ABSTRACTS

Czyzyk, A.; and Ostrowski, K. (Dept. III of Intern. Dis., Medical Academy, Warsaw, Poland): REACTIVITY OF THE VEINS IN DIABETES. Diabetologia *8*:99-103, 1972.

Verbatim summary. In thirty-two patients with juvenile-onset diabetes and thirty-two healthy subjects, venous reflexes were studied by determination of the peripheral venous pressure, forearm blood flow and venous tone at rest and after application of the following stimuli: passive change in the position of the legs, cooling of the opposite forearm, intravenous injection of Bamethan sulfate and of phentolamine.

The changes in the measured parameters induced by spasmolytic drugs were similar in both groups, whereas the effect of a drug blocking the alpha receptors and of the stimuli acting reflexively, was markedly less pronounced in diabetics.

The present results are interpreted as indicating specific venous changes in diabetes (venopathia diabetica), expressed as a decrease in the venous tone, impairment of the venous reflexes and rise of the venous pressure. The differences of the venous reflexes after blocking of the alpha receptors may indicate that changes in vessel innervation are the primary cause of diabetic venopathy.

Edwards, J. C.; Hellerström, C.; Petersson, B., and Taylor, K. W. (Histol. Dept., Univ. of Uppsala, Uppsala, Sweden and Sch. of Biol. Sci., Univ. of Sussex, Brighton, England): OXIDATION OF GLUCOSE AND FATTY ACIDS IN NORMAL AND IN A_2-CELL RICH PANCREATIC ISLETS ISOLATED FROM GUINEA PIGS. Diabetologia *8*:93-98, 1972.

Verbatim summary. Glucose and fatty acid oxidation has been measured in normal guinea-pig islets of Langerhans, and in A_2-cell rich islets from streptozotocin-treated guinea pigs. The rate of oxidation of these compounds in guinea pig A_2-cells and B-cells has been estimated. In the B-cells, the oxidation of glucose and octanoic acid responded markedly to changes in the extracellular levels of these substrates. Palmitic acid did not appear to be oxidized by the B-cells. In contrast, the oxidation of octanoic acid and palmitic acid in the A_2-cells was very sensitive to changes in the extracellular fatty acid concentration. The sensitivity of glucose oxidation to changes in the glucose concentration was small by comparison. The high rate of oxidation of fatty acids in the A_2-cells supports the view that the rate of fatty acid metabolism in these cells plays an important role in the regulation of glucagon release.

Fahlén, M.; Stenberg, J.; and Björntorp, P. (First Med. Service, Sahlgren's Hospital, Univ. of Gothenburg, Gothenburg, Sweden): INSULIN SECRETION IN OBESITY AFTER EXERCISE. Diabetologia *8*:141-44, 1972.

Verbatim summary. Blood glucose and plasma insulin during glucose loads were measured in nine obese patients before, and twice the days after, a submaximal work of long duration. All subjects showed lower plasma insulin values the day after exercise. The insulin/glucose ratio was decreased indicating an increased insulin sensitivity. The effect could be demonstrated with the peroral as well as with the intravenous glucose test. The effect was remaining for four to six days after exercise in seven of the nine patients studied. The insulin concentration the day after exercise was well within the range of values of nonobese, nonexercising controls. No parallel lowering of plasma triglycerides was observed. It was concluded that an acute, submaximal, prolonged work produces a considerable decrease of plasma insulin levels during several days in hyperinsulinemic obese patients.

Fernstrom, J. D.; and Wurtman, R. J. (Lab. of Neuroendocrine Regulation, Dept. of Nutrition and Food Science, Mass. Inst. of Technology, Cambridge, Mass.): ELEVATION OF PLASMA TRYPTOPHAN BY INSULIN IN RAT. Metabolism *21*: 337-42, April 1972.

In rat plasma, the levels of tryptophan are strikingly increased in fasted animals after the administration of insulin or after a carbohydrate meal. The levels of all other amino acids are decreased by these measures. Large doses of glucagon reduce plasma tryptophan concentrations while small doses are without effect. The sources of plasma tryptophan responsible for its elevation after insulin have not been identified. C.R.S.

Fischer, U.; Hommel, H.; Ziegler, M.; and Michael, R. (Zentralinstitut für Diabetes "Gerhardt Katsch," Bereich experimentelle Diabetesforschung Karlsburg/Greifswald, Germany): THE MECHANISM OF INSULIN SECRETION AFTER ORAL GLUCOSE ADMINISTRATION. I. MULTIPHASIC COURSE OF INSULIN MOBILIZATION AFTER ORAL ADMINISTRATION OF GLUCOSE IN CONSCIOUS DOGS. DIFFERENCES TO THE BEHAVIOR AFTER INTRAVENOUS ADMINISTRATION. Diabetologia *8*:104-10, 1972.

Verbatim summary. In conscious, trained dogs (Alsatians) the IRI concentration in the peripheral venous blood after oral administration of glucose increases when the blood glucose is still unchanged. After one or two peaks during the first twenty minutes IRI increases parallel to the blood sugar increase. In relation to the intravenous injection of glucose, the IRI maximum after oral administration occurs earlier. Furthermore the ratio of the IRI to blood sugar areas is raised. Without any blood sugar change the IRI concentration after oral application of tap water increases with one or two peaks. These peaks correspond to the first peaks after oral administration of glucose. These findings are discussed in the sense of a "feed-forward" of insulin secretion after feeding via N. vagus as well as via enterohormones. More attention should be paid to the IRI course during the early phase of the oral glucose tolerance test.

Gorden, Phillip; Freychet, Pierre; and Nankin, Howard (Diabetes Sect., Clin. Endocr. Branch, National Inst. of Arthritis and Metabolic Diseases, N. I. H., Bethesda, Md.): A UNIQUE FORM OF CIRCULATING INSULIN IN HUMAN ISLET CELL CARCINOMA. J. Clin. Endocrinol. Metab. *33*:983-87, December 1971.

The authors have partially characterized the circulating insulin components from a patient with islet cell carcinoma. The proinsulin-like component is larger in size, less reactive by radioimmunoassay, and more reactive by bioassay than identical preparations from a nontumor patient. The insulin component is less reactive by radioimmunoassay, but otherwise indistinguishable from the nontumor component. These unique circulating insulin components either represent a specific mutation in an individual patient or a more general heterogeneity of the insulin components in disease states.

T.J.M.

Griffiths, Anthony D.; and Bryant, Gillean M. (North Monmouthshire Hosp. Management Committee, Nevill Hall Hosp., Monmouthshire, and Dept. of Child Health, Welsh National Sch. of Med., Cardiff, Wales): ASSESSMENT OF EFFECTS OF NEONATAL HYPOGLYCEMIA. Arch. Dis. Child. *46*:819-27, December 1971.

Forty-one children who had experienced neonatal hypoglycemia (blood glucose less than 20 mg./100 ml.) and a group of matched normoglycemic controls were evaluated at a mean age of fifty-one months. There was no significant difference between the two groups in evidence of cerebral damage, mean I.Q., locomotor scores, behavior disorders, or convulsions. Twelve children had had asymptomatic hypoglycemia, and none showed evidence of cerebral damage. It is concluded that while it is important to treat symptomatic hypoglycemia in the newborn, most infants tolerate hypoglycemia without sequelae. P.S.R.

Group of Physicians of the Newcastle-upon-Tyne Region. TRIAL OF CLOFIBRATE IN THE TREATMENT OF ISCHAEMIC HEART DISEASE. Brit. Med. J. *4*:767-75, Dec. 25, 1971.

This collaborative study by twenty-two medical consultants was initiated in 1964-65 and terminated on August 31, 1969. Like the Scottish study, its aim was to evaluate the effectiveness of clofibrate on the secondary prevention of ischemic heart disease. It differed primarily in the criteria for patient selection and diagnosis of myocardial infarction. The Newcastle design was in general not as rigid with its requirements for patient age, number of previous myocardial infarctions, duration of angina pectoris or insistence upon abnormal electrocardiograms. The participating physicians used their own criteria for electrocardiogram evaluations.

In the Newcastle trial there was a significant over-all reduction in mortality (57 per cent) in the clofibrate-treated group (244) compared to the placebo group (253), $p = 0.02$. Like the Scottish data, the most beneficial effect of clofibrate was seen principally in the angina group. The drug effect on reducing serum cholesterol was maintained for over four years but again could not be causally related to the improved prognosis. Although cholesterol effects may still be very important, favorable drug actions on platelet adhesiveness, blood flow, or plasma free fatty acids should also be considered. P.H.S.

Guder, Walter; Wiesner, Wolfgang; Stukowski, Barbara; and Wieland, Otto (Inst. Clin. Chem., Municipal Hosp., Muenchen-Schwabing and Diabetes Res. Unit, Muenchen, Germany): METABOLISM OF ISOLATED KIDNEY TUBULES: OXYGEN CONSUMPTION, GLUCONEOGENESIS AND THE EFFECT OF CYCLIC NUCLEOTIDES IN TUBULES FROM STARVED RATS. Hoppe Seyler Z. Physiol. Chem. *352*:1319-28, October 1971.

Rates of renal gluconeogenesis were investigated under a variety of experimental conditions. Because gluconeogenesis in the whole kidney may be difficult to interpret, in that part of the glucose formed can be re-utilized by the medulla, isolated rat tubules were used in this investigation. The rates of gluconeogenesis from eleven substrates were generally higher than those obtained with kidney cortex slices. Except for pyruvate, gluconeogenesis was paralleled by a simultaneous increase in oxygen consumption.

In this renal tubule test system, cyclic AMP in a concentration range from 10^{-5} to 10^{-3} M stimulated glucose formation from all substrates entering the pathway via phosphopyruvate carboxylase (not from glycerol, dihydroxyacetone and fructose), without changing the oxygen consumption.

Of the other nucleotides tested (dibutyryl-adenosine-, cytidine-, guanosine-, inosine-, and uridine -3′, 5′ -monophosphate), only cyclic GMP which is known to be formed in the kidney, inhibited gluconeogenesis from lactate. This would tend to support the concept of Hardman et al.—that cyclic GMP is regulated independently from cyclic AMP. K.H.D.

Haeckel, R.; and Haeckel, H. (Institut für Klinische Chemie, Medizinische Hochschule Hannover, Hannover, Germany): INHIBITION OF GLUCONEOGENESIS FROM LACTATE BY PHENYLETHYLBIGUANIDE IN THE PERFUSED GUINEA PIG LIVER. Diabetologia *8*:117-24, 1972.

Verbatim summary. 1. Two hours after the intraperitoneal injection of 12 mg./kg. 1-β-phenylethylbiguanide (DBI) to guinea pigs fasted forty-eight hours, the 3-hydroxybutyrate/acetoacetate ratio and the concentration of both lactate and pyruvate were increased in the blood of the vena cava. The glucose level and the lactate/pyruvate ratio were not altered. In perfused livers taken from these animals immediately after the blood samples were withdrawn, the rate of glucose formation from lactate was not inhibited. However, the addition of 2×10^{-5} M DBI to the perfusate caused a 60 per cent suppression of gluconeogenesis under these conditions.

2. The accumulation of hepatic acetyl-S-Co A with a concomitant decrease of the citrate- and of the 2-oxoglutarate concentration in the presence of DBI indicated an impaired synthesis of citrate. A slight reduction of hepatic oxygen consumption was also consistent with an inhibition of the citric acid cycle. It is concluded that biguanides primarily suppressed hepatic cell respiration, which led to an accumulation of reducing equivalents inside the mitochondria. This may have caused a lack of oxalacetate for mitochondrial citrate synthesis.

3. The pattern of hepatic metabolite concentrations did not clearly show the rate-limiting step of glucose formation from lactate in the presence of biguanides; however, some evidence was found that the conversion of pyruvate to phosphenolpyruvate was affected.

4. No exact correlation was found between the effect of DBI on gluconeogenesis and on the hepatic ATP/ADP ratio.

Hellman, Bo; Lernmark, Åke; Sehlin, Janove; and Taljedal, Inge-Bert (Dept. of Histology, Univ. of Umea, Umea, Sweden): EFFECTS OF PHLORIZIN ON METABOLISM AND FUNCTION OF PANCREATIC B-CELL. Metabolism *21*:60-66, January 1972.

Uremia resulting from nephrectomy performed in rats was associated with a significant depression in pancreatic insulin stores. Despite diminished pancreatic insulin and the presence

of abnormal glucose tolerance tests in these animals, the serum insulin levels were appropriate for the serum glucose levels. Whether these animals are able to secrete insulin in response to stress and increased glucose levels in a normal pattern, or whether such factors as increased parathormone activity or guanidine compounds found in uremic plasma represent the stimulatory factors for insulin release, are questions which remain to be studied. C.R.S.

Hellman, Bo; Sehlin, Janove; and Taljedal, Inge-Bert (Dept. of Histology, Univ. of Umea, Umea, Sweden): THE INTRACELLULAR pH OF MAMMALIAN PANCREATIC B-CELLS. Endocrinology 90:335-37, January 1972.

The intracellular pH of pancreatic beta cells was estimated by the uptake of C-14-labeled 5,5-dimethyloxazolidine -2, 4 dione in microdissected islets of obese-hyperglycemic rats. Epinephrine, diazoxide, anoxia and variable glucose concentrations had no effect on intracellular pH. Factors other than low cytoplasmic pH must be involved to explain the intracellular integrity of beta granules. Insulin release does not appear to be related to alterations of the intracellular pH of the beta cells. C.R.S.

Hommel, H.; Fischer, U.; Retzlaff, K.; and Knöfler, H. (Zentralinstitut für Diabetes "Gerhardt Katsch," Bereich experimentelle Diabetesforschung, DDR-2201 Karlsburg and Kreiskrankenhaus Wolgast, DDR-222 Wolgast, Germany): THE MECHANISM OF INSULIN SECRETION AFTER ORAL GLUCOSE ADMINISTRATION. II. REFLEX INSULIN SECRETION IN CONSCIOUS DOGS BEARING FISTULAS OF THE DIGESTIVE TRACT BY SHAM FEEDING OF GLUCOSE OR TAP WATER. Diabetologia 8:111-16, 1972.

Verbatim summary. After sham feeding of glucose, conscious trained dogs bearing double-barrelled fistulas of the esophagus or of the stomach do not show any blood sugar increase. Nevertheless their IRI levels in the peripheral venous blood increased considerably. This increase consists of two peaks of short duration between the fifth and the tenth as well as the fifteenth and the twenty-fifth minutes. Such IRI peaks occurred also after sham feeding of tap water, but to a smaller extent. Their temporal order corresponds to the early IRI peaks after oral glucose administration in intact animals, but before the blood glucose increase which was observed by us previously. After the application of glucose into the oral opening of the esophageal fistula the first IRI peak does not occur, the second and the third peaks appeared to the same extent. A feed-forward of insulin secretion induced by oral ingestion is suggested. It may be interpreted within the scope of the "entero-insular axis" of the mechanism of insulin secretion.

