ABSTRACTS

Altszuler, N.; Morrison, A.; Gottlieb, B.; Bjerknes, C.; Rathgeb, I.; and Steele, R. (Dept. of Pharmacol., N.Y.U. Sch. of Med., N.Y., N.Y., and the Biol. Dept., Brookhaven Natl. Lab., Upton, N.Y.): ALTERATION BY FASTING OF THE EFFECTS OF METHYLPREDNISOLONE ON CARBOHYDRATE METABOLISM IN THE NORMAL DOG. Metabolism *23*:369-74, 1974.

Administration of pharmacologic doses of methylprednisolone produced an increased glucose turnover with no significant change in plasma glucose concentration in the normal dog in the postabsorptive state. Plasma lactate and insulin concentrations were raised, and the hepatic glycogen content showed a marked increase. Fasting resulted in decreased glucose turnover, liver glycogen and plasma insulin, with little change in plasma glucose or lactate levels. Administration of methylprednisolone with continued fasting caused an increase in insulin levels and a striking rise in liver glycogen to values exceeding those in the postabsorptive state. Despite the elevated glycogen content, hepatic glucose release was not increased above the depressed values of the long-fasting state. C.R.S.

Anthony, L. E.; and Faloona, G. R. (Dept. of Biochem., Univ. of Texas Southwestern Med. Sch. and V. A. Hosp., Dallas, Texas): PLASMA INSULIN AND GLUCAGON LEVELS IN PROTEIN-MALNOURISHED RATS. Metabolism *23*:303-06, 1974.

Plasma concentrations of insulin and glucagon were determined in protein-malnourished rats. Plasma insulin levels were markedly reduced while plasma glucagon levels were comparable to adequately fed control rats. In experimental protein malnutrition, low levels of serum amino acids do not appear to depress plasma glucagon levels. The low insulin/glucagon ratio is consistent with the hypothesis that glucagon serves as a catabolic hormone in states characterized by protein breakdown. C.R.S.

Aubry, F.; Marcel, Y. L.; and Davignon, J. (Dept. of Lipid Metab. and Atherosclerosis Res., Clin. Res. Inst. of Montreal and Dept. of Med., Hotel-Dieu Hosp., Montreal, Quebec, Canada): EFFECTS OF GLUCAGON ON PLASMA LIPIDS IN DIFFERENT TYPES OF PRIMARY HYPERLIPOPROTEINEMIA. Metabolism *23*:225-38, 1974.

Single doses of intramuscular glucagon lowered plasma triglyceride (TG) within four hours in patients with primary hyperlipoproteinemia of types IIa, IIb or V but had no effect on plasma cholesterol. Glucagon given for ten days lowered plasma cholesterol in types IIa, IIb, III and V, but did not change the cholesterol in II homozygous or IV. Glucagon lowered plasma TG in types III and V, but produced only a transient fall followed by a progressive rise in types IIa, IIb, and IV. In all subjects studied, a positive correlation between the increase in plasma glucose at 120 minutes after a single dose of glucagon and the decrease in TG during its chronic administration was observed. The mechanisms involved in lipid alterations induced by glucagon may be related to the stimulation of insulin secretion as well as to a direct effect of the hormone upon lipid-glucose metabolism. C.S.

Boden, G.; Essa, N.; Owen, O. E.; and Reichle, F. A. (Temple Univ. Health Sciences Center, Philadelphia, Pa.): EFFECTS OF INTRADUODENAL ADMINISTRATION OF HCl AND GLUCOSE ON CIRCULATING IMMUNOREACTIVE SECRETIN AND INSULIN CONCENTRATIONS. J. Clin. Invest. *53*:1185-93, April 1974.

In a study concerned with the normal dynamics of endogenous secretin release and degradation, the authors have also examined some relationships of secretin and carbohydrate metabolism. Intraduodenal hydrochloric acid produced a prompt increase in immunoreactive secretin in the portal and femoral veins of anesthetized dogs along with a concomitant increase in pancreatic exocrine function. In this system the portal venous insulin levels rose significantly in response to intraduodenal hydrochloric acid; the rise was not great enough, however, to affect peripheral venous insulin, serum glucose, or free fatty acid levels. Furthermore, intraduodenal glucose had no effect on portal venous secretin levels.

The authors have suggested that the insulin response to hydrochloric acid may be a result of endogenous secretin release. It is difficult to draw these conclusions, however, as there may be many unknown effects of intestinal acidification; the effect, however, was so minimal as to discount its physiologic significance. The authors have demonstrated well that secretin is not the gut factor responsible for insulin secretion in response to the presence of glucose in the gastrointestinal tract. R.R.

Brook, C. G. D.; and Loyld, J. K. (Inst. of Child Health, London): ADIPOSE CELL SIZE AND GLUCOSE TOLERANCE IN OBESE CHILDREN AND EFFECTS OF DIET. Arch. Dis. Child. *48*:301, 1973.

Verbatim summary. Adipose cell size and the glucose and insulin responses to an oral glucose load have been studied in twenty-six obese children. Adipose cells were found to be enlarged, and hyperinsulinaemia was demonstrated both in the fasting state and also after oral glucose. The degree of hyperinsulinaemia could not be predicted by adipose cell size.

In fourteen children studies were repeated after a period of weight loss. A marked fall in fasting serum insulin levels occurred in all children during the first week of treatment. A reduction in adipose cell size was demonstrated over a longer period, but there was no change in the total number of adipose cells. In seven children who were still losing weight when a second glucose tolerance test was performed, insulin levels after oral glucose were reduced, but there was no reduction in insulin levels in seven children studied after they had stopped losing weight. The reduction in body fat and adipose cell size in these two groups of children was no different. Thus it was not possible to predict the fall in insulin levels from changes in body composition or adipose cell size.

These data do not support the hypothesis of a direct causal relation between the increase in adipose cell size and the hyperinsulinaemia of obesity.

Felig, P.; Wahren, J.; Hendler, R.; and Brundin, T. (Yale Univ. Sch. of Med., New Haven, Conn., and the Karolinska Inst., Serafimer Hosp., Stockholm, Sweden): SPLANCHNIC GLUCOSE AND AMINO ACID METABOLISM IN OBESITY. J. Clin. Invest. *53*:582-90, February 1974.

In order to study the effects of obesity on splanchnic glucose

production and the uptake of gluconeogenic precursors, the authors simultaneously catheterized the hepatic vein and the brachial artery in the thirteen obese male subjects and twelve nonobese male control subjects in the fasting state. An increase in arterial concentration of glycerol, free fatty acids, pyruvate, insulin, and a number of amino acids, most notably alanine, was noted in the obese subjects. While the net splanchnic glucose production was not significantly different in the two groups, the splanchnic uptake of lactate, glycerol, free fatty acids, alanine, and oxygen was 50 to 160 per cent greater in the obese subjects; gluconeogenic precursors could thus account for 33 per cent of the splanchnic glucose output in the obese subjects as compared with 19 per cent in the control subjects. In order to estimate hepatic responsiveness to endogenous insulin secretion, glucose was administered in a peripheral vein at a dose to cause a 75 per cent reduction in splanchnic glucose output in the control subjects; a similar rate of glucose infusion in the obese subjects resulted in a similar reduction in splanchnic glucose output but at the cost of a significantly increased arterial insulin increment. When the arterial insulin increment in the obese subjects was matched to the control subjects by adjusting the rate of glucose infusion, the fall in splanchnic glucose output in the obese subjects was significantly less. The authors suggest that these data are consistent with hepatic resistance to insulin in obesity. R.R.

Genuth, S. M.; and Castro, J. (The Saltzman Inst. for Clin Invest., Mt. Sinai Hosp. of Cleveland, Cleveland, Ohio): EFFECT OF ORAL ALANINE ON BLOOD BETA-HYDROXYBUTYRATE AND PLASMA GLUCOSE, INSULIN, FREE FATTY ACIDS, AND GROWTH HORMONE IN NORMAL AND DIABETIC SUBJECTS. Metabolism *23*:375-86, 1974.

Oral administration of alanine to normal subjects and untreated adult diabetic patients resulted in a decrease in blood beta-hydroxybutyrate levels. This reduction occurred in two phases, the first associated with a rise in plasma insulin and the second with a fall in free fatty acids. The latter phase was observed only with a high dose of alanine (0.5 gm. per kilogram). In diabetic patients made ketotic by insulin withdrawal, the first phase was clearly demonstrable suggesting that alanine is capable of inhibiting ketosis by an extra-insulin mechanism. In these patients, alanine produced a rise in free fatty acid levels as blood levels of beta-hydroxybutyrate decreased. Plasma glucose remained stable in normal control and untreated diabetic subjects but rose significantly in insulin-dependent diabetic subjects. Alanine produced a delayed rise in levels of growth hormone at ninety minutes in normal and insulin-dependent diabetic subjects; this effect was correlated with a preceding fall in free fatty acid levels. The basis for the antiketogenic effect of alanine is not yet established and may involve oxidative deamination of alanine to pyruvate with subsequent conversion to lactate, glycerol and phosphate or to oxalacetate. The possibility exists also that alanine may alter the flux of free fatty acids into the mitochrondria. The present study suggests that ketogenesis in conjunction with gluconeogenesis may be regulated by alanine supply which has been shown to be reduced in diabetic ketoacidosis. C.R.S.

Holm, J.; Dahllof, A. G.; Bjorntorp, P.; and Scherstén, T. (Dept. of Surg. II, Dept. of Clin. Rehab. II, and The Clin. Metab. Lab. of the First Med. Serv., Sahlgren's Hosp., Univ. of Gothenburg, Gothenburg, Sweden): GLUCOSE TOLERANCE, PLASMA INSULIN, AND LIPIDS IN INTERMITTENT CLAUDICATION WITH REFERENCE TO MUSCLE METABOLISM. Metabolism *22*:1395-1402, 1973.

Nondiabetic patients with intermittent claudication (IC) due to peripheral arterial insufficiency and healthy, well trained men had similar plasma insulin and glucose responses during an oral glucose tolerance test, i.e. both manifested values well below those seen in control subjects. The low plasma insulin levels were more pronounced in those with proximal arterial stenosis compared to those with distal disease. The plasma triglyceride concentrations were lower in the former group. The normal glucose tolerance and low plasma insulin level in the IC patients and well trained men indicate enhanced insulin sensivitity in the peripheral tissues. Succinic oxidase activity as well as incorporation of glucose carbon into glycogen, lipids, and carbon dioxide were increased in muscle specimens from IC patients and well trained men. These observations indicate that adaptation of muscle metabolism is of importance for insulin sensitivity after physical training and may involve enzymatic adaptation of low oxygen tension. A similar situation applies in patients with proximal arterial stenosis with a larger mass of adapted muscle tissue showing the most pronounced increase in insulin sensitivity. The parallelism between the degree of insulin sensitivity and the quantity of adapted muscle favors the view that muscle tissue is of importance in the insulin sensitivity of the organism. C.R.S.

Like, A. A.; and Chick, W. L. (Elliott P. Joslin Res. Lab. Joslin Diabetes Foundation, and Dept. of Pathol., Peter Bent Brigham Hosp., and Harvard Med. Sch., Boston, Mass.): PANCREATIC BETA CELL REPLICATION INDUCED BY GLUCOCORTICOIDS IN SUBHUMAN PRIMATES. Am. J. Pathol. *75*:329-48, 1974.

Verbatim summary. Pancreatic islets were studied by means of light microscopy, autoradiography and electron microscopy in untreated Macaca cyclopis monkeys and after the administration of large quantities of adrenal glucocorticoids. Mild hyperglycemia and profound elevations of the serum immunoreactive insulin level were induced by glucocorticoid injections of one to three weeks' duration, with a gradual return to pretreatment levels within two months after cessation of treatment. Morphologic alterations included degranulation and hyperplasia of pancreatic beta cells. These were noted in association with increased numbers of labeled islet cells after the administration of ^{3}H-thymidine and beta cells undergoing mitotic division, and they could be correlated directly with the magnitude of serum insulin elevation. Evidence of acinar-islet or duct-islet cell transformation was absent. Beta cell regranulation and the twofold increase in extractable pancreatic insulin which followed the cessation of injections demonstrated the survival and functional integrity of the newly formed beta cells.

Rosenmann, E.; Palti, Z.; Teitelbaum, A.; and Cohen, A. M. (Diabetic Unit and Isotope Lab. for Endocr. Res., Dept. of Pathol. and Dept. of Obs./Gynec., Hadassah Univ. Hosp. and Hebrew Univ. Hadassah Med. Sch., Jerusalem, Israel): TESTICULAR DEGENERATION IN GENETICALLY SELECTED SUCROSE-FED DIABETIC RATS. Metabolism *23*:343-48, 1974.

Diabetes induced in rats by genetic selection and sucrose feeding was found to be associated with diabetic retinopathy and intercapillary glomerulosclerosis. Starch-fed siblings of these rats did not develop similar abnormalities. In the present study, testicular degeneration was observed in sucrose-fed diabetic rats. The changes consisted of atrophy of seminiferous tubules, thickening of tubular basement membrane, reduced spermatogenesis and Leydig cell hyperplasia. None of these changes were noted in the starch-fed siblings. C.R.S.