

ABSTRACTS

Berchtold, P.; Meier, V.; Büber, V.; Felber, J.-P.; and Keiser, G. (Medizinische Abteilung, Bürgerspital, Zug/Schweiz Département de Biochimie Clinique, Clinique Médical Universitaire, Lausanne, Switzerland): COMPARATIVE INVESTIGATIONS CONCERNING THE ORAL AND INTRAVENOUS TOLBUTAMIDE TESTS I. CLINICAL STUDIES ON MIDDLE-AGED PATIENTS. *Diabetologia* 7:73-76, 1971.

Verbatim summary. The duration of the oral tolbutamide test (OTT) was extended to 140 min. to allow the observation of the rebound following the blood sugar fall and the comparison with the IVTT. The undesired effects of the hypoglycemia observed after the ingestion of 2 gm. tolbutamide were prevented by reducing the dose of the drug to 1 gm. in eighteen patients and to 1.5 gm. in thirty-one others. Tolbutamide was given together with the double amount of sodium bicarbonate. The agreement of IVTT and OTT was good in 35 per cent, fair in 38 per cent, and poor in 27 per cent of the cases. It is suggested that these unsatisfactory results are due to different tolbutamide absorption rates. The use of the prolonged OTT is not recommended as a tool for the diagnosis of diabetes.

Berchtold, P.; Büber, V.; Meier, V.; Felber, J.-P.; and Keiser, G. (Medizinische Abteilung, Bürgerspital, Zug/Schweiz und Département de Biochimie Clinique, Clinique Médical Universitaire, Lausanne, Switzerland): COMPARATIVE INVESTIGATIONS CONCERNING THE ORAL AND INTRAVENOUS TOLBUTAMIDE TESTS. II. DETERMINATION OF GLUCOSE, SERUM INSULIN AND SERUM TOLBUTAMIDE IN NORMAL YOUNG SUBJECTS. *Diabetologia* 7:77-81, 1971.

Verbatim summary. In twelve normal subjects the OTT and IVTT were studied by simultaneous determination of blood glucose, serum insulin (IRI) and serum tolbutamide. From the results it is possible to deduce two different mechanisms for the action of the orally administered tolbutamide. They are dependent on the absorption rate of the drug. When tolbutamide is absorbed quickly, insulin secretion follows. It is responsible for the fall of blood sugar. When the tolbutamide absorption is slow, insulin secretion is small, but the blood sugar level is still falling. The three following hypotheses are proposed: the insulin which appears in the pancreatic vein cannot be measured at the periphery and acts mostly in the liver; the low concentration of tolbutamide in the serum causes only a slight secretion of insulin; and an important inhibition of the secretion of glucagon is responsible for the observed hypoglycemia. Extrapankreatic action of sulfonylurea compounds, particularly on muscle tissue, may too play an important role in explaining the results.

Brånemark, P.-I.; Langer, L.; Fagerberg, S.-E.; and Breine, U. (Lab. of Exper. Biol., First Med. Serv. and Plastic Surg. Serv., Sahlgrenska Sjukhuset, Univ. of Göteborg, Sweden): STUDIES IN RHEOLOGY OF HUMAN DIABETES MELLITUS. *Diabetologia* 7:107-112, 1971.

Verbatim summary. The rheology of blood cells studied intravascularly, and the relation between blood cells and endothelium was analyzed in vivo by high resolution, vital microscopy in four diabetic patients with varying duration of the disease. In a dipedicled, tubed skin-flap a titanium chamber with optics was implanted. A thin layer of tissue in this chamber was observed microscopically over a period of up to four months. Microvascular structure and function were analyzed under normal flow conditions as well as in various test situations with reduced or completely blocked flow in lipemia and when slight local tissue trauma was added. It was found, contrary to what has hitherto been considered in the literature, that there is no aggregation of blood cells in diabetes, unless the metabolic balance is heavily upset as in acidosis. The rheology of the various types of blood cells is normal even in long-standing diabetes.

Brodoff, B. N.; Kagan, A.; Slotnik, B.; Hagedorn, J. (Dept. of Med., The New York Med. Coll., Div. of Endocr., Coney Island Hosp., Dept. of Psych., Columbia Univ., and Dept. of Anat., The New York Med. Coll., New York): THE EFFECT OF HYPOTHALAMIC LESION IN THE SAND RAT MAINTAINED ON A HIGH FAT DIET. *Diabetologia* 7:59-67, 1971.

Verbatim summary. Nine sand rats maintained on a high fat diet gained weight, developed endogenous hyperinsulinemia and resistance to exogenous insulin without further deterioration in glucose tolerance. A four-hour postglucose hyperinsulinemia, noted in some animals on both diets, may represent a chronic stress to the islets in these intermittent feeders. Five animals survived post lesion. Results were consistent with previous findings that lesions in the posterior median eminence portion of the periventricular arcuate system were associated with an improved glucose tolerance, and also in the present study, an increased sensitivity to exogenous insulin. A possible explanation for the mechanism of these effects on carbohydrate metabolism is suggested.

Devey, Madeleine; Carter, D.; Sanderson, D. J.; and Coombs, R. R. A. (Immunology Div., Dept. of Path., Univ. of Cambridge, Cambridge, England): IgD ANTIBODY TO INSULIN. *Lancet* 2:1280-83, Dec. 19, 1970.

Sera from six diabetic patients, two of whom had insulin resistance, were studied for the presence of a specific IgD anti-

body to insulin. The method involved coupling of crystalline bovine insulin to a Salmonella lipopolysaccharide to serve as the antigen. All patients had IgG antibodies to insulin but further tests showed that three of the six had very low but specific antibodies of the IgD class. The highest titer of IgD antibody reacting with beef insulin was 1:32. The patient having it was a sixty-eight-year-old woman who had been treated briefly two years previously with beef insulin and recently with a small dose of Regular insulin. She reacted to this by vomiting and developing signs of shock which were reversed by hydrocortisone therapy. Retreatment with insulin resulted in a generalized urticarial reaction. The study suggests that injections of insulin may in some way stimulate IgD producing cells. T.G.S.

Dunn, J. P.; Ipsen, J.; Elsom, K. O.; and Ohtani, M. (Periodic Health Examination Res. Proj., Dept. of Community Med., Sch. of Med., Univ. of Pennsylvania, Philadelphia, Pa.): RISK FACTORS IN CORONARY ARTERY DISEASE, HYPERTENSION AND DIABETES. *Amer. J. Med. Sci.* 259:309-22, May 1970.

Verbatim summary. Risk factors for coronary artery disease, diabetes and hypertension were determined among 13,148 men participating in periodic health examination programs between 1950 and 1964. During the period of observation there were 401 new events of coronary artery disease, 241 new events of diabetes and 988 new events of hypertension based on the criteria used in this study. Important risk factors for coronary artery disease were elevated serum cholesterol and systolic blood pressure and hemoglobin values above 17 g per cent. For diabetes the important risk factors were blood sugar, family history of diabetes, elevated serum cholesterol and increased relative weight. For hypertension the factors were systolic blood pressure, increased relative weight, cigarette smoking, elevated serum cholesterol and the diagnosis of diabetes. The effect of some of the risk factors varied with age. Elevated serum cholesterol was the one risk factor common to all three conditions.

Elkeles, R. S.; Blach, R. K.; and Joplin, G. F. (Dept. of Med., Royal Postgrad. Med. Sch., London, England): COMPARISON OF THE PROGRESS OF FLAT NEW VESSELS ON THE OPTIC DISC WITH THOSE ON THE RETINA IN PATIENTS TREATED BY PITUITARY ABLATION. *Diabetologia* 7:102-06, 1971.

Verbatim summary. The progress of new vessels arising on the disc has been compared with the progress of new vessels arising elsewhere on the retina from photographs of twenty-nine eyes from twenty-three patients followed for a mean period of fourteen months. Only new vessels flat on the disc and unassociated with significant fibrosis were studied. Progress of the new vessels in each of these two locations was based on grading of severity from corresponding sets of standard photographs. The direction of change whether regression or deterioration, was found to be the same for disc vessels and retinal vessels in all but one eye. It was found that this similarity in behavior of new vessels in the two locations applied equally to the twenty-two eyes of sixteen patients treated by pituitary ablation where the direction of change was usually improvement, and to the seven eyes of seven nonoperated patients in which there was usually either no change or deterioration. Vitreous hemorrhage precluded a second assessment of six further operated and three further control eyes. Disc vessels improved in sixteen of the twenty-two assessable eyes from patients treated

by pituitary ablation. Thus, the presence and type of new vessels on the disc should be one of the features assessed in a patient with diabetic retinopathy being considered for treatment with pituitary ablation.

Engelhardt, A.; Gries, F. A.; Liebermeister, H.; and Jabnke, K. (Medizinische Universitätsklinik und Diabetes-Forschungsinstitut an der Universität Düsseldorf, Germany): SIZE, LIPID AND ENZYME CONTENT OF ISOLATED HUMAN ADIPOCYTES IN RELATION TO NUTRITIONAL STATE. *Diabetologia* 7:51-58, 1971.

Verbatim summary. The following parameters have been determined or calculated in isolated adipocytes from subcutaneous human adipose tissue from normal weight and obese subjects, obtained during surgical interventions or from volunteers who received local anesthesia: mean cell diameter, mean cellular lipid content, mean fat cell volume, and volume of lipid-free space. In fat cell extracts the activities of the following enzymes were measured: glucose-6-phosphate-dehydrogenase, phosphoglucumutase, fructose-6-phosphatekinase, hexose-phosphate-isomerase, aldolase, glycerolaldehyde-phosphate-dehydrogenase, phosphoglycerate-kinase, pyruvate-kinase, lactate-dehydrogenase. In subjects with more than 50 per cent overweight, the mean fat cell diameter was significantly increased. Mean fat cell volume calculated from fat cell diameter increased from $376 \pm 115 \text{ mm}^3 \times 10^{-6}$ in normal weight to $799 \pm 99.5 \text{ mm}^3 \times 10^{-6}$ in obesity. In obese subjects the mean lipid content of individual adipocytes was twice as high as in normal weight subjects. The lipid-free residual space was also significantly larger in obesity. Nevertheless, this lipid-free space occupied a significantly smaller percentage of a defined fat cell mass in obese than in normal weight subjects. Related to triglyceride content, the activities of HIM, G6PDH, and aldolase were significantly reduced in adipocytes of subjects with more than 50 per cent overweight; in a second series this was true for LDH also. There were significant negative correlations of the logarithms of these enzymes to the logarithm of overweight. There was an increased mean absolute enzyme content in adipocytes of obese subjects compared with those of normal weight persons. However, this increase was significant for LDH and HIM only. It is not certain that the enzyme pattern in the fat cells of obese subjects is related to the increase in cell volume. When related to a defined fat cell mass after correction for extra-cellular space, diminished activities for aldolase, G6PDH, HIM, and LDH were found.

Fain, John N.; Dodd, Anita; and Novack, Leila (Div. of Biological & Med. Sci., Brown Univ., Providence, R.I.): RELATIONSHIP OF PROTEIN SYNTHESIS AND CYCLE AMP TO LIPOLYTIC ACTION OF GROWTH HORMONE AND GLUCOCORTICOIDS. *Metabolism* 20:109-18, February 1971.

Lipolysis in isolated white fat cells from rats to which are added growth hormone (GH) and glucocorticoid occurs after a lag period of one to two hours which is presumably the time required for synthesis of protein via a mechanism of DNA-dependent RNA formation. When cycloheximide, an inhibitor of protein synthesis, is added the lipolytic effects of GH and glucocorticoids are blocked; its effects are reversible and occur during an early period after addition of the hormones. Leucine incorporation into fat cell protein is inhibited by GH and glucocorticoids during the first two hours and stimulated during the second two hours of incubation. GH but not dexamethasone increases the maximum accumulation of cyclic AMP seen in response to lipolytic agents. Incubation

of cells with insulin prior to addition of epinephrine and theophylline resulted in an absence of cyclic AMP accumulation within five minutes except in the presence of GH. In cells incubated with insulin and lipolytic agents for fifteen minutes there was marked inhibition of cyclic AMP accumulation under all conditions. C.R.S.

Felig, P.; and Lynch, V. (Yale Univ. Med. Sch., New Haven, Conn.): STARVATION IN HUMAN PREGNANCY: HYPOGLYCEMIA, HYPOINSULINEMIA, AND HYPERKETONEMIA. *Science* 170:990-92, Nov. 27, 1970.

Verbatim summary. In women fasted during the second trimester of pregnancy, concentrations of glucose and insulin in the plasma fell to a greater extent and ketone acid concentrations in the blood rose more rapidly than in nonpregnant controls. Nitrogen excretion in the urine, particularly ammonia, was increased in the pregnant group. Continuous glucose utilization by the conceptus may exaggerate and accelerate the metabolic consequences of starvation.

Friedman, Bernice; Goodman, Edward H., Jr.; Saunders, Harry L.; Kostos, Vincent; and Weinhouse, Sidney (Fels Res. Inst., Temple Univ. Sch. of Med., Philadelphia, Pa.): ESTIMATION OF PYRUVATE RECYCLING DURING GLUCONEOGENESIS IN PERFUSED RAT LIVER. *Metabolism* 20:2-12, January 1971.

The recycling of labeled pyruvate during gluconeogenesis was described in experiments using the perfused rat liver with measurement of the radioactive carbon in glucose lactate and pyruvate isolated after one hour of perfusion. Recycling was estimated from incorporation of labeled carbon in sites 1 and 3 of the 3-carbon acids. In fasted rats nearly twice as much carbon was converted to glucose as was recycled, while in livers from fed rats only one fourth as much was converted to glucose as was recycled. Addition of octanoate to the perfusate did not alter the recycling patterns. The results suggest a marked inhibition of pyruvate kinase as a probable factor in the conversion of pyruvate to glucose in fasted rat liver.

C.R.S.

Goberna, R.; Fussgänger, R. D.; Raptis, S.; Telib, M.; and Pfeiffer, E. F. (Dept. of Endocr. and Metab., Center of Internal Medicine and Pediatrics, Univ. of Ulm, Germany): THE ROLE OF THE EXOCRINE PANCREAS IN THE STIMULATION OF INSULIN SECRETION BY INTESTINAL HORMONES. II. INSULIN RESPONSES TO SECRETIN AND PANCREOZYMIN IN EXPERIMENTALLY-INDUCED PANCREATIC EXOCRINE INSUFFICIENCY. *Diabetologia* 7:68-72, 1971.

Verbatim summary. A comparison was made of the effects of the intestinal hormones secretin and pancreozymin on insulin secretion in nondiabetic rats with experimentally induced exocrine pancreatic insufficiency and in control animals. The rats with exocrine pancreatic insufficiency exhibited normal disappearance of glucose and secretion of insulin. In rats with exocrine pancreatic insufficiency secretin did not lead to any increase in insulin secretion in contrast to its effect in the controls. In rats with exocrine pancreatic insufficiency pancreozymin evoked secretion of insulin to the same extent as in the normal animals. From these results it is inferred that the effect of secretion upon the β cells of the rat is dependent upon the presence of intact exocrine pancreatic tissue. However, pancreozymin and glucose exert their effects upon the β cells directly without the involvement of the exocrine portion of the pancreas. All of these findings made under conditions in vivo are

in perfect accord with studies made on isolated islets of rats subjected to the same stimuli in the preparation in vitro.

Goldman, Jack A.; and Eckerling, Benjamin (Dept. of Obstet. and Gynec., Beilinson Med. Center, Petah Tikva; and Tel Aviv Univ. Med. Sch., Israel): BLOOD GLUCOSE LEVELS AND GLUCOSE TOLERANCE IN PREDIABETIC AND SUBCLINICAL DIABETIC WOMEN ON A LOW DOSE PROGESTOGEN CONTRACEPTIVE. *Israel J. Med. Sci.* 6:703-07, November-December 1970.

Verbatim summary. Fasting blood glucose and blood glucose disappearance rate, with the aid of intravenous glucose tolerance tests (IVGTT), were measured in two groups of women treated with a new low dose progestogen oral contraceptive agent: thirty-two women with presumed prediabetes and twelve women with subclinical diabetes. In each subject an IVGTT was performed, before oral contraceptive therapy was started and after three months of therapy. Fasting blood glucose was again tested three months after therapy was stopped. The mean fasting blood glucose was significantly changed during therapy in both groups. However, three months after therapy was stopped the mean fasting blood glucose had returned to normal. The plasma glucose disappearance constant (k) during IVGTT was unchanged in both groups during three months of oral contraceptive therapy. No woman of either group required insulin during therapy.

Gray, Jean G.; Pratt, William B.; and Aronow, L. (Dept. of Pharmacol., Stanford Univ. Sch. of Med., Stanford, Calif.): EFFECT OF GLUCOCORTICOIDS ON HEXOSE UPTAKE BY MOUSE FIBROBLASTS IN VITRO. *Biochemistry* 10:277-84, Jan. 19, 1971.

Verbatim summary. Triamcinolone acetonide (10^{-7} M) has been found to inhibit the uptake of radioactive galactose by L929 cells suspended in a salt solution. The uptakes of glucose and deoxyglucose, hexoses which utilize the same uptake process as galactose, are also inhibited. Glucocorticoids also inhibit amino acid transport although the effect is delayed relative to the effect on hexose uptake. The structure-activity relationships of the steroids active in growth inhibition is paralleled by their ability to inhibit hexose uptake. Cells which are resistant to glucocorticoids demonstrate no inhibition of hexose uptake when exposed to triamcinolone acetonide. Fructose will support L cell growth provided its external concentration is high, but it is not taken into the cell by the same process as galactose or glucose. Fructose supported growth is shown to be as sensitive to inhibitions by triamcinolone acetonide as growth on glucose. These data indicate that steroid-mediated inhibition of hexose uptake is probably secondary to some other effect of the steroid, possibly an alteration in the phosphorylation or energy yielding metabolic fate of carbohydrates in these cells.

Greenberg, Robert E.; and Christiansen, Robert O. (Dept. of Pediat., Stanford Univ. Sch. of Med., Stanford, Calif.): THE CRITICALLY ILL CHILD: HYPOGLYCEMIA. *Pediatrics* 46:915-20, December 1970.

This article is a brief review of the problems in diagnosis and treatment of various forms of hypoglycemia in the pediatric patient. R.K.K.

Greene, M. L.; Glueck, C. J.; Fumimoto, W. Y.; Seegmiller, J. E. (Human Biochemical Genetics, Nat. Inst. of Arthritis and Metabolic Diseases, Lab. of Molecular Disease, N.I.H., Bethesda, Md.): BENIGN SYMMETRIC LIPOMATOSIS (LAUNOIS-BENSAUDE ADENOLIPOMATOSIS) WITH GOUT AND HYPER-

LIPOPROTEINEMIA. *Amer. J. Med.* 48:239-46, February 1970.

Verbatim summary. A thirty-year-old woman with Launois-Bensaude adenolipomatosis, a disease characterized by diffuse symmetric deposits of adipose tissue on the neck, back and upper trunk, has been studied. Gouty arthritis developed at age seventeen, and oligomenorrhea and muscle cramps were prominent symptoms. Pes cavus and extensor plantar reflexes were present.

