influence of other nonrelated diseases extant should also be judged on an individual basis.

It is expected that individual employers may modify these standards in order to cope with individual situations. The recommendations do not necessarily represent criteria of the American Diabetes Association for treatment of individual patients. The Committee on Employment and Insurance of the American Diabetes Association is willing to act in an advisory capacity regarding these recommended standards of employability.

ABSTRACTS

Barter, Philip J.; Nestel, Paul J.; and Carroll, Kevin F. (Dept. of Clin. Science, The John Curtin Sch. of Med. Res., The Australian National Univ., Canberra, Australia): PRECURSORS OF PLASMA TRIGLYCERIDE FATTY ACID IN HUMANS. EFFECTS OF GLUCOSE CONSUMPTION, CLOFIBRATE ADMINISTRATION, AND ALCOHOLIC FATTY LIVER. Metabolism *21*:117-24, February 1972.

The conversion of plasma FFA to plasma triglyceride fatty acid (TGFA) was examined following infusion of labeled palmitates. In healthy volunteers and patients with hypertriglyceridemia the ratio of the specific activity of VLDL TGFA to that in plasma FFA was 80 to 100 per cent. In patients with alcoholic fatty liver and subjects on clofibrate therapy the ratios were 50 per cent and 40 per cent respectively. After cessation of clofibrate the ratios returned to normal. In normal subjects prolonged glucose consumption resulted in a decrease of the ratio to 30 to 60 per cent. Simultaneous infusion of labeled glucose revealed that 80 per cent of the C-14 label appearing in plasma triglyceride was in the fatty acid moiety (TGFA). In normally fed subjects after overnite fast C-14-glucose label appeared only in the glycerol of plasma triglyceride. It appears that in healthy subjects on normal diets, plasma TGFA is derived primarily from plasma FFA. During glucose consumption hepatic lipogenesis contributes significantly to TGFA. The source of plasma TGFA in those treated with clofibrate or in patients with hepatic steatosis appears to be stored hepatic fatty acids. C.R.S.

Brown, Joseph D.; Steele, Ann A.; Stone, Daniel B.; and Steele, Forest A. (Dept. of Intern. Med., University Hosp., Iowa City, Iowa): THE EFFECT OF TOLBUTAMIDE ON LIPOLYSIS AND CYCLIC AMP CONCENTRATION IN WHITE FAT CELLS. Endocrinology 90:47-51, January 1972.

Isolated white fat cells from epididymal adipose tissue were incubated in the presence of DL-arterenol and theophylline to stimulate lipolysis. After eight minutes of incubation, the addition of tolbutamide inhibited lipolysis induced by these agents but, in contrast to insulin, it raised the concentration of cyclic AMP. Tolbutamide inhibited basal or theophylline-induced lipolysis but alone or in combination with theophylline had no effect on cyclic AMP concentrations. The finding of inhibition of lipolysis with increased intracellular cyclic AMP concentration indicates that the antilipolytic effect of tolbutamide results from inhibition of the lipolytic enzymes system activated by cyclic AMP. C.R.S.

Canfield, Robert E.; Kaye, Gordon I.; and West, Susan B. (Dept. of Med. and the F. H. Cabot Lab. of the Div. of Surg. Path., Dept. of Surg. and Path., Coll. of Physicians and Surg., Columbia Univ., New York, N.Y.): THE PREPARATION AND EVALUATION OF TRITIATED POLYALANYL INSULIN DERIVATIVES. Endocrinology 90:112-22, January 1972.

The polyalanyl insulin derivatives retain full biological activity as determined by the rat epididymal fat pad assay. Phenylisothiocyanate degradation studies were performed indicating that 87 per cent of the insulin molecules probably possess at least one added alanine. Tritiated polyalanyl insulin of high specific activity was synthesized and shown to have high biological activity by the fat pad assay. Autoradiographic studies using this insulin derivative demonstrated that the hormone is bound to sarcolemmal membranes of both striated and cardiac muscle. Tritiated polyalanyl insulin was also concentrated in the proximal tubules of the kidney but was barely detectable in the liver after intravenous injection. C.R.S.

