are self-disciplined, they often become outstanding workers in whatever positions they occupy.
3. In the rehabilitation of the diabetic, education, training and skill are important factors in improving job opportunity and security.
4. The majority of diabetic patients have adapted themselves and their condition to the demands of daily living and are functioning effectively in their communities. They are good examples of successful rehabilitation. P.S.E.

Hunter, W. M.; Clarke, B. F.; and Duncan, L. J. P. (Med. Res. Council Clin. Endocr. Res. Unit, Edinburgh; and the Diabetic and Dietetic Dept., Royal Infirmary of Edinburgh, Scotland): PLASMA GROWTH HORMONE AFTER AN OVER-

NIGHT FAST AND FOLLOWING GLUCOSE LOADING IN HEALTHY AND DIABETIC SUBJECTS. *Metabolism* 15:596-607, July 1966.

Plasma growth hormone (HGH) levels of healthy and newly diagnosed diabetics, fasted overnight, did not differ significantly. Glucose loading inhibited HGH release in both groups within two hours, with a secondary rise occurring during the next four hours. The stimulus for the secondary rise was neither the amount nor the rapidity of blood glucose fall but rather its decline below a threshold value. In diabetic patients this threshold was higher than in the normals and usually exceeded the fasting blood glucose of the patient. The secondary rise in HGH in the diabetic patient at higher blood sugar levels may reflect the relative intracellular glucose deficiency (reduced tissue glucose assimilation threshold) described in diabetes mellitus. C.R.S.

Jakob, A.; Bürgi, H.; Froesch, E. R.; and Labhart, A. (Stoffwechsellabteilung der Medizinischen Universitätsklinik, Kantonsspital, Zurich, Switzerland): THE ANTIBODY NONSUPPRESSIBLE SERUM INSULIN-LIKE ACTIVITY. *Deutsch. Med. Wschr.* 91:1314-19, July 1966.

A review of the state of insulin in blood with special reference to the so-called "nonsuppressible" form of insulin-like activity. The purified principle shares with crystalline insulin many biological properties, including that of glycogen synthesis, but physico-chemical studies have indicated that the active principle is a polypeptide different from insulin. O.V.S.

Katsuki, Shibanosuke; and Ito, Mitsuo (Second Dept. of Intern. Med., Kyushu Univ., Fukuoka, Japan): ANTIDIURETIC EFFECT OF DIGUANIDES. *Lancet* 2:530-32, Sept. 3, 1966.

The authors observed that the diguanide, metformin, appeared to have an antidiuretic effect when given to a patient with coexisting diabetes mellitus and diabetes insipidus. They then investigated the response of twelve other subjects with diabetes insipidus to prolonged administration of diguanides. The usual dose was 1.0 to 1.5 gm. per day of metformin or 0.1 gm. per day of phenformin. A reduction of urine flow of 32 per cent per day was found in five of eight patients with idiopathic diabetes insipidus. No effect was seen in subjects with nephrogenic diabetes insipidus. Administration of diguanides augmented the antidiuretic action of both vasopressin and thiazides. The characteristic action of metformin was delayed and its maximum effect occurred several days after the drug was started. The mode of action of diguanides in diabetes insipidus is not known, but the authors speculate that idiopathic diabetes may be caused by an abnormally high rate of degradation of antidiuretic hormone by the liver. The diguanides could ameliorate the disease by inhibiting the enzyme responsible for this degradation. T.G.S.

Lippmann, Heinz I. (Albert Einstein Coll. of Med., New York, N.Y.): SYMPOSIUM: TOTAL CARE OF DIABETIC PATIENT FROM PHYSIATRIST'S POINT OF VIEW. PHYSIATRIST'S ROLE IN CARE OF DIABETES. *N.Y. J. Med.* 66:1649-50, June 15, 1966.

The general role of the physiatrist in treating diabetics is cited. The need to establish foot-care programs is stressed. In a 500-bed old-age home no amputations were performed for the two years following the inception of such a program. Previously there was an average of four or five a year. P.S.E.

Mekanik, Ghodsi; Smith, R. Lawrence; and MacLeod, Robert M. (Depts. of Pediat., Anatomic Path. and Intern. Med. of the Univ. of Virginia Sch. of Med., Charlottesville, Va.): ENZYME PATTERNS IN GLYCOGEN STORAGE DISEASE TYPE II (POMPE'S DISEASE). *Metabolism* 15:641-48, July 1966.

The enzyme defects detected in the tissues of a patient with Type II glycogen storage disease are described. There was a virtual absence of α -glucosidase in heart, skeletal muscle, thyroid, adrenal and liver, although the enzyme was present in kidney tissue. Phosphorylase activity was depressed as were amylo-1, 6-glucosidase and glucose-6-phosphatase; however, they were easily detectable in the tissues analyzed. Remarkable changes were described in heart, skeletal muscle, glia and neurons of the central nervous system resulting from glycogen deposition. C.R.S.

Oken, Donald E. (Depts. of Med., Peter Bent Brigham Hosp. and Harvard Med. Sch., Boston, Mass.): CHRONIC RENAL DISEASES AND PREGNANCY: A REVIEW. *Amer. J. Obst. Gynec.* 94:1023-43, April 1, 1966.

The author presents a review of chronic renal diseases and pregnancy. He has endeavored to determine the relationship between a variety of chronic renal diseases and the outcome of the pregnancy and whether or not the pregnancy increased the severity of the renal disease. E.A.W.