Metabolic studies with the patient on a purine-free diet demonstrated hyperuricemia, a marked increase in the whole body miscible pool and daily turnover of uric acid, augmented extrarenal disposal of uric acid and excessive incorporation of glycine-1-C-14 into urinary uric acid. Azathioprine therapy resulted in moderate suppression of purine synthesis; this suppression was not as marked as that observed in gouty patients studied previously. Glucose tolerance in this patient was abnormal, and immunoreactive insulin response during an oral glucose tolerance test was exaggerated. Plasma triglyceride levels were elevated, and a type IV lipoprotein pattern was present. The patient's sister had a similar symmetric lipomatosis, elevated uric acid to creatinine ratio in the urine, hypertriglyceridemia and type IV lipoprotein pattern on electrophoresis.

Guthrie, Richard and Van Leeuwen, G. (Dept. of Pediat., Univ. of Missouri, Columbia, Mo.; and Dept. of Pediat., Univ. of Nebraska, Omaha, Neb.): THE FREQUENCY OF ASYMPTOMATIC HYPOGLYCEMIA IN HIGH RISK NEWBORN INFANTS. *Pediatrics* 46:933-36, December 1970.

Verbatim summary. Serial blood glucose determinations were performed on 109 high risk and twenty-five normal term infants. Eight of these risk infants (7.3 per cent) had at least two glucose determinations of less than 20 mg./100 ml.; twenty (18 per cent) had at least one determination less than 20 mg./100 ml. Although no documented clinical significance of transient asymptomatic hypoglycemia is known to date, it occurs very frequently in high risk infants. Therefore, we advocate that the current practice of very early oral or intravascular feeding in risk infants be continued.

Hadden, D. R.; Harley, J. M. G.; Kajtar, T. J.; and Montgomery, D. A. D. (Metabolic Unit, Royal Victoria Hosp., and Antenatal Diabetes Clinic Royal Maternity Hosp., Belfast, Northern Ireland): A PROSPECTIVE STUDY OF THREE TESTS OF GLUCOSE TOLERANCE IN PREGNANT WOMEN SELECTED FOR POTENTIAL DIABETES WITH REFERENCE TO THE FOETAL OUTCOME. *Diabetologia* 7:87-93, 1971.

Verbatim summary. Results of glucose tolerance tests in a selected group of 1,718 patients studied at the thirty-second week of gestation are related, (a) mainly to the maternal weight, and (b) in part to the maternal age, fetal maturity at delivery and fetal weight at delivery. No clear preference between the three tests emerges, but the K value (glucose disappearance rate after intravenous glucose) appears to be most sensitive to the variables studied. It is not possible to predict the fetal outcome with information obtained from a glucose tolerance test carried out at the thirty-second week of gestation.

Hanson, R. W.; Patel, M. S.; Jomain-Baum, M.; and Ballard, F. J. (Fels Res. Inst., and Dept. of Biochem., Temple Univ. Sch. of Med., Philadelphia, Pa.): ROLE OF MITOCHONDRIA IN METABOLISM OF PYRUVATE AND LACTATE BY RAT ADIPOSE TISSUE. *Metabolism* 20:27-42, January 1971.

Fatty acid synthesis in rat adipose tissue from pyruvate or lactate is dependent in part on the oxidation-reduction potential of cytosolic nicotinamide coenzymes as well as by production and efflux from the mitochondria of key intermediates. The transfer of malate and citrate across mitochondrial membranes may result in transfer of excess reducing equivalents into mitochondria via malate, with a simultaneous efflux of citrate into the cytosol. A forward flow of citrate to α -ketoglutarate in the cytosol may generate NADPH through the action of isocitric dehydrogenase. C.R.S.

Kaess, H.; Schlierf, G.; Eblers, W.; von Mikulicz-Radecki, J.-G.; Hassenstein, P.; Walter, K.; Brech, W.; and Hengstmann, J. (Medizinische Universitätsklinik (Ludolf-Krehl-Klinik) Heidelberg, Germany): THE CARBOHYDRATE METABOLISM OF NORMAL SUBJECTS DURING POTASSIUM DEPLETION. *Diabetologia* 7:82-86, 1971.

Verbatim summary. A potassium loss of 3 to 11 per cent (6.0 ± 2.7 per cent) of total body potassium was produced in six normal subjects during the course of a metabolic balance study of thirteen to sixteen days duration using a supplemented formula diet. This resulted in the development of a marked hypokaliemic alkalosis. There were no significant changes of blood sugar, free fatty acid and plasma insulin concentrations during intravenous (0.5 gm./kg.) or oral (100 gm.) glucose tolerance tests for control and experimental periods.

Lev-Ran, A.; Laor, J.; Vins, M.; and Simon, E. (Diabetes Clin., Dept. of Int. Med. D; Isotopes Dept.; Anesthesia Dept., Beilinson Hosp., Peta Tikvah, and Biodynamics Dept., Weizmann Inst. of Science, Rehovot, Israel): EFFECT OF INTRAVENOUS INFUSION OF D-MANNOHEPTULOSE ON BLOOD GLUCOSE AND INSULIN LEVELS IN MAN. *J. Endocr.* 47:137-38, May 1970.

To further evaluate the effect of mannoheptulose on insulin secretion in man, the following study was performed on a thirty-eight-year-old, male physician volunteer. After an overnight fast, a constant infusion of 5 per cent glucose was begun and approximately five hours later a second infusion of 200 ml. of a 10 per cent solution of mannoheptulose was given over seventy minutes. Fifty minutes following the termination of the mannoheptulose infusion, 1.5 gm. of tolbutamide was injected intravenously.

Immediately following the initiation of the mannoheptulose infusion, serum insulin dropped to near zero and the blood glucose level rose. While the latter was still rising, the tolbutamide was given with an immediate insulin response and fall in blood glucose. Thus mannoheptulose is a useful tool for blockade of insulin release in man which can be overcome by tolbutamide as previously shown in animal experiments. No untoward effects were observed in the volunteer. D.R.C.

Loridan, Liliane; Sadeghi-Nejad, A.; and Senior, Boris. (Pediat. Endocrine-Metabolic Serv. of the Tufts-New England Med. Center Hosp. [Boston Floating Hosp. for Infants and Children], Boston, Mass.): HYPERSECRETION OF INSULIN AFTER THE ADMINISTRATION OF L-LEUCINE TO OBESE CHILDREN. *J. Pediat.* 78:53-58, January 1971.

Verbatim summary. The administration of L-leucine by mouth to eight markedly obese children resulted in elevations in the concentrations of insulin in the blood which were strikingly greater than those observed in control subjects. Such changes were not dependent on differences in the absolute doses of leucine. Despite the marked elevations of insulin after administration of leucine, the fall in concentrations of glucose

differed little from that in the control subjects, reflecting a relative insensitivity to insulin in obese subjects. The increased secretion of insulin after administration of leucine to obese subjects correlates with an increased basal secretory capability of the islets and appears to be in keeping with a hyper-responsiveness of the islets of Langerhans to a variety of stimuli.

Mehnert, H. (Third Med. Div., City Hosp., Munich Schwabing, and Diabetic Research Group, Munich, Germany): ORAL THERAPY OF DIABETES MELLITUS. *Germ. Med. Mth.* 15: 747-48, 1970.

Professor Mehnert expresses his views on the use of oral agents in this brief article. Patients who can be treated by diet alone must not be given hypoglycemic drugs. As a second step, should control be unsatisfactory on diet, he suggests a low dose of a "second generation" hypoglycemic drug such as glibenclamide or a mild preparation of the "first generation" such as tolbutamide. Upgrading to more potent agents might be necessary. Only at this point and should control continue to be unsatisfactory, does he add a biguanide. Insulin is used as a last step if necessary. D.R.C.

Pyke, D. A.; Cassar, I.; Todd, Janet; and Taylor, K. W. (Univ. of Sussex, Diabetic Dept., King's Coll. Hosp., London, England): GLUCOSE TOLERANCE AND SERUM INSULIN IN IDENTICAL TWINS OF DIABETICS. *Brit. Med. J.* 4:649-51, Dec. 12, 1970.