Chevalier, M.; Wiley, J. H.; and Leveille, G. A. (Lab. of Nutritional Biochem., Dept. of Animal Sci., Univ. of Illinois at Urbana-Champaign, Urbana, Ill.): THE AGE-DEPENDENT RESPONSE OF SERUM TRIGLYCERIDES TO DIETARY FRUCTOSE. Proc. Soc. Exp. Biol. Med. *139*:220-22, January 1972.

Diets containing 70.1 per cent glucose, starch, sucrose, or fructose were fed to weanling and mature rats. Fructose or sucrose increased serum triglyceride levels in mature but not in weanling rats. J.D.G.

Chlouverakis, C. (Dept. of Med., State Univ. New York at Buffalo and E. J. Meyer Memorial Hosp., Buffalo, N.Y.): EFFECT OF CALORIC RESTRICTION ON BODY WEIGHT LOSS AND BODY FAT UTILIZATION IN OBESE HYPERGLYCEMIC MICE (obob). Metabolism *21*:10-17, January 1972.

Caloric restriction imposed upon obese-hyperglycemic mice (obob) and lean littermates resulted initially in loss of body weight which gradually diminished until the weights stabilized at a new level. The cumulative body mass loss was greater in the obese than in lean animals. The composition of body mass lost by food deprivation differed markedly between obob and lean controls, the proportion of fat being much greater in the former. These data do not support the hypothesis that impairment of fat mobilization from fat depots of calorically restricted obob mice leads to decreased rates of energy utilization by their tissues. C.R.S.

Chow, Kye-Wing; and Pond, Wilson G. (Dept. of Animal Sci., and Graduate Sch. of Nutrition, Cornell Univ., Ithaca, N.Y.).: BIOCHEMICAL AND MORPHOLOGICAL ASPECTS OF MITOCHONDRIAL SWELLING IN AMMONIA TOXICITY. Proc. Soc. Exp. Biol. Med. *139*:150-56, January 1972.

Molecular aspects of ammonia intoxication were studied with rat liver mitochondria swelling spontaneously in buffered iso-

tonic sucrose solution containing 45-Ca label. Small concentrations of NH_4Cl added to swelling media markedly decreased labeling of mitochondria. Decreased labeling was due to increased efflux of label. Ammonia also increased loss of intramitochondrial magnesium and phosphate. Ammonium, phosphate and magnesium reduced 45-Ca labeling of swelling mitochondria. When all three ions were present, reduction in labeling was not additive. A crystalline material was isolated from supernatant of mitochondria swelling in medium containing Mg, PO_4 and NH_4 ions. The material was identified as magnesium ammonium phosphate. Electron micrographs of hyperammonemic rat liver revealed radical changes to fine structure of liver cell. Mitochondria were swollen with considerable loss of matrix. Disorganization of endoplasmic reticulum was apparent. Effect of ammonia on respiring mitochondria may not only be substrate and cofactor depletion but may also be due to change in membrane structure through magnesium loss. J.D.G.

Cremer, Guillermo M.; Molnar, George D.; Taylor, William F.; Moxness, Karen E.; Service, F. John; Gatewood, Laël C.; Ackerman, Eugene; and Rosevear, John W. (Mayo Clin. and Mayo Foundation, Rochester, Minn., and Univ. of Minnesota, Minneapolis, Minn.): STUDIES OF DIABETIC INSTABILITY. II. TESTS OF INSULINOGENIC RESERVE WITH INFUSIONS OF ARGININE, GLUCAGON, EPINEPHRINE, AND SALINE. Metabolism 20:1083-98, December 1971.

Insulinogenic reserve was tested with arginine, glucagon and epinephrine in unstable and stable diabetics as well as control subjects by determining plasma IRI concentrations before and after administration of test substances and saline. The changes observed in IRI concentration were correlated with changes in blood glucose, serum FFA and ketone body concentrations. No significant blood glucose fluctuations occurred in any subject during the saline test while fasting. During ambulatory-fed conditions the blood glucose and ketone bodies in unstable diabetics rose steadily while receiving saline in contrast to stable diabetics and normals where they remained unchanged. A correlation was observed between insulin secretory ability under resting-fasting conditions and blood glucose regulatory stability during ambulatory-resting conditions. Unstable diabetics had no demonstrable insulinogenic reserve, except for one maturity-onset patient. Stable diabetics had demonstrable insulinogenic reserve but less than that of normals. C.R.S.

Fain, John N.; Rosenthal, Judith W.; and Ward, Walter F. (Div. of Biological and Med. Sciences, Brown Univ., Providence, R.I.): ANTI-LIPOLYTIC ACTION OF TOLBUTAMIDE ON BROWN FAT CELLS. Endocrinology 90:52-59, January 1972.

Lipolytic effects of epinephrine, theophylline and dibutyryl cyclic AMP were blocked in isolated brown fat cells from rats by the addition of tolbutamide. In the presence of epinephrine, tolbutamide enhanced cyclic AMP accumulation but inhibited lipolysis. The addition of theophylline to incubates containing a concentration of epinephrine sufficient to activate lipolysis without cyclic AMP rises resulted in marked rise in cyclic AMP without inducing further lipolysis. Tolbutamide had no significant effect on phosphodiesterase in brown fat cell homogenates. The inhibition of the lipolytic effect of dibutyryl cyclic AMP by tolbutamide and its ability to increase cyclic AMP accumulation under conditions of inhibition of lipolysis suggest that it affects the intracellular systems involved in the actions of cyclic AMP. C.R.S.

Fredholm, Bertil B. (Dept. of Pharmacol., Karolinska Inst., Stockholm, Sweden): INHIBITION BY β-HYDROXYBUTYRATE OF LIPOLYSIS INDUCED BY SYMPATHETIC NERVE ACTIVITY IN CANINE SUBCUTANEOUS ADIPOSE TISSUE IN SITU. Metabolism 21:125-31, February 1972.

Beta-hydroxybutyrate infused intra-arterially was found to increase glucose uptake by subcutaneous fat tissue while decreasing basal FFA release despite unchanged mobilization of glycerol. The mobilization of FFA and glycerol induced by nerve stimulation was inhibited significantly by β-hydroxybutyrate although there was no antagonism of the vasoconstrictor effect of nerve stimulation. The results indicated that β-hydroxybutyrate in concentrations such as occur with fasting inhibited activation of lipolysis by nerve stimulation but has little effect on basal lipolysis. C.R.S.

Furner, R. L.; Neville, E. D.; Talarico, K. S.; and Feller, D. D. (Environmental Biology Div., Ames Res. Center, NASA, Moffett Field, Calif.): EFFECTS OF PENTOBARBITAL ON PLASMA GLUCOSE AND FREE FATTY ACIDS IN THE RAT. Proc. Soc. Exp. Biol. Med. 139:231-34, January 1972.

Hyperglycemia and hypolipemia were observed in rats after injection of sodium pentobarbital. Changes were independent of whether blood was collected by decapitation or by needle puncture of aorta. Hyperglycemic response was caused by stress of injection, per se, and pharmacological action of the drug. Hyperlipemia was observed at five minutes postinjection; however, plasma free fatty acids decreased by fifteen minutes postinjection. Both hyperglycemia and hypolipemia responses were dose dependent. J.D.G.

Ghilchik, Margaret W.; and Morris, A. S. (Surg. Unit, St. Mary's Hosp., London, England): ABNORMAL INSULIN RESPONSE IN PATIENTS WITH SMALL-VESSEL DISEASE. Lancet 2:1227-29, Dec. 4, 1971.

It has been hypothesized that one of the factors causing atherogenesis is an increased insulin response to glucose which stimulates lipogenesis and raises serum lipid concentrations. In this study twenty-five patients having peripheral vascular disease involving small vessels and presenting with gangrene, pre-gangrene of the toes, or rest-pain but normal foot pulses were examined. The subjects were tested by observing their immunoreactive insulin response to an oral 50 gm. glucose load. The tolerance to glucose of these individuals was normal but surprisingly their serum insulin response was subnormal. While normal subjects showed peak serum insulin responses which averaged six times basal insulin levels, nine of the patients with small-vessel disease had no increase in insulin and six had peak insulins which were less than three times basal. The hyporesponsiveness was studied in addition when eight small-vessel disease patients were given 1 gm. of tolbutamide intravenously. In the group, blood glucose fell from 0 to 45 per cent at twenty minutes and 10 to 60 per cent at thirty minutes compared to control patients whose glucose fell from 58 to 65 per cent at twenty minutes and 60 to 90 per cent at thirty minutes. The authors postulate that the small-vessel disease patients lack an ability to release insulin in a pulsatile fashion in response to the normal stimulus of a glucose load. This deficiency could result in deficient uptake of nutrients by small vessels which lack vasa vasorum and could suffer a relative insulin insufficiency. T.G.S.

Ghilchik, Margaret W.; and Morris, A. S. (Surg. Unit, St. Mary's Hospital, London, England): INSULIN RESPONSE TO GLUCOSE IN PATIENTS WITH PERIPHERAL VASCULAR

DISEASE, ARTERITIS, AND RAYNAUD'S PHENOMENON. Lancet 2:1229-31, Dec. 4, 1971.

In a previous study the authors found that nondiabetic patients with peripheral small-vessel disease either did not secrete insulin or secreted less insulin in response to a glucose load than did control subjects. In this study they compared insulin responses to glucose in twenty-three patients with peripheral vascular disease who had atheromatous occlusion of large vessels, four patients with Takayasu's or other arteritis and twenty patients with Raynaud's phenomenon. Of the twenty-three atherosclerotic patients, 40 per cent had normal glucose tolerance and normal insulin responses; 35 per cent had "prediabetic" glucose tolerance and higher than average peak insulin levels; 25 per cent had normal glucose tolerance curves with "flat insulin responses." Three of the four patients with arteritis had normal OGTT and one had a diabetic OGTT. The twenty patients with Raynaud's phenomenon had normal glucose tolerance curves and normal basal insulin levels and after glucose six had peak insulin values which exceeded normal. This study failed to confirm the high and late insulin secretion reported by other workers in studies of patients with peripheral vascular disease and challenges the concept that excessive insulin secretion may be a causative factor in atheroma formation. T.G.S.

Heird, William C.; Driscoll, John M., Jr.; Schullinger, John N.; Grebin, Burton; and Winters, Robert W. (Depts. of Pediat. and Surg., Columbia Univ., Coll. of Physicians and Surg.; and Babies Hosp., Columbia-Presbyterian Med. Center, New York, N.Y.): INTRAVENOUS ALIMENTATION IN PEDIATRIC PATIENTS. J. Pediatr. 80:351-72, March 1972.

The authors present a useful, comprehensive review of the theory, technics, results and complications of intravenous hyperalimentation in children. It is pointed out that some infants, especially prematures, tolerate the large glucose loads poorly. Plasma hyperosmolality due to hyperglycemia is the most common complication and careful monitoring of blood glucose, with administration of insulin if necessary, is essential. P.S.R.

Hellman, Bo; Sehlin, Janove; and Täljedal, Inge-Bert (Dept. of Histology, Univ. of Umeå, Umeå, Sweden): CALCIUM UPTAKE BY PANCREATIC β-CELLS AS MEASURED WITH THE AID OF CA-45 AND MANNITOL-H-3. Am. J. Physiol. 221:1795-1801, December 1971.