Johansen, Klaus; and Ornsholt, Jorgen (Second Univ. Clin. of Intern. Med.; Aarhus Univ. Sch. of Med., Kommunehospitalet, Aarhus, Denmark; and the Surg. Dept., Vejle Town and Country Hosp., Denmark): FREQUENCY OF DIABETES AFTER ACUTE PANCREATITIS. Metabolism 21:291-96, April 1972.

Diabetes mellitus, diagnosed by glucose tolerance tests, was found in four of twenty-two patients after one or two attacks of acute pancreatitis. These patients with mild diabetes were under thirty-five years of age and manifested blood glucose abnormalities of less severity than usually seen in genetic diabetes in this age group, which may be attributable to destruction of both alpha and beta cells in patients with pancreatitis. The plasma insulin response following glucose was abnormal, three showing hypoinsulinism and one a delayed hyper-response. C.R.S.

Kansal, Prakash C.; Buse, John; Talbert, O. Rhett; and Buse, Maria G. (Med. Serv., V.A. Hosp.; and Departs. of Med. and Neurol., Med. Univ. of South Carolina, Charleston, S.C.): THE EFFECT OF L-DOPA ON PLASMA GROWTH HORMONE, INSULIN AND THYROXINE. J. Clin. Endocrinol. Metab. 34: 99-105, January 1972.

The effect of L-dopa on glucose, insulin, growth hormone and thyroxine in plasma was studied in eight normal patients and in seven subjects with Parkinson's disease.

Growth hormone increased 60 to 110 min. following a single oral dose of 500 mg. of L-dopa. Stimulation of growth hormone release by L-dopa was inhibited by the intravenous infusion of phentolamine, an α-adrenergic blocking agent. The single dose of L-dopa had no effect on the concentration of glucose, insulin or thyroxine.

In patients with Parkinson's disease, treated with 2 to 3 gm. L-dopa daily for two to three weeks, fasting levels of glucose and growth hormone remained unchanged. The "k" of glucose disappearance and insulin levels in plasma after an intravenous glucose load were not significantly affected. Fasting plasma insulin and thyroxine increased during L-dopa therapy. Maximum plasma growth hormone levels after intravenous insulin were less during L-dopa treatment than during the control period.

The results confirm that a single dose of L-dopa stimulates growth hormone secretion. This stimulatory effect appears to be mediated through adrenergic α-receptors. T.J.M.

Klöppel, G.; Freytag, G.; and Bommer, G. (Dept. of Path., Univ. of Hamburg, Hamburg, Germany): ENZYMEHISTOCHEMICAL STUDIES ON THE PANCREATIC ISLETS IN MICE INJECTED WITH ANTI-INSULIN SERUM. Diabetologia 8:19-28, 1972.

Verbatim summary. Islets of Langerhans in white mice with a diabetic syndrome after single and repeated injections of anti-insulin serum were studied by enzymehistochemical methods and compared with controls. Changes in activity of some enzymes were noted in the islet area in accordance with the histopathological findings of severe degranulation and hypersecretory changes of the beta cells. The α-glycerophosphate oxidase (GPOX) showed the most sensitive and severe decrease of activity whereas the acid phosphatase (ACPase) was only slightly decreased. Compared with the enzyme activity in normal mice, no significant changes of glucose-6-phosphate dehydrogenase (G-6-PD) could be observed. The only enzyme showing an increased activity was the glucose-6-phosphatase (G-6-Pase). The studies of the cytochrome oxidase (CCOX), lactic dehydrogenase (LDH), succinic dehydrogenase (SDH), acid phosphatase (ACPase), alkaline phosphatase (APase) and adenosine triphosphatase (ATPase) revealed no alterations of the enzyme patterns under these experimental conditions. The findings are discussed with regard to the hypothetical relations between the pentose phosphate shunt (indicator enzyme: G-6-PD), the glycerophosphate cycle (indicator enzyme: GPOX) and the phosphorylation of glucose (indicator enzyme: G-6-Pase) to insulin synthesis and release.

Koschinsky, Theodor; and Gries, F. Arnold (Second Dept. of Intern. Med. and Diabetes Res. Inst., Univ. of Duesseldorf, W. Germany): GLYCEROL KINASE AND LIPOLYSIS IN HU-

MAN ADIPOSE TISSUE IN RELATION TO RELATIVE BODY WEIGHT. Hoppe Seyler Z. Physiol. Chem. *352*:430-32, March 1971.

