

# ABSTRACTS

*Andersen, O. Orved* (Steno Memorial Hosp., Gentofte, Denmark): INSULIN ANTIBODY FORMATION: I. THE INFLUENCE OF AGE, SEX, INFECTIONS, INSULIN DOSAGE AND REGULATION OF DIABETES. *Acta Endocr.* 71:126-40, September 1972.

Plasma concentrations of insulin antibodies were determined in fifty-one patients with diabetes mellitus, who were being treated with daily injections of 4-68 (mean 28) units of crystalline suspension of porcine Protamine insulin. In a group of seventeen patients, the antibody concentrations were determined before and at frequent intervals after the initiation of insulin therapy. In 76 per cent of these patients, antibodies were detected one to three months after the beginning of treatment. The concentration of antibodies attained a maximal level four to nine months after the onset of treatment and remained at that level during the period of observation of up to three years. The antibody concentrations were similar among both sexes; patients less than twenty-five years of age had higher concentrations. A direct correlation was observed between the antibody concentration and the dosage of insulin corrected for body weight. The adequacy of the control of diabetes did not appear to be related to the antibody levels. Intercurrent infections did not influence the antibody concentrations. S.P.

*Atkinson, J. N. C.; and Randle, P. J.* (Dept. of Biochem., Univ. of Bristol, Bristol, England): AN ABNORMALITY OF ADRENALINE, PHENTOLAMINE STIMULATED LIPOLYSIS IN ADIPOSE TISSUE FROM OBESE, MATURITY-ONSET DIABETICS. *Diabetologia* 8:371-76, December, 1972.

*Verbatim summary.* Abnormalities of fat metabolism from in vitro and in vivo experiments have elsewhere been described in both diabetes and obesity. In these studