ABSTRACTS

Alberti, K. G. M. M.; Darley, J. H.; Emerson, Pauline M.; and Hockaday, T. D. R. (Nuffield Dept. of Med., Dept. of Hematology and Div. of Med., Radcliffe Infirmary, Oxford, England): 2,3-DIPHOSPHOGLYCERATE AND TISSUE OXYGENATION IN UNCONTROLLED DIABETES MELLITUS. Lancet 2:391-95, August 26, 1972.

Decreased levels of red cell 2,3-diphosphoglycerate (2,3-DPG) causes impaired oxyhemoglobin dissociation and may result in tissue anoxia. In this study 2,3-DPG, pH, blood gasses, lactate, pyruvate, 3-hydroxybutyrate acetoacetate, glucose and phosphate were measured in fifteen patients with ketoacidosis or ketoacidosis plus lactic acidosis. On admission, mean 2,3-DPG was 2.2 ± 0.4 mmoles/L. (normal 4.5 ± 0.5)—the low level correlated positively with blood pH and negatively with lactate pyruvate ratios and total ketones. Because the lowered pH improved oxyhemaglobin dissociation to about the same extent as the lowered 2,3-DPG concentration, it was thought that there was little effect on tissue oxygen supply. With fluid and insulin treatment, up to five days were needed before 2,3-DPG returned to normal. The authors postulate that this delay may have been secondary to a prolonged low plasma phosphate. In patients treated with intravenous bicarbonate, there was a rapid correction of pH and an acute fall in calculated availability of oxygen to tissues. The investigators suggest that intravenous regimens for the treatment of uncontrolled diabetes include phosphate and exclude bicarbonate. **T.G.S.**

Arnold, R.; Deuticke, U.; Frerichs, H.; and Creutzfeldt, W. (Dept. of Med., Div. of Gastroenterology and Metabolism, Univ. of Goettingen, W. Germany): IMMUNOHISTOLOGIC INVESTIGATIONS OF HUMAN INSULINOMAS. Diabetologia 8: 250-59, August 1972.

Verbatim summary. Fourteen subjects with insulinomas were examined immunohistologically using the peroxidase labeled antibody method. Eight tumors were investigated immediately after extirpation. Seven of these reacted with insulin and porcine-C-peptide antisera but not with glucagon antiserum. Only a B-cell carcinoma with an unusually low insulin concentration was negative. One year after embedding in paraffin, the immunohistologic reaction with insulin antiserum had markedly decreased in the tumors; however, not in the islet of the adjacent pancreas. From six patients one to four years old, paraffin-embedded material of the tumor and the normal pancreas was available. In this group, four tumors with an elevated insulin concentration reacted immunohistologically only weakly with an insulin antiserum, and two tumors (one with high and one with low insulin concentration) were immunohistologically negative, while the islets of the adjacent pancreas of all six cases showed a strong reaction. Thus the immunohistologic reaction of insulin in B-cell tumors but not in normal islets depends on the time elapsed between the paraffin embedding and the examination. Only tumors fixed in Bouin's fluid but not in Karnovsky's solution gave a positive immunohistologic reaction, while the islets of the adjacent pancreas reacted postively also after fixation in Karnovsky's solution. These findings suggest differences between the normal and the tumor insulin. A correlation between aldehyde-thionine stain and immunohistology indicates the superiority of immunohistology in identifying insulin-producing tumor cells.

Asplund, K. (Histol. Dept., Univ. of Uppsala, Uppsala, Sweden): EFFECTS OF POSTNATAL FEEDING ON THE FUNCTIONAL MATURATION OF PANCREATIC ISLET B-CELLS OF NEONATAL RATS. Diabetologia 8:153-59, June 1972.

Verbatim summary. The insulin response to glucose stimulation has been investigated in vivo and in vitro in suckling rats from small and large litters. In two-day-old animals from small litters there was a marked increase in serum insulin levels after an intraperitoneal glucose injection, while the insulin response to glucose in animals from large litters was low and sluggish. The weak insulin response to glucose in the two-day-old rats from large litters was further substantiated in studies in vitro in which the insulin release of isolated pancreatic glands was measured after incubation in a low or a high glucose concentration. On the third and fourth postnatal days there was an increased insulin secretion in response to the glucose challenge both in vivo and in vitro in the two groups of animals. The results indicate that postnatal feeding modulates the development of the glucose-mediated insulin release.

Bässler, K. H.; Horbach, L.; and Wagner, K. (Physiologisch-chemisches Institut und Institut für Medizinische Statistik und Dokumentation der Johannes Gutenberg, Universität Mainz, Mainz, Germany): DYNAMICS OF KETONE BODY METABOLISM IN DIABETIC RATS. Diabetologia 8:211-14, June 1972.

Verbatim summary. Steady state blood levels of ketone bodies during infusions of acetoacetate at various rates have been compared in healthy and diabetic rats. The characteristics of the metabolic elimination of ketone bodies from the blood are completely changed in diabetic rats. Whereas steady state levels of ketone bodies increase linearly with the infusion rate in healthy rats, this increase is exponential in diabetic animals. This difference, which is due to an impaired metabolic elimination, becomes evident only above a dosage of 50 μmoles acetoacetate per kilogram per minute. Chronic treatment with insulin for four to six days, but not acute insulin injection, restores the capacity of diabetic rats to metabolize ketone bodies at normal rates. The results are discussed with regard to the difference between the stable ketosis of starvation and the labile diabetic ketoacidosis.

Birkbeck, J. A. (Dept. of Pediat., Univ. of British Columbia, Vancouver, Canada): GROWTH IN JUVENILE DIABETES MELLITUS. Diabetologia 8:221-24, June 1972.

Verbatim summary. Height, weight, height velocity and skeletal maturity information were collected on a group of ninety-four juvenile diabetics in a mixed longitudinal study, and compared to a control population. Familial growth trends were taken into consideration where possible. Although the hormonal environment in the juvenile diabetic is probably unusual and fluctuating, there is no evidence that juvenile dia-

betes is likely to interfere with growth, provided a reasonable degree of control is maintained.

Boquist, L. (Inst. of Path., Univ. of Umeå, Umeå, Sweden): OBESITY AND PANCREATIC ISLET HYPERPLASIA IN THE MONGOLIAN GERBIL. Diabetologia *8*:274-82, August 1972.

Verbatim summary. In a colony of Mongolian gerbils maintained on a standard laboratory diet, obese animals were found occasionally. Obesity developed in animals of both sexes and was either transitory or permanent. The mean fasting blood glucose level in nonobese and obese gerbils was 83 and 105 mg./100 ml., respectively. Glucosuria and hyperglycemia were found only in a few obese animals, whereas the glucose tolerance was decreased in most obese gerbils.

The endocrine pancreas of the obese animals was morphologically either normal or more often hyperplastic, sometimes with the appearance of adenomatous islets. The β-cells possessed prominent Golgi complex and endoplasmic reticulum, and sparse granulation. Large, granule-poor cells and mitotic figures were seen in the islets. Degenerative changes occurred in the β-cells of diabetic animals.

It is suggested that the maintenance of the gerbils under laboratory conditions with free access to laboratory diet plays a major role in the development of obesity and that the endocrine pancreas of these animals has a good capacity for hyperplasia that often is sufficient to maintain normoglycemia in obese animals, although the glucose tolerance is decreased.

Boyett, June D.; and Hofert, J. F. (Dept. of Biochem., Univ. of Nebraska Coll. of Med., Omaha, Nebr.): STUDIES CONCERNING THE INHIBITION OF GLUCOSE METABOLISM IN THYMUS LYMPHOCYTES BY CORTISOL AND EPINEPHRINE. Endocrinology *91*:233-39, July 1972.

Thymic lymphocytes from adrenalectomized rats manifested depressed glucose uptake, lactate production and glycogen levels during aerobic incubation in the presence of cortisol. The depression of glucose uptake was greater than the decrease in CO_2 production from labeled glucose, resulting in an increased specific yield of 14-CO_2 in the presence of steroid. The fraction of glucose metabolized by pentose pathway was increased by cortisol, but absolute amounts of glucose metabolized by this pathway were unaltered. Cortisol had no effect upon anaerobic glycolysis. The lack of inhibition was not due to anoxic cellular damage. Epinephrine depressed glucose uptake and lactate production only in the presence of cortisol suggesting that epinephrine can only affect glucose metabolism in thymocytes if cells are exposed to glucocorticoid. C.R.S.

Chlouverakis, C.; and Bernardis, L. L. (E. J. Meyer Memorial Hosp., Dept. of Med., State Univ. of N. Y., Buffalo, N.Y.): VENTROLATERAL HYPOTHALAMIC LESIONS IN OBESE-HYPERGLYCEMIC MICE (OBOB). Diabetologia *8*:179-84, June 1972.

Verbatim summary. Bilateral electrolytic lesions were induced on the ventrolateral nucleus (VLN) of obese-hyperglycemic mice (*obob*) and lean litter mates, with or without previous body weight reduction. All lean animals with VLN damage died within the first four postoperative days. In contrast, all obese mice (*obob*) with no prior body weight reduction recovered, following an initial period of aphagia and rapid body weight loss. Three out of five reduced *obob* mice died following VLN lesions.

Two months after the operation the body weight of all lesioned *obob* mice stabilized at a level significantly lower than that of the "sham" operated obese; their serum immunoreactive insulin and blood glucose levels were also lower.

These data indicate that *obob* mice respond normally to bilateral lesions of VLN and that their excess adiposity, by protecting them during the early postoperative period, facilitates their recovery. The final stabilization of the body weight of lesioned *obob* at a level lower than that of control mice is compatible with the view that the VLN acts as the low set point controller in the regulation of body weight.

Cresto, J. C.; Dujovne, I. L.; Castellani, P. I.; Mitta, E. A.; de Majo, S. F.; and Foglia, V. G. (Dept. of Endocr., "Dr. Pedro de Elizalde" Pediat. Hosp.; Labeled Molecules Div., C.N.E.A.; Instituto de Fisiología, U.N.B.A., Buenos Aires, Argentina): INSULIN RADIOIMMUNOASSAY BY THE CHARCOAL-DEXTRAN TECHNIC. Diabetologia *8*:292-95, August 1972.

Verbatim summary. The influence exerted by the inactive support (charcoal-dextran) and the proteins in the medium, on the separation of free from antibody-bound 125-I-insulin by the charcoal-dextran insulin radioimmunoassay method was studied. The behavior of both fractions in the presence of different concentrations of albumin, dextran, normal guinea pig serum, and normal human serum was observed, and the conditions were established under which maximum charcoal adsorption of free insulin and minimum adsorption of bound insulin occur. The results obtained were compared with those yielded by the double antibody technic.

Under these working conditions it is possible to determine insulin in an unknown serum at 1/20 or 1/10 dilutions with a sensibility of 0.5 μU.

Dean, P. M.; and Matthews, E. K. (Dept. of Pharmacol., Univ. of Cambridge, Hills Road, Cambridge, England): THE BIOELECTRICAL PROPERTIES OF PANCREATIC ISLET CELLS: EFFECT OF DIABETOGENIC AGENTS. Diabetologia *8*:173-78, June 1972.

Verbatim summary. Alloxan, 5 mM, depolarized the islet but not the acinar cells of mouse pancreatic segments in vitro. This effect was prevented by D-glucose but not by glutathione, 3,0,methyl-α-D-glucose, D-glucosamine, D-mannoheptulose, or L-leucine. Pretreatment of islet β-cells with streptozotocin, 20 mM, caused no depolarization but inhibited the generation of action potentials by D-glucose, L-leucine, D-mannose and D-glyceraldehyde, whereas tolbutamide-induced action potentials were not blocked; the alkylating moiety of streptozotocin, N-nitroso-N-methyl urea produced similar effects. Prior exposure of the islet cells to nicotinamide, 4.1 mM, conferred protection against streptozotocin action. These observations are discussed in relation to the diabetogenic action of alloxan and streptozotocin.

Dzúriková, Viera; Niederland, T. R.; Brixová, Eva; Dzúrik, R.; Hupková, Viera; and Holomán, J. (Lab. of Exp. Ther. III. Med. Clin. Comenius Univ. Med. Sch., Bratislava, Czechoslovakia): ABNORMAL CARBOHYDRATE METABOLISM IN PATIENTS WITH LIVER CIRRHOSIS; IN VITRO STUDY. Diabetologia *8*:202-05, June 1972.

Verbatim summary. The serum of patients with liver cirrhosis inhibits glucose utilization in rat diaphragm. Inhibition is not caused by increased glycogenolysis or decreased glycogen synthesis. Lactate production and fructose utilization are not changed, indicating that the inhibition of glucose utilization is localized at the level of transmembrane transport of glucose

or at the level of hexose phosphates. The inhibitory activity of cirrhotic serum, fractionated by gel filtration is displaced by peptides and amino acids, excluding the significance of FFA and of growth hormone.

Felig, Philip; Wahren, John; Hendler, Rosa; and Ahlborg, Gunvor (Dept. of Intern. Med., Yale Univ. Sch. of Med., New Haven, Conn., and Dept. of Clin. Physiol. of the Karolinska Inst., Stockholm, Sweden): PLASMA GLUCAGON LEVELS IN EXERCISING MAN. N. Engl. J. Med. 287:184-85, July 27, 1972.

Seven nonobese, healthy males were exercised at half speed for forty minutes after an overnight fast. The plasma glucagon values increased in six out of the seven subjects with exercise; the mean maximal increase was 46 ± 13 pg./ml. The blood sugar of these individuals increased from 72 to 94 mg./100 ml., and there was a 110 per cent increase in the plasma alanine levels. The authors discuss the role this increase in glucagon plays in exercise, and whether this increase is due to the rise in alanine or to other factors. H.G.M.

Foucar, Eliott; and Field, James B. (Clin. Res. Unit and Dept. of Med., Univ. of Pittsburgh Sch. of Med., Pittsburgh, Pa.): EFFECT OF CONTROL OF HYPERGLYCEMIA ON PLASMA INSULIN RESPONSES TO VARIOUS STIMULI IN NEWLY DIAGNOSED KETOSIS-PRONE DIABETIC PATIENTS. J. Clin. Endocr. 35:288-98, August, 1972.

The effect of prompt re-establishment of normoglycemia on insulin was examined in newly diagnosed ketosis-prone diabetic patients. The patients were studied with an oral glucose tolerance test (GTT), a tolbutamide tolerance test (TTT) and a maximum insulin stimulation test (MIST) at the initiation of insulin treatment (mean fasting blood glucose = 268 ± 26 mg./100 ml.), and again after control of hyperglycemia (mean fasting blood glucose = 142 ± 13 mg./100 ml.). Initially, the patients' insulin responses to the three tests were absent or markedly below normal except for three patients' responses to tolbutamide. Glucose administration prior to control of hyperglycemia induced a mean insulin response which was only 6.7 per cent of the normals' response.

Treatment of hyperglycemia was followed by variable insulin responses. Three patients experienced a temporary remission of their diabetes and had insulin responses on the second GTT of 241 per cent, 204 per cent and 82 per cent of the normals' response. These patients also demonstrated marked improvement of their insulin response to tolbutamide and the MIST. Two other patients, who did not experience remission of their diabetes, demonstrated some improvement in insulin secretion on the second GTT, while the remaining patients showed no improvement. In general, but not always, the results of the ITT and MIST paralleled the results of the GTT.

These results demonstrated that while ketosis-prone diabetics initially have little insulin response to provocative stimuli, correction of hyperglycemia is followed by a wide range of insulin responses. Remissions were associated with significantly improved insulin secretion. It was not possible to correlate the improved insulin secretion with such factors as the patients' age, duration of symptoms, level of initial hyperglycemia, duration of insulin therapy or the degree of control of the hyperglycemia. T.J.M.

Gellady, Andrew M.; and Greenwood, Ronald D. (Childrens Memorial Hosp. and Dept. of Pediat., Northwestern Univ. Med. Sch., Chicago, Ill.): G-6-PD HEMOLYTIC ANEMIA COMPLICATING DIABETIC KETOACIDOSIS. J. Pediat. 80:1037-38, June 1972.

The authors report a ten-year-old boy who presented with diabetic ketoacidosis and who demonstrated evidence of acute hemolysis. G-6-PD deficiency was demonstrated. No drugs were given that are known to cause hemolysis in G-6-PD deficient patients. Ten previously reported patients have had episodes of hemolysis during diabetic ketoacidosis in the absence of drugs. Since G-6-PD deficiency and diabetes are both common disorders, the complication of hemolytic anemia should be considered in patients with diabetic ketoacidosis. P.S.R.

Glueck, Charles J.; Scheel, Deborah; Fishback, James; and Steiner, Paula (Gen. Clin. Res. Center, Univ. of Cincinnati Coll. of Med., Dept. of Intern. Med., Cincinnati Gen. Hosp., Cincinnati, Ohio): ESTROGEN-INDUCED PANCREATITIS IN PATIENTS WITH PREVIOUSLY COVERT FAMILIAL TYPE V HYPERLIPOPROTEINEMIA. Metabolism 21:657-66, July 1972.

Estrogen administration to three women and one man resulted in the development of pancreatitis at which time a previously covert familial type V hyperlipoproteinemia became overt. Exogenous and endogenous hypertriglyceridemias were exacerbated, carbohydrate tolerance diminished and the activity of postheparin lipolytic enzymes was depressed. Amelioration of pancreatitis and reversal of the biochemical abnormalities followed cessation of estrogenic therapy. It may be advisable to determine the level of serum triglycerides prior to administration of estrogens in order to avoid estrogen-induced pancreatitis. C.R.S.

Goldfine, I. D.; Cerasi, E.; and Luft, R. (Dept. of Endocr. and Metabolism, Karolinska Hosp., Stockholm, Sweden): GLUCAGON STIMULATION OF INSULIN RELEASE IN MAN: INHIBITION DURING HYPOGLYCEMIA. J. Clin. Endocr. 35: 312-15, August, 1972.

The plasma insulin response to intravenous administration of glucagon was studied in five healthy subjects both in the basal state and during insulin-induced hypoglycemia. Insulin response to glucagon was blunted when the blood glucose level was decreased. This inhibition was not entirely mediated by catecholamines liberated during hypoglycemia, since the alpha adrenergic blocking agent, phentolamine, could not restore the effect of glucagon. Phentolamine itself, in the absence of hypoglycemia, had no significant effect on glucagon-induced insulin release.

The authors conclude that, in man, the insulin releasing action of glucagon is dependent on the presence of a normal blood glucose concentration. T.J.M.

Goldman, J. K.; Schnatz, J. D.; Bernardis, L. L.; and Frohman, L. A. (Depts. of Med. and Path., State Univ. of N. Y. at Buffalo and the V. A. Hosp., Buffalo, N. Y.): IN VIVO AND IN VITRO METABOLISM IN HYPOTHALAMIC OBESITY. Diabetologia 8:160-64, June 1972.

Verbatim summary. U-14-C-glucose was injected into weanling rats two weeks after electrolytic destruction of the ventromedial hypothalamic nuclei. Incorporation of radioactivity into plasma lipids as well as liver, adipose tissue, diaphragm and carcass glycogen, total lipid and saponifiable fatty acids was measured. On a fat free as well as on a chow diet, rats with lesions incorporated more radioactivity into all adipose tissue components and into liver fatty acids but not into liver glyco-

gen. On the fat-containing diet (chow), radioactivity of plasma lipid was increased and that of total liver lipid unchanged, whereas on a fat-free diet, incorporation into plasma lipid was not increased while that into liver lipid was. Total diaphragm lipid and fatty acid radioactivity was increased while that of diaphragm glycogen was not. Carcass lipid, fatty acid and glycogen radioactivity were increased.

Diaphragm was also incubated in vitro with U-14-C-glucose or 1-14-C-palmitate. Glucose incorporation into total lipid and fatty acid was increased whereas oxidation and incorporation into glycogen were not. Palmitate oxidation and incorporation into phospholipid were decreased while incorporation into triglyceride was increased.

Results have been discussed in the light of similar changes previously noted with adipose tissue in vitro.

Hales, C. N. (Dept. of Chem. Path., Welsh National Sch. of Med., Cardiff, Wales): IMMUNOLOGICAL TECHNICS IN DIABETES RESEARCH, THE MINKOWSKI AWARD LECTURE. Diabetologia *8*:229-35, August 1972.

Verbatim summary. Solid phase biochemical systems have many technical advantages. The lecture reviews a number of ways in which solid phase immunological methods may be used in diabetes research. Solid phase antibodies are very convenient for use in radioimmunoassay. The immunoradiometric assay involves the isolation of antibodies onto solid phase antigen, the iodination of the antibodies while combined with the solid phase antigen, the elution of the iodinated antibodies and finally their use as a reagent for the measurement of antigen. The two site assay utilizes solid phase antibodies to extract and concentrate antigen from solutions such as plasma. The extracted antigen may then be assayed while combined with solid phase antigen if a second site on the antigen is available for reaction with I-125-labeled antibody. High specific activity, purified labeled antibodies may also be used for antigen localization, antibody estimation and for labeling cell membranes. Cell membrane purification using solid phase antibodies is considered as a further development of this methodology.

Heding, Lise G. (Novo Res. Inst., Copenhagen, Denmark): DETERMINATION OF TOTAL SERUM INSULIN (IRI) IN INSULIN-TREATED DIABETIC PATIENTS. Diabetologia *8*:260-66, August 1972.

Verbatim summary. A routine method is described for the determination of total IRI (immunoreactive insulin) in insulin-treated diabetics. The method involves an easy acid-ethanol extraction, whereby antibody-bound IRI is dissociated and separated, together with the "free" IRI from the serum proteins and the antibodies. The recovery of IRI in this procedure is about 80 per cent. After the separation, the total isolated IRI is measured in an immunoassay using ethanol for the separation of free and antibody-bound 125-I-insulin. In 169 diabetic patients treated with insulin in doses of from 6 to 120 U./day, the total fasting serum IRI was between 6 and 4,374 μU./ml., with a mean of 392 μU./ml. During treatment with insulin, the level of total IRI increased from normal values, registered during the first two months, to a higher level which became stable after about five months of treatment. The increase in IRI occurred simultaneously with the formation of antibodies. Insulin-resistant patients showed very high IRI levels.

Himsworth, R. L.; Carmel, P. W.; and Frantz, A. G. (Depts. of Med. and Neurosurgery, Coll. of Physicians and Surgeons of Columbia Univ., New York, N.Y.): THE LOCATION OF THE CHEMORECEPTOR CONTROLLING GROWTH HORMONE SECRETION DURING HYPOGLYCEMIA IN PRIMATES. Endocrinology *91*:217-26, July 1972.

Monkeys, prepared with intracranial cannulae and sedated with phencyclidine, have persistently low basal growth hormone (GH) levels and are found to secrete GH and cortisol in response to insulin-induced hypoglycemia or to intravenous deoxy-D-glucose (2-DG). Microinjections of 2-DG into many hypothalamic sites in these animals, including ventromedial nucleus and third ventricle, did not affect GH secretion. Injection of 2-DG into the lateral hypothalamic area adjacent to midventromedial nucleus invariably caused a sustained rise in GH secretion comparable to that seen with hypoglycemia. It is inferred that chemoreceptors which control GH secretory responses are located in that area. C.R.S.

Kahlenberg, Arthur; Dolansky, Donna; and Rohrlick, Ruth (Lady Davis Inst. for Med. Res., Jewish Gen. Hosp. and Dept. of Exp. Med., McGill Univ., Montreal, Quebec): D-GLUCOSE UPTAKE BY ISOLATED HUMAN ERYTHROCYTE MEMBRANES VERSUS D-GLUCOSE TRANSPORT BY HUMAN ERYTHROCYTES. J. Biol. Chem. *247*:4572-76, July 25, 1972.

The authors compared the effects of proteolytic and phospholipase A_2 digestion on the transport of D-glucose by intact RBC and by isolated RBC membranes. In intact RBC's exposed to these enzymes, and membranes isolated from cells previously treated with these enzymes, D-glucose uptake was not altered. When membranes were exposed after isolation to limited proteolytic digestion, there was a three- to fivefold increase in D-glucose uptake and a twofold increase in the apparent dissociation constant for the D-glucose membrane complex.

Overall, the studies were compatible with the fact that limited proteolytic digestion of isolated membrane exposes latent D-glucose binding sites, which are masked by a protease-sensitive covering on the surface of the isolated membrane. T.J.M.

Kaijser, L.; Lassers, B. W.; Wahlqvist, M. L.; and Carlson, L. A. (Dept. of Geriatrics, Uppsala Univ., Uppsala; Dept. of Clin. Physiol., Karolinska Hosp., Stockholm; and King Gustav V Res. Inst., Stockholm, Sweden): MYOCARDIAL LIPID AND CARBOHYDRATE METABOLISM IN FASTING MEN DURING PROLONGED EXERCISE. J. Appl. Physiol. *32*:847-58, June 1972.

Verbatim summary. Myocardial metabolism was studied at rest and during prolonged exercise in fifteen healthy subjects by measurement of arterial-coronary sinus concentration differences and the intravenous infusion of palmitate-3-H as a free fatty acid (FFA) tracer. During prolonged exercise, the relative participation of total blood lipid and carbohydrate substrates in myocardial oxidative metabolism, as assessed by the oxygen extraction ratios, did not differ from the pattern at rest. Arterial-coronary sinus difference in oxygen content increased with exercise and was significantly correlated with heart rate. Myocardial extractions of FFA, glucose, and pyruvate, but not lactate, were significantly correlated with their respective arterial concentrations at rest. During prolonged exercise, myocardial extractions of pyruvate and lactate, but not FFA and glucose, were correlated with their arterial concentrations. However, the results suggested that rate of glu-

cose upake might be enhanced during exercise. Radiopalmitate measurements were interpreted as indicating efflux of fatty acids into the coronary sinus blood from endogenous lipid stores. The release of free glycerol during exercise raised the possibility of increased turnover of these stores during exercise.

Kreisberg, Robert A. (Dept. of Med., V.A. Hosp. and Univ. of Alabama in Birmingham, Birmingham, Ala.): GLUCOSE-LACTATE INTERRELATIONS IN MAN. N. Engl. J. Med. *287*: 132-37, July 20, 1972.

The author reviews his studies and those of others concerning the interrelationships between the metabolism of lactate and glucose in man. He points out that the average production of lactate is 140 gm./day as estimated by isotopic lactate turnover studies. The major sites of lactate production are skeletal muscle and erythrocytes, with the brain, renal medulla, leucocytes, skin and gastrointestinal tract also contributing. Glucose is the major source, accounting for 50 per cent of the lactate produced in man. Alanine is also a prime source of lactate with the remainder coming presumably from other amino acids and muscle glycogen. Lactate is recycled into glucose, with approximately 20 per cent of the glucose being derived from this source. During starvation the conversion of lactate to glucose increases 50 per cent, so that lactate becomes the major source of glucose during prolonged starvation in man. In his studies of the effect of ethanol on lactate and glucose turnover, the author found no increase in the production of lactate, but there was a marked decrease in the conversion of lactate to glucose. This occurred both in the starved and the nonstarved state demonstrating that depletion of glycogen stores is a prerequisite for alcohol-induced hypoglycemia. The author also mentions that changes in glucose and lactate interrelations occur with phenformin, but does not discuss this topic. **H.G.M.**

Langslow, D. R.; and Freeman, B. M. (Houghton Poultry Res. Station, Houghton, Huntingdon, England): PARTIAL PANCREATECTOMY AND THE ROLE OF INSULIN IN CARBOHYDRATE METABOLISM IN GALLUS DOMESTICUS. Diabetologia *8*:206-10, June 1972.

Verbatim summary. A technic for the partial pancreatectomy of the chicken is described. Following surgery the plasma insulin concentration falls from 78 μU./ml. to 17.5 μU./ml. and remains at that level for the subsequent two days of observations. No persistent hyperglycemia was noted, and the birds became hypoglycemic after two days. Plasma FFA concentration was significantly reduced throughout. The partially pancreatectomized chicken was found to have a severely impaired glucose tolerance and there was only a slight, nonsignificant increase in plasma insulin after glucose loading. Its response to glucagon changed little. It is concluded that insulin plays an essential role in the utilization of glucose, but the site of its action remains to be identified.

Leonhardt, W.; Hanefeld, M.; Schneider, H.; and Haller, H. (Dept. of Intern. Med., Med. Acad. of Dresden, Germany): HUMAN ADIPOCYTE VOLUMES: MAXIMUM SIZE, AND CORRELATION TO WEIGHT INDEX IN MATURITY-ONSET DIABETES. Diabetologia *8*:287-91, August 1972.