Role of calcium in insulin release was studied by incubating islets of obese hyperglycemic mice with Ca-45. Glucose stimulated Ca-45 uptake but had no effect on steady-state level. Glucose also made β-cells retain increased amounts of Ca-45 during washing. Other insulin secretagogues failed to enhance initial Ca-45 uptake. Uptake was stimulated by diazoxide and by removal of sodium from medium. Excess sodium or potassium as well as potassium deficiency inhibited uptake. Insulin release may be associated with allocation of calcium to less mobile compartments of the β-cell. J.D.G.

Jordan, Scott W.; and Perley, Michael J. (Dept. of Path., Univ. of New Mexico Sch. of Med., Albuquerque, N. Mex.): MICROANGIOPATHY IN DIABETES MELLITUS AND AGING. Arch. Pathol. 93:261-65, March 1972.

Verbatim summary. Measurements of basement membrane thickness (BMT) in skeletal muscle biopsies, done without knowledge of clinical features, are presented for fifty patients. Most diabetics aged forty or older showed capillary basement thickening, while this change was rarely present below age forty. There was significant difference between mean BMT of diabetics forty years old or older and those under age forty ($P < .005$). However, many nondiabetic patients over age forty showed similar thickening. The difference between average BMT in diabetics over forty years old and nondiabetic patients was statistically significant ($P < .01$). However, because of the marked individual variation, BMT measurement does not appear to be useful as a tool for diagnosing diabetes in a specific patient. Additional investigation is needed to further evaluate the relationship of BMT and disability in both diabetic and nondiabetic patients.

Kabara, J. J.; Chapman, Betty B.; and Borin, Bruce M. (Mich. State Univ., Coll. of Osteopathic Med., Pontiac, Mich.; Wayne State Univ., Coll. of Med., Detroit, Mich.; and Univ. of Detroit, Detroit, Mich.): EFFECT OF HYPOCHOLESTEREMIC DRUGS ON TUMOR-BEARING MICE. Proc. Soc. Exp. Biol. Med. 139:100-04, January 1972.

Hypocholesteremic drugs (methylphenidate, clofibrate and 20, 25-diazacholesterol) lower the mean life span of tumor-bearing animals. A similar drug (AY9944) did not have a significant effect. The drug, Elipten, produced an opposite effect (mean life span was significantly increased). J.D.G.

Louis, Laurence H.; and Conn, Jerome W. (Dept. of Intern. Med., Div. of Endocr. and Metabolism, and the Metabolism Res. Unit, Univ. of Michigan Med. Sch., Ann Arbor, Mich.): DIABETOGENIC POLYPEPTIDE FROM HUMAN PITUITARIES SIMILAR TO THAT EXCRETED BY PROTEINURIC DIABETIC PATIENTS. Metabolism 21:1-9, January 1972.

A procedure described previously for the isolation of a polypeptide from hypophyses of several animal species was modified to achieve isolation of a similar polypeptide with anti-insulin and diabetogenic properties from human pituitary glands. The isoelectric point of the compound was the same as that of the compound isolated from animal adenohypophyses, from the urine of patients with lipoatrophic diabetes and proteinuric diabetics without lipoatrophy. Administration of the polypeptide to dogs resulted in intolerance to glucose and resistance to exogenous insulin. Glucose tolerance tests in the same animals showed a greater diabetogenic potential following administration of the polypeptide than following human growth hormone or ovine prolactin. The molecular weight of the material determined by gel electrophoresis is 20,600 and a modified procedure for its isolation has been outlined. C.R.S.