Verbatim summary. Glucose tolerance with serum insulin assay has been carried out in twenty-four apparently unaffected identical twins of diabetics. Glucose values were significantly higher and insulin values significantly lower than in control subjects, but there was considerable individual variation and in half the cases glucose tolerance was normal. There was no case of increased insulin response. In these twins glucose tolerance and insulin response were not correlated with weight, family history of diabetes, age at diagnosis of diabetes in the affected twin, time since that diagnosis, nor with age at testing the unaffected twin. On retesting twelve of the twins after two years no significant differences were found from the first testing.

The authors conclude that not all these twins are likely to develop diabetes, that the assumption that identical twins of diabetics are necessarily "prediabetic" is probably erroneous, and that factors other than genetic ones are important in the etiology of diabetes.

Raju, K. G. (Dept. of Physiol. and Pharmacol., Sch. of Vet. Med., Tuskegee Inst., Ala): METABOLISM OF ACETATE, PROPIONATE, BUTYRATE, AND GLUCOSE BY BOVINE CEREBRAL CORTEX SLICES. *Amer. J. Physiol.* 219:1739-41, December 1970.

Verbatim summary. Cerebral cortex slices from bovines of five different age groups (15 days, 2 months, 4 months, 6 months, and 2 years) were incubated in Krebs-Ringer phosphate buffer at pH 7.4 with C-14-labeled acetate, butyrate,

propionate, and glucose. The rate of oxygen uptakes and the utilization of C-14-labeled substrates were measured. In all age groups oxygen uptakes were much higher with glucose and fatty acids in comparison with no added substrates. Glucose supported the highest rate of oxygen uptake followed by propionate, acetate, and butyrate in that order. The cerebral tissue from animals of all age groups utilized more glucose in comparison with fatty acids. However, in the brain tissues from animals over six months of age utilization of fatty acids was significant ($P < 0.001$) in comparison with younger age groups. These results suggest that the primary source of energy for the bovine brain is glucose but in mature animals short-chain fatty acids may be important contributors of energy along with glucose.

Smith, C. K.; Stoll, R. W.; Vance, J.; Ricketts, H.; and Williams, R. H. (Depts. of Med. and Radiol., Sch. of Med., Univ. of Washington, Washington, D.C.): TREATMENT OF MALIGNANT INSULINOMA WITH STREPTOZOTOCIN. *Diabetologia* 7: 118-24, 1971.

Verbatim summary. Two patients with malignant insulinoma and hepatic metastases were treated with streptozotocin, administered directly into the celiac artery. Decreases in tumor size were documented radiographically. One patient was in a terminal state when first treated, but the other patient was in moderately good general health and responded well. Some side-effects, including renal tubular damage, were observed but were relatively minor. Streptozotocin therapy offers some benefit in patients with malignant insulinoma.

Terkildsen, A. B.; and Christensen, N. J. (Sec. Clin. of Int. Med., Kommunehospitalet, Århus Univ. Sch. of Med., Århus, Denmark): REVERSIBLE NERVOUS ABNORMALITIES IN JUVENILE DIABETICS WITH RECENTLY DIAGNOSED DIABETES. *Diabetologia* 7:113-17, 1971.

Verbatim summary. It has been well documented that diabetic patients retain vibratory perception during a longer period of ischemia than nondiabetics. This neurological abnormality is present at the time of the clinical appearance of diabetes and can be normalized by treatment with insulin. In the present study the vibratory perception threshold was studied during ischemia in six diabetics before and after treatment with insulin and in six nondiabetics. Threshold values were measured in the big toe, and ischemia induced by inflating a pressure cuff placed either above the knee or at the level of the ankle. The results obtained show that a normal function of only a part of the length of the nerve fiber is required to obtain a normal ischemic response throughout the length of the nerve, presumably because this part will stop conduction as if the whole nerve fiber were fully repaired. Furthermore, it is demonstrated that during treatment with insulin, normalization occurs at a greater rate in the proximal parts of the nerves compared with the more distal parts. The ischemic abnormalities are believed to be due to a defective myelin sheath.