Verbatim summary. Adipocytes of man and rat were isolated by incubation with collagenase. Their size distributions were measured with the pulse counter ZG 2 and evaluated on a lognormal base. Empirically, we have found that the standard deviations of the distributions are negatively correlated with the cell diameter. By extrapolation of the standard deviations to zero, we calculated upper limits of the adipocyte volumes to be $v_m = 0.93$ nl. (subcutaneous adipose tissue of the abdomen in man) and $v_m = 0.49$ nl. (epididymal and retroperitoneal adipose tissue in white Wistar rats). Larger adipocyte volumes in these tissues have not been observed. The correlations between adipocyte volume (v) and relative body weight (m/m_0) have been measured in nondiabetics (I) and maturity-onset diabetics (II) separately: $m/m_0 = 2.34\ v + 0.45$ (I), and $m/m_0 = 0.576\ v + 0.95$ (II). The regression coefficients in both equations are significantly different: adipocyte volumes increase more directly with weight index in maturity-onset diabetics. Supposing that overweight is an excess of adipocyte mass, we have derived a general relation between weight index m/m_0, adipocyte volume v and N/m_0, the adipocyte number per kilogram body mass: $m/m_0 = 0.93\ Nv/m_0 + 0.79$. It follows with the above-mentioned regression coefficients that obese maturity-onset diabetics have smaller adipocyte numbers than obese nondiabetics. This means that the predisposition to maturity-onset diabetes is extreme in those obese persons who became overweight after the end of adolescence.

Lin, Boniface J.; Nagy, Barbara R.; and Haist, Reginald E. (Dept. of Physiol., Univ. of Toronto, Toronto, Canada): EFFECT OF VARIOUS CONCENTRATIONS OF GLUCOSE ON INSULIN BIOSYNTHESIS. Endocrinology *91*:309-11, July 1972.

Glucose concentrations in media containing isolated islets from the rat influenced the rates of proinsulin synthesis and conversion to insulin. At low concentrations of glucose, proinsulin synthesis proceeds at a low, basal level; at higher concentrations, biosynthesis is markedly accelerated. The rate of conversion to insulin is also accelerated but less than proinsulin production. The results suggest that there is a threshold of glucose concentration effective in promoting proinsulin biosynthesis and that the conversion of proinsulin to insulin may be rate-limiting in insulin production. **C.R.S.**

Luyckx, A. S.; Massi-Benedetti, F.; Falorni, A.; Lefebvre, P. J. (Sect. of Diabetes, Inst. of Med., Univ. of Liège, Belgium and Dept. of Pediat., Univ. of Perugia, Italy): PRESENCE OF PANCREATIC GLUCAGON IN THE PORTAL PLASMA OF HUMAN NEONATES. DIFFERENCES IN THE INSULIN AND GLUCAGON RESPONSES TO GLUCOSE BETWEEN NORMAL INFANTS AND INFANTS FROM DIABETIC MOTHERS. Diabetologia *8*:296-300, August 1972.

Verbatim summary. Human neonates have been studied during the first hours of life. Blood glucose, portal plasma insulin and glucagon have been determined both at regular intervals up to twenty-four hours after birth and during an intravenous glucose load performed at the twenty-fourth hour. A material presenting the immunological characteristics of pancreatic glucagon has been found in the portal plasma of both normal infants and infants from diabetic mothers (IDM). The intravenous glucose load did not suppress plasma glucagon in the normal neonates nor in the IDM. Higher portal plasma glucagon values were observed in the late phase of the intravenous glucose load in normal neonates compared to IDM. Portal plasma insulin has been found higher in IDM both at the twenty-fourth hour of life and during the early phase of the intravenous glucose tolerance test. The hypothesis is put

forward that the behavior difference in glucagon secretion might be a consequence of the relative hyperinsulinism of IDM with insulin facilitating the entry of glucose into the α cell thus permitting a more effective glucagon suppression.

Rasio, E.; Whichelow, M. J.; Butterfield, W. J. H.; Hicks, B. H. (Dept. of Pathophysiol., Univ. of Brussels, Brussels, Belgium, and Dept. of Med., Guy's Hosp. Med. Sch., London, England): INSULIN FIXATION AND GLUCOSE UPTAKE BY FOREARM TISSUES IN RESPONSE TO INFUSIONS OF PHYSIOLOGICAL AMOUNTS OF INSULIN IN NONDIABETIC SUBJECTS. Diabetologia *8*:244-49, August 1972.

Verbatim summary. Insulin fixation and glucose uptake have been studied in the forearm tissues of nine lean nondiabetic men for three consecutive hours, during a fasting state, an intra-arterial infusion of a small dose of insulin (25 to 100 mU.), and a recovery period. When insulin was administered, the arterial plasma immunoreactive insulin rose to levels ranging from 15 to 65 μU./ml.; the tissue insulin fixation was significantly increased during this period, but no effect on tissue glucose uptake was observed. A close correlation was found between the arterial plasma insulin concentration and the tissue insulin fixation. The injection of 200 mg. glucose intra-arterially at the end of the study resulted in a reversal of the arteriovenous gradient of plasma insulin concentration.