Paul, T. N. (Redhill Gen. Hosp., Redhill, Surrey, England): TREATMENT BY LOCAL APPLICATION OF INSULIN OF AN INFECTED WOUND IN A DIABETIC. *Lancet* 2:574-76, Sept. 10, 1966.

A fifty-six year old woman with diabetes, retinopathy, azotemia and peripheral vascular insufficiency developed gangrene of the leg which required below the knee amputation. After surgery the stump failed to heal and became chronically infected with staphylococcus aureus. Measures which included large doses of insulin and appropriate antibiotics were unsuccessful over a sixty-day period. After applications of a gauze dressing to which 20 U. Regular Insulin had been used for three to four days, the appearance of the wound improved, and after eighteen days it showed signs of healing. A second course of insulin applications was associated with complete healing. The mode of action of locally applied insulin is unexplained. T.G.S.

Robertson, Patrick D. (Dept. of Intern. Med., Univ. of Iowa, College of Med., Iowa City, Iowa): CARBOHYDRATE INTOLERANCE IN POSTGASTRECTOMY PATIENTS. *Arch. Intern. Med.* 117:764-68, June 1966.

Verbatim Summary. After a gastric operation for peptic ulcer an abnormal response to the oral glucose tolerance test may be found. Seven patients with previous gastric surgery for peptic ulcer were studied. Five had been previously investigated for hypoglycemia and a further two because of glycosuria. None of the patients had dumping symptoms. All seven patients had abnormal oral glucose tolerance tests, but the shape of the blood sugar curve showed a rapid rise and fall dissimilar to that seen in established diabetes.

Abnormal intravenous glucose tolerance tests were found in six of the seven patients studied. This study suggests that in patients who have had a gastric operation for peptic ulcer, and who have an abnormal oral glucose tolerance test curve showing a rapid rise and fall of blood sugar levels, there is carbohydrate intolerance unrelated to defective absorption of glucose. P.S.E.

Rodbell, Martin (Lab. of Nutrition and Endocr., Nat. Inst. of Arthritis and Metabolic Dis., Nat. Inst. of Health, Bethesda, Md.): THE METABOLISM OF ISOLATED FAT CELLS. IV. REGULATION OF RELEASE OF PROTEIN BY LIPOLYTIC HORMONES AND INSULIN. *J. Biol. Chem.* 241:3909-17, Sept. 10, 1966.

Using fat cells isolated from rat epididymal fat pads, it was found that endogenously labeled proteins and certain enzymes are released in increased amounts under the influence of lipolytic hormones (ACTH, glucagon and epinephrine) and theophylline, and that release is inhibited by addition of glucose and insulin to the medium. Evidence is presented to suggest that increased release of intact molecules of protein is due to increased intracellular concentrations of free fatty acids. P.H.W.

Steinke, Jurgen; Miki, Eisbi; and Cabill, George F., Jr. (Elliott P. Joslin Res. Lab.; Dept. of Med., Harvard Med. Sch.; the Diabetes Found., Inc.; and the Peter Bent Brigham Hosp., Boston, Mass.): ASSAY OF CRYSTALLINE INSULIN AND OF SERUM INSULIN-LIKE ACTIVITY OF DIFFERENT SPECIES ON ADIPOSE TISSUE OF THE RAT, MOUSE AND GUINEA PIG. *New Eng. J. Med.* 273:1464-67, Dec. 30, 1965.

Epididymal adipose tissue of the rat, mouse and guinea pig was incubated with and without 500 μ U. of human, pork, beef, rat or tuna fish insulin per milliliter. On a unit basis these insulins, regardless of origin, exhibited an identical effect on the adipose tissue of a given species. The absolute magnitude of the response to crystalline insulin varied from species to species; it was largest in the rat and smallest in the guinea pig. Pooled serum from rat, mouse and guinea pig, as well as individual human sera, had a variable effect on adipose tissue of these three different species; there was no consistent pattern. The response of rat adipose tissue to 500 μ U. of crystalline insulin was seven times, of mouse adipose tissue it was three times, and of guinea pig adipose tissue, 20 per cent above the baseline activity of the respective tissues. The steep insulin response curve of rat adipose tissue therefore makes this animal superior to either the mouse or the guinea pig for assay purposes, since the precision of the assay depends to a large extent on the slope of the response curve. B.R.B.

Wilder, Joseph R.; Ascoli, Nino; Sturchio, Edward A.; and Popowitz, Leonard (Dept. of Surg., Hosp. for Joint Diseases and Med. Center, New York, N.Y.): SYMPOSIUM: TOTAL CARE OF DIABETIC PATIENT FROM PHYSIATRIST'S POINT OF VIEW. MANAGEMENT OF DIABETES WITH VASCULAR DISEASE OF LOWER EXTREMITIES. *N.Y. J. Med.* 66:1651-58, June 15, 1966.

It is pointed out that the combination of increased longevity and an expanding population is resulting in increasingly greater numbers of diabetic patients with vascular disease of the lower extremities. The morbidity rate, for unknown reasons, is much higher in the diabetic than the nondiabetic with comparable vascular disease. A correlation was found between morbidity and the socioeconomic status of the patient. The great advances in vascular surgery have not greatly helped the diabetic because the diffuse nature of the vascular disease makes them poor candidates for reconstructive surgery. Prophylactic care is emphasized. Greater efforts must be made to bring these patients into the mainstream of hospital care rather than treating them as hopeless cases doomed to amputation and helplessness. P.S.E.