Marco, J.; Baroja, I. M.; Diaz-Fierros, M.; Villanueva, M. L.; and Valverde, I. (Clinica Puerta de Hierro and Fundacion Jimenez-Diaz, Universidad Autonoma de Madrid, Madrid, Spain): RELATIONSHIP BETWEEN INSULIN AND GUT GLUCAGON-LIKE IMMUNOREACTIVITY AND GASTRECTOMIZED SUBJECTS. J. Clin. Endocrinol. Metab. 34:188-91, January 1972.

Since there exists in the gut a material with glucagon-like immunoreactivity (GLI) which is released during glucose absorption, it was thought that it could have an insulin-releasing activity, as does glucagon, and therefore be a component of the enteroinsular axis.

In order to study the relationship between insulin and GLI secretion, the authors studied both of these responses to an oral glucose load in a series of eighteen normal subjects and in another of eight gastrectomized patients.

It was found that in normal subjects, after oral glucose,

plasma GLI increased slightly but consistently from 1.5 ng./ml. to 2.3 ng./ml. In the gastrectomized patients, plasma GLI rose more intensively, from 1.7 ng./ml. to 5.8 ng./ml. However, in these patients, in spite of the higher blood sugar values and the higher plasma GLI levels during the OGTT, the insulin response was practically identical to that of normal subjects during the first hour of the test. It was significantly higher at only one point (seventy-five minutes). This relatively lower insulin response, when compared to the elevation of the glycemia, is compatible with a deterioration of the gastroenteroinsular axis caused by the gastrectomy. The fact that GLI hypersecretion is not accompanied by a greater insulin response, even in the presence of hyperglycemia, seems to indicate that GLI is not a major intestinal insulin-releasing factor, if indeed it has any such activity. T.J.M.

Orci, L.; Gabbay, K. H.; and Malaisse, W. J. (Inst. of Histology and Clin. Biochem., Univ. of Geneva, Geneva, Switzerland; and Joslin Res. Lab., Harvard Med. Sch., Boston, Mass.; Children's Hosp. Med. Center, Boston, Mass.; Lab. of Exp. Med., Univ. of Brussels, Brussels, Belgium): PANCREATIC BETA-CELL WEB: ITS POSSIBLE ROLE IN INSULIN SECRETION. Science 175:1128-30, Mar. 10, 1972.

A cortical band of fine microfilaments is consistently observed in beta cells of rat pancreas. Alteration of this web by cytochalasin B is associated with enhanced glucose-induced secretion of insulin by isolated islets. This web may play an important role in emiocytosis of insulin secretory granules, by controlling their access to cell membrane. J.D.G.

Pannbacker, R. G.; Fleischman, D. E.; and Reed, D. W. (Charles F. Kettering Res. Lab., Yellow Springs, Ohio): CYCLIC NUCLEOTIDE PHOSPHODIESTERASE: HIGH ACTIVITY IN A MAMMALIAN PHOTORECEPTOR. Science 175:757-58, Feb. 18, 1972.

Purified outer segments of bovine rods exhibit phosphodiesterase activity against cyclic AMP and cyclic GMP, hydrolyzing cyclic GMP more rapidly than cyclic AMP at low substrate concentrations. High phosphodiesterase activity in this specialized organelle suggests this enzyme functions in control of cyclic nucleotide concentration during visual excitation or adaptation. J.D.G.

Passa, P.; Gourgon, R.; Motte, G.; Lorente, P.; Maria, J.; and and Canivet, J. (Paris, France): PHEOCHROMOCYTOMA WITH INSULIN-DEPENDENT DIABETES REVEALED BY ACUTE CIRCULATORY FAILURE. Nouv. Presse Med. 1:245-48, January 22, 1972.

The authors report a case of pheochromocytoma in a forty-one year old woman in whom acute cardiovascular failure was followed by hyperglycemia and ketoacidosis. Diabetic control was achieved with 20 U. of Lente insulin. The diabetes disappeared after surgical removal of a 7 X 9 cm. tumor from the left adrenal gland. The present theories on the pathogenesis of glucose intolerance in patients with catecholamine secreting tumors are discussed. G.B.