In genetically obese mice (ob/ob) the activity of glycerol kinase in fat cells is tenfold greater than that seen in lean littermates. The elevated level of intracellular glycerolphosphate can lead to an increased rate of re-esterification which in turn results in the accumulation of fat. The authors establish that glycerol-kinase is present in human subcutaneous adipose tissue, and in obese persons is ten times more active than in persons of normal weight. In genetically obese mice the enzyme activity is sufficient to phosphorylate 20 per cent of the glycerol liberated during lipolysis. However, in overweight persons only about 5 per cent of the released glycerol can be phosphorylated by the enzyme. It is concluded that the mechanisms leading to obesity in genetically obese mice are different from those in obese humans. K.H.D.

Lafrance, Louise; Rousseau, Suzanne; Begin-Heick, Nicole; and LeBlanc, Jacques (Depts. of Physiol. and Biochem., Sch. of Med., Laval University, Quebec, Canada): BLOOD GLUCOSE AND FREE FATTY ACID (FFA) RESPONSES TO CATECHOLAMINES IN RATS TREATED CHRONICALLY WITH NORADRENALINE OR ADRENALINE. Proc. Soc. Exp. Biol. Med. *139*:157-60, January 1972.

Controls and rats injected twice a day with noradrenaline or adrenaline in olive oil were used. After twenty-eight days, blood glucose, lactic acid and plasma free fatty acid (FFA) were measured in response to noradrenaline or adrenaline in saline. In controls, effect of noradrenaline is more pronounced on FFA levels, while effect of adrenaline is greater on glucose and lactic acid. Responses were diminished in animals treated chronically with either noradrenaline or adrenaline. In view of enhanced oxygen consumption response to noradrenaline or adrenaline in noradrenaline-treated rats, it seems that lower levels of FFA and glucose obtained could indicate enhanced utilization of those substrates. Since catecholamines inhibit insulin liberation, it is possible that chronic treatment with catecholamines preferentially enhances lipid rather than glucose utilization in response to noradrenaline or adrenaline. J.D.G.

Levey, Gerald S.; Schmidt, William M. I.; and Mintz, Daniel H. (Div. of Endocr. and Metabolism, Dept. of Med., Univ. of Miami Sch. of Med., Miami Fla.): ACTIVATION OF ADENYL CYCLASE IN A PANCREATIC ISLET CELL ADENOMA BY GLUCAGON AND TOLBUTAMIDE. Metabolism *21*:93-98, February 1972.

The effect of glucagon, tolbutamide, glucose, arginine and leucine on adenyl cyclase in a particulate preparation of an islet cell adenoma was determined by measuring the conversion of labeled ATP to cyclic AMP. Maximum increases in cyclic AMP production were obtained with glucagon and tolbutamide. Glucose and L-arginine did not increase cyclic AMP formation while leucine produced a 40 per cent increase in its accumulation. Insulin release from islet cell tissue and activation of adenyl cyclase were observed with glucagon and tolbutamide suggesting that the insulinogenic action of sulfonylurea drugs may reside in the stimulation of adenyl cyclase. C.R.S.

Loubatières, A.; Mariani, M. M.; Ribes, G.; Alric, R.; and Agot, H. (Faculté de Médecine, Institut de Biologie, Montpellier, France): PHARMACOLOGICAL STUDY OF A NEW HYPOGLYCEMIC SULFONAMIDE: GLISOXEPID (RP 22410). Diabetologia *8*:29-36, 1972.

Verbatim summary. Glisoxepid or RP 22410 is a new, very active hypoglycemic sulfonylurea. In the normal conscious dog, RP 22410 administered intravenously was eighty-one or 131 times more active than tolbutamide, depending on whether the dose is expressed in grams or in moles. The hypoglycemic effect did not occur in the totally pancreatectomized dog.

RP 22410 stimulated insulin secretion. In vivo in the anesthetized or conscious dog, the action of the drug (whether it be administered intravenously or orally) resulted in a rapid and considerable increase of the amount of insulin secreted by the pancreas. This action lasted several hours. In vitro the direct action of the product on the pancreas was demonstrated on the isolated and perfused rat pancreas, even at very low concentrations.

In the mouse, prolonged oral administration of RP 22410 stimulated neogenesis of the islets of Langerhans and of the beta cells. It therefore possesses betacytotrophic action.

Martin, David E.; Wolf, Richard C.; and Meyer, Roland K. (Dept. of Physiol. and Wisconsin Regional Primate Res. Center, Univ. of Wisconsin, Madison, Wis.): THE EFFECTS OF PREGNANCY ON BILIARY LIPIDS IN RHESUS MONKEYS. Proc. Soc. Exp. Biol. Med. *139*:115-17, January 1972.

To determine whether alterations in biliary excretion of lipids could explain marked hypolipemia seen during pregnancy in rhesus monkey, concentrations of cholesterol, phospholipids, and total lipids were measured at stages of gestation. No significant changes in biliary lipid levels were observed, indicating increased biliary concentration of lipids probably does not occur during pregnancy. J.D.G.

Molsted-Pedersen, Lars (Diabetes Centre, Royal Maternity Dept. B, Rigshospitalet; and the Central Lab., Sundby Hosp., Copenhagen, Denmark): ASPECTS OF CARBOHYDRATE METABOLISM IN NEWBORN INFANTS OF DIABETIC MOTHERS. I. INTRAVENOUS GLUCOSE TOLERANCE TESTS. Acta Endocrinol. (Kbh.) *69*:174-88, January 1972.

The rate of disappearance of intravenously administered glucose was investigated within six hours after birth in thirty-four infants of insulin-treated and sixteen infants of noninsulin-treated diabetic mothers and sixty infants of nondiabetic mothers. In infants of insulin-treated diabetic mothers glucose was cleared from plasma at a rate significantly faster than that in the other two groups. In infants of insulin-treated diabetic mothers, glucose was cleared more rapidly in those infants who had lower fasting plasma levels of glucose. In all three groups glucose was cleared more rapidly in infants with greater birth weights. The rapidity of glucose clearance in infants of diabetic mothers may reflect the hyperinsulinism which occurs in these infants in response to maternal hyperglycemia. The correlation between the efficiency of glucose clearance and birth weight suggests that the state of hyperinsulinism may promote fetal growth and that maternal blood levels of glucose may modulate the fetal growth rate. S.P.

Muller, Walter A.; Faloona, Gerald R.; and Unger, Roger H. (Dept. of Intern. Med., Univ. of Texas Southwestern Med. Sch. at Dallas, and VA Hosp., Dallas, Tex.): THE INFLUENCE OF THE ANTECEDENT DIET UPON GLUCAGON AND INSULIN SECRETION. N. Engl. J. Med. *285*:1450-54, Dec. 23, 1971.

The authors report the effect of a tenfold alteration in the carbohydrate content of the diet upon the plasma insulin and

glucagon and their response to a protein meal. The fasting insulin values decreased from 18 to 11 μU./ml. and their glucagon values increased from 100 to 136 pg./ml. on the low carbohydrate diet. The protein meal evoked a peak insulin increase of 7 μU./ml. at ninety minutes and a glucagon increase of 107 pg./ml. After restoration of the carbohydrate intake to normal, the peak insulin response to a protein meal increased to 27 μU./ml. at sixty minutes. The glucagon response was the same but the final level achieved was less because of the lower fasting level. The insulin-glucagon molar ratio declined to 1.6 on the low carbohydrate diet and did not change after a protein meal. With a normal carbohydrate intake the fasting ratio increased to 4.3 and rose to 8.2 after a protein meal. H.G.M.

Nobis, H.; Fischer, M.; Fuchs, F. S.; and Korp, W. (III. Medizinische Abteilung für Stoffwechselerkrankungen, Urologische Abteilung und Zentrallaboratorium des Krankenhauses der Stadt Wien, Lainz, Vienna, Austria): FIBRINOLYSIS AND PERITONEAL DIALYSIS IN THE TREATMENT OF DIABETIC COMA, COMPLICATED BY SEVERE SHOCK. A CASE REPORT. Diabetologia 8:145-47, 1972.

Verbatim summary. The case of a nineteen year old patient with gestational diabetes is reported who has developed diabetes five months after delivery in severe insulin-resistant ketoacidosis complicated by persistent shock. Since routine coma- and heparin therapy failed, fibrinolysis was applied and peritoneal dialysis was performed because of renal failure. Therapy resulted in a complete recovery of the patient.

Osterby, R. (Univ. Inst. of Path. and the Second Univ. Clin. of Intern. Med., Kommunehospitalet, Århus, Denmark): MORPHOMETRIC STUDIES OF THE PERIPHERAL GLOMERULAR BASEMENT MEMBRANE IN EARLY JUVENILE DIABETES. I. DEVELOPMENT OF INITIAL BASEMENT MEMBRANE THICKENING. Diabetologia 8:84-92, 1972.

Verbatim summary. An extension of a previously reported quantitative electronmicroscopic study of the glomerular basement membrane in juvenile diabetes is presented. The initial phase in the development of basement membrane thickening in diabetic glomeruli has also been studied.

Measurements of the basement membrane were obtained from photomontages of glomerular cross-sections produced from electron micrographs. A total of sixteen glomeruli from five nondiabetics and eighty-three glomeruli from fifteen diabetics were measured.

The results showed that the peripheral glomerular basement membrane is normal at the onset of acute, juvenile diabetes, but a thickening is demonstrable in patients with a duration of the disease of about two years.

These findings support the hypothesis that diabetic angiopathy is a consequence of the metabolic derangement in diabetics.

Parker, Donal C.; Rossman, Lawrence G.; and Vanderlaan, Eileen F. (Endocrine Div., Scripps Clin. and Res. Foundation, La Jolla, Calif. and the Univ. of Calif. at San Diego Sch. of Med., San Diego, Calif.): PERSISTENCE OF RHYTHMIC HUMAN GROWTH HORMONE RELEASE DURING SLEEP IN FASTED AND NONISOCALORICALLY FED NORMAL SUBJECTS. Metabolism 21:241-52, March 1972.

Human growth hormone (HGH), insulin, glucose and nonesterified fatty acid (NEFA) were determined in plasma obtained at intervals during monitored sleep from women after fasting or nonisocaloric feeding schedules. Normal patterns of HGH release in sleep occurred during periods of high caloric intake as well as during fasting, which produced an increased peak of HGH concentration. The amplification of HGH release during fasting occurred despite a fall in glucose levels, undetectable IRI, elevated NEFA and weight loss. A sharp decrease in NEFA at sleep onset during fasting suggested an alteration in the adrenergic mechanism during entry into sleep. There was no rise in glucose or NEFA following the early sleep HGH peak such as is seen typically with HGH release. These data suggest that sleep release of HGH is a primary neural rhythm independent of substrate concentration. Neuronal adaptation to utilization of nonglucose substrate in fasting may lead to enhanced rhythmic activity and increased amplitude of HGH release rhythm in sleep. C.R.S.

Pfeiffer, E. F.; and Raptis, S. (Dept. of Endocrinol. and Metab., Center of Intern. Med. and Pediat., Univ. of Ulm, Germany): CONTROLLED EXTENSION OF ORAL ANTIDIABETIC THERAPY ON FORMER INSULIN-DEPENDENT DIABETICS BY MEANS OF THE COMBINED INTRAVENOUS GLIBENCLAMIDE-GLUCOSE-RESPONSE-TEST. Diabetologia 8:41-47, 1972.

Verbatim summary. A new sulfonylurea response test is described for predicting the results of long-term treatment with a recently developed sulfonylurea compound, glibenclamide, particularly in insulin-dependent tolbutamide-nonresponsive elderly diabetics. The test is based on the observation that the insulin-stimulating capacity of glucose and the determination of the insulin increases are strikingly potentiated following glibenclamide plus glucose intravenously (25 γ plus 0.33 gm./kg. body weight) in serum samples where insulin binding antibodies have been removed. Eleven out of forty diabetics demonstrating between sixty and ninety minutes following injection, a mean increase of insulin of more than 500 per cent above the initial values, correlated satisfactorily with successful long-term oral treatment with glibenclamide. A positive glibenclamide-glucose-response test contrasted with primary failure of glibenclamide therapy in only one patient suffering from hemochromatosis. Oral treatment with glibenclamide may have certain advantages over insulin therapy, especially in elderly diabetics suffering from visual impairment, who are unable to inject themselves with insulin.

Saxton, C.; Majid, P. A.; Clough, G.; and Taylor, S. H. (Cardiovascular Unit, Univ. Dept. of Med., Gen. Infirmary, Leeds, England): EFFECT OF OUABAIN ON INSULIN SECRETION IN MAN. Clin. Sci. 42:57-62, January 1972.

Ouabain, administered intravenously at the maximum recommended therapeutic dose, did not influence plasma levels of insulin or blood glucose in the basal state or with the intravenous injection of tolbutamide in ten healthy subjects. With ouabain, urinary free catecholamines decreased significantly in the basal state. The hyperinsulinemic and hypoglycemic effects of ouabain reported by other investigators may have been related to the use of much greater doses of this digitalis glycoside. The improvement of insulin secretory capacity during digitalis-induced remission in heart failure must be due predominantly to the improved circulatory state of the patient rather than to a direct effect of the glucoside on the beta cell. The mechanisms responsible for the decreased urinary excretion of catecholamine with ouabain remain to be explained. S.P.

Schotz, Michael C.; Baker, Nome; and Salvatierra, Cairo (Res. V.A. Wadsworth Hosp., Los Angeles, Calif., and Dept. of Biological Chem., Univ. of Calif. at Los Angeles Sch. of Med., Los Angeles, Calif.): EFFECT OF GLUCOSE AND INSULIN ON FATTY ACID SYNTHETASE ACTIVITY IN RAT ADIPOCYTES. Hoppe Seyler Z. Physiol. Chem. *352*:991-96, July 1971.

To evaluate the mechanisms by which glucose and insulin increase lipogenesis in adipose tissue, the authors measured fatty acid synthetase activity in rat adipocytes. In rats fed ad libitum, glucose and insulin increased fatty acid synthetase activity in the first two hours. With prolonged incubation, fatty acid synthetase activity diminished, although glucose and insulin retarded the decrease in enzymatic activity. Adipocytes from fasted rats showed no increase in fatty acid synthetase activity with the addition of glucose and insulin.

Cycloheximide and actinomycin D inhibited the initial rise, and retrograded the fall of fatty acid synthetase activity in the late phase of incubation. This latter effect was observed in experiments in which only the inhibitors were evaluated as well as with glucose and insulin present.

Although addition of glucose or insulin alone increased the fatty acid synthetase activity, they were less effective than the combination in maintaining the augmented levels of enzymatic activity.