The results show that large amounts of circulating insulin can be bound to the forearm tissues without exerting an effect on glucose uptake. It is suggested that the binding of insulin occurs at the vascular endothelium and that it is reversible by increased concentrations of blood glucose.

Rosak, C.; Bartelt, K. M.; Beyer, J.; and Schöffling, K. (Center of Intern. Med., Johann Wolfgang Goethe-Univ., Frankfurt/Main, Dept. of Endocr., Frankfurt/M., Germany): STUDIES ON THE SITE OF ACTION OF TOLBUTAMIDE IN THE LIPOLYTIC SYSTEM. Diabetologia *8*:185-88, June 1972.

Verbatim summary. The antilipolytic effect of tolbutamide was studied under different conditions in isolated rat adipose tissue, using norepinephrine, theophylline and dibutyryl 3′,5′-AMP as lipolysis-stimulating agents. A selective blockade was performed with alpha and beta-blocking agents (phentolamine and Kö 592) to investigate a possible relation of tolbutamide to the adrenoceptive structures of the fat cell. (1) Tolbutamide exerts an antilipolytic effect on norepinephrine and theophylline-stimulated lipolysis in two different concentration ranges. (2) When using dibutyryl 3′,5′-AMP, this biphasic pattern disappears. (3) Tolbutamide shows an additional antilipolytic activity in adipose tissue pretreated with the beta blocker Kö 592, whereas this effect could not be obtained after pretreatment with the alpha blocker phentolamine.

From the results obtained the conclusion is drawn that tolbutamide, like phentolamine, at least in concentrations ranging from 12.5 to 50 μg/ml., influences a reaction subsequent to the formation of cyclic 3′,5′-AMP.

Shigeta, Yukio; Shichiri, Motoaki; Okada, Akira; and Karasaki, Kenkichi (First Dept. of Med., Osaka Univ. Med. Sch. Osaka, Japan): PLASMA IMMUNOREACTIVE INSULIN AFTER INTESTINAL ADMINISTRATION OF B-NAPHTHYL-AZO-POLYSTYRENE INSULIN TO THE RABBIT. Endocrinology *91*:320-22, July 1972.

Insulin was bound to diazopolystyrene quenched with B-naphthal. When this complexed insulin was administered into the jejunum of rabbits, there was a significant rise in plasma IRI followed by a fall in blood glucose. The plasma IRI elevations seen after administration of B-naphthyl-azo-polystyrene-insulin were two to three times higher than those following infusions of Regular insulin. These results suggest a means of protecting the insulin molecule from digestive destruction. C.R.S.

Silcock, D. H.; Hadden, D. R.; and Neill, D . W. (Royal Victoria Hosp., Belfast, N. Ireland): COMPUTER ANALYSIS OF INTRAVENOUS GLUCOSE TOLERANCE TESTS. Diabetologia *8*: 301-04, August 1972.

Verbatim summary. A computer program which simultaneously calculates glucose disappearance rates after intravenous injection using three different mathematical equations is described. This program has been applied to the results obtained from several groups of pregnant women. The reasons for suggesting that the "absolute K value" may be preferable on practical grounds are discussed. This program, written in Fortran, is available on application to D. W. Neill.

Tasman, William (Retina Service, Wills Eye Hosp., Philadelphia, Pa.): RETINAL DETACHMENT SECONDARY TO PROLIFERATIVE DIABETIC RETINOPATHY. Arch. Ophthal. *87*:286-89, March 1972.

Verbatim summary. Twenty-nine patients representing thirty-three retinal detachments secondary to diabetic retinopathy were examined. Eighteen of the eyes had definite retinal breaks located in the posterior pole near the optic nervehead and were salvageable if the retinal break could be closed by surgery. In fifteen eyes no retinal break could be found. Five of these eyes spontaneously reattached over a period of six to fourteen months without treatment, one with extremely good visual return. All of the detachments appeared to be secondary to vitreous traction.

Young, D. A. B.; and Balant, L. (Inst. de Biochimie Clinique, Univ. of Geneva, Switzerland, and Nuffield Inst. of Comparative Med., Zoological Soc. of London, England): INTRAPERITONEAL TEST OF INSULIN ACTIVITY ON THE RAT DIAPHRAGM IN VIVO: FACTORS CONTROLLING THE VARIABILITY OF RESPONSE. Acta Endocr. *71*:103-14, September 1972.

Rafaelsen had described a sensitive in vivo method of measuring insulin activity which was based upon injection of media containing insulin together with 14-C-labeled glucose intraperitoneally to rats and determination of incorporation of radioglucose into glycogen of diaphragmatic muscle and into lipids of epididymal adipose tissue. To make this bioassay more precise and reproducible, the authors investigated the principal steps of the method with respect to glycogen formation in the muscle. The nutritional state and the weight range of the animals were identified as variables influencing the results importantly. Modifications of the assay designed to minimize these variables resulted in improved precision and sensitivity. S.P.