Redetzki, H. M.; Hughes, J. R.; and Redetzki, J. E. (Dept. of Pharmacol., La. State Univ. Sch. of Med. in Shreveport; and V.A. Hosp., Shreveport, La.): DIFFERENCES BETWEEN SERUM AND PLASMA OSMOLALITIES AND THEIR RELATIONSHIP TO LACTIC ACID VALUES. Proc. Soc. Exp. Biol. Med. 139: 315-18, January 1972.

Significant increases in osmolality can be observed when blood samples are allowed to remain from one to four hours at room temperature before serum is separated from corpuscular elements. The increase is related to production of lactic acid caused by persistent glycolytic activity of erythrocytes and leukocytes. Error can be reduced by immediate cooling of samples or by using plasma separated from blood cells within twenty minutes after collection. J.D.G.

Research Committee of the Scottish Society of Physicians. ISCHAEMIC HEART DISEASE: A SECONDARY PREVENTION TRIAL USING CLOFIBRATE. Brit. Med. J. 4:775-84, Dec. 25, 1971.

This important collaborative study was designed as a secondary prevention trial in patients with pre-existing ischemic heart disease. Men (593) and women (124), aged forty to sixty-nine years with angina pectoris and/or recent myocardial infarction were randomized into two groups receiving either clofibrate (350) or placebo (367). Diabetics were excluded from this study. Withdrawal rates were low and evenly balanced from both groups. After forty-eight months there was a striking reduction (62 per cent) in the mortality of clofibrate-treated patients with angina pectoris. However, the beneficial effect of clofibrate on patients with myocardial infarction was not seen, perhaps due to the unusually low mortality in the placebo group. The only serum lipid analyzed at regular intervals was cholesterol and neither initial levels nor response to drug were significantly related to the incidence of cardiac events.

These over-all findings are even more encouraging when evaluated together with the companion study from England reported in the same issue of this journal. P.H.S.

Song, Sun K.; and Rubin, Emanuel (Dept. of Path., Mount Sinai Sch. of Med., New York, N.Y.): ETHANOL PRODUCES MUSCLE DAMAGE IN HUMAN VOLUNTEERS. Science 175: 327-38, Jan. 21, 1972.

Ethanol (42 per cent of total calories) for twenty-eight days increased serum creatine phosphokinase activity and produced ultra-structural changes in skeletal muscle of human volunteers. Data suggest myopathy results from ethanol toxicity rather than nutritional or other factors. J.D.G.

York, David A.; Steinke, Jurgen; and Bray, George A. (Depts. of Med., New England Med. Center Hosp.; Tufts Univ. Sch. of Med., Elliott P. Joslin Res. Labs., and Harvard Med. Sch., Boston, Mass.; and the Dept. of Med., UCLA Sch. of Med., Los Angeles, Calif.; and Harbor Gen. Hosp., Torrance, Calif.): HYPERINSULINEMIA AND INSULIN RESISTANCE IN GENETICALLY OBESE RATS. Metabolism 21:277-84, April 1972.

Serum immunoreactive insulin (IRI) was elevated in genetically obese rats and in rats with obesity following electrolytic lesions placed in hypothalamic ventromedial regions. The administration of exogenous insulin to these two groups of obese rats revealed that lesioned animals retained normal sensitivity to insulin with prompt falls in glucose and FFA while genetically obese rats displayed only a slight hypoglycemic effect with rise in FFA. A characteristic hypertrophy of the pancreatic beta cells was seen in both groups of obese animals. Thus, obesity in both groups of rats is accompanied by increased circulating IRI, higher concentrations of FFA, and hypertrophy of islet tissue, suggesting both increased insulin synthesis and slight resistance to endogenous insulin. Whether hyperinsulinemia is the cause or the result of obesity remains undetermined although it is suggested that, with increased insulin synthesis in lesioned animals, the degree of obesity depends upon the circulating insulin levels. C.R.S.