The increased NADPH oxidation was thought to reflect an increase in fatty acid synthetase activity induced by glucose and insulin.

It is postulated that the glucose and insulin effects on enzymatic activity are dependent upon mRNA synthesis and new protein synthesis. K.H.D.

Spalding, J. F.; and Brooks, Mary R. (Biomedical Res. Group, Los Alamos Scientific Lab., Univ. of California, Los Alamos, N. Mex.): LONGEVITY AND MORTALITY DISTRIBUTIONS OF MICE WITH AND WITHOUT X-RAY EXPOSURE TO FORTY-FIVE GENERATIONS OF MALE PROGENITORS. Proc. Soc. Exp. Biol. Med. *139*:15-18, January 1972.

Longevity and mortality distributions were observed on two H-2 genotype substrains of mice within each of two lines. Two substrains were from forty-five generations of X-irradiated male progenitors, and two were from nonirradiated progenitors with same degree of inbreeding. Life span differed significantly for H-2 genotypes within two lines but not for same genotypes between lines. Life shortening was not a genetic consequence of forty-five generations of exposure to over 4,500 times background radiation level. Data suggest a single-gene effect on longevity. J.D.G.

Tsang, Reginald C.; Kleinman, Leonard I.; Sutherland, James M.; and Light, Irwin J. (Dept. of Pediat., Univ. of Cincinnati, Coll. of Med., Cincinnati, Ohio): HYPOCALCEMIA IN INFANTS OF DIABETIC MOTHERS. J. Pediat. *80*:384-95, March 1972.

Hypocalcemia has been reported to occur in infants of diabetic mothers. The authors studied twenty-eight infants of diabetic mothers and twenty-eight infants of nondiabetic mothers prospectively matched for gestational age and perinatal complications. The incidence of hypocalcemia was significantly increased in the infants of diabetic mothers. There was no difference in the urinary excretion of calcium, magnesium or phosphorus. Serum phosphate was higher in the infants of diabetic mothers. Serum calcium responded normally to administration of exogenous parathormone. Although serum calcium was higher in the diabetic mothers than in the nondiabetics, both groups had serum calciums which were below normal. The authors suggest that diabetic mothers may have "relative" hyperparathyroidism, leading to fetal hypoparathyroidism in a manner analogous to that seen in infants of women with parathyroid adenomata. This seems unlikely, however, since absolute hypercalcemia was not observed in the diabetic mothers. P.S.R.

Vermeulen, A.; and Rottiers, R. (Dept. of Endocrin. and Metab., Med. Clin., Akademisch Ziekenhuis, Ghent, Belgium): INFLUENCE OF DIMETHYLBIGUANIDE (METFORMIN) ON CARBOHYDRATE METABOLISM IN OBESE, NONDIABETIC WOMEN. Diabetologia *8*:8-11, 1972.

Verbatim summary. The authors have studied the influence of two weeks' treatment of fifteen nondiabetic, obese subjects with 2 gm. of Metformin daily, on intravenous glucose tolerance and plasma insulin levels. Blood glucose fasting and during the IVGTT were not influenced by treatment, but the insulin levels and the insulin/glucose ratios were significantly decreased. This points to a decreased insulin resistance.

Whittingham, Senga; and Mackay, Ian R. (The Clin. Res. Unit of The Walter and Eliza Hall Inst. of Med. Res., and The Royal Melbourne Hosp., Victoria, Australia): THE ICEBERG ANALOGY OF AUTOIMMUNITY. Postgrad. M. J. *48*:95-97, February 1972.

Verbatim summary. The *iceberg analogy of autoimmunity* is presented to illustrate in human populations the totality of autoimmune disorders, that which is clinically overt and that which is clinically silent with only histological stigmata. The *iceberg analogy of autoimmunity* can be applied to co-existences of autoimmune diseases in one individual and associations of different autoimmune diseases in families. This is particularly exemplified by the familial occurrence of clinical or serological features of Hashimoto's thyroiditis, pernicious anaemia and other diseases in the 'thyrogastric cluster.' The clinician, on seeing multiple features of autoimmunity in a particular patient or on eliciting a family history of autoimmune disorder, may not only explore the surface but also plumb the depths of this remarkable complex of diseases.

Ziegler, M.; Hahn, H. J.; and Klatt, D. (Zentralinstitut für Diabetes "Gerhardt Katsch," Karlsburg, Germany): INFLUENCE OF ISOLATED INSULIN ANTIBODIES ON THE INSULIN SECRETION OF THE ISLETS OF LANGERHANS IN VITRO. Diabetologia *8*:148-49, 1972.

Verbatim summary. Mouse islets of Langerhans, isolated by microdissection after treatment with collagenase, were incubated either with pure insulin antibodies (IAB), which were prepared by immune precipitation, or with exogenous insulin. Insulin release was enhanced with increased concentrations of IAB and was inhibited by exogenous insulin. The results suggest that it was not the insulin per se, but probably its biological effect on the β-cells that influenced insulin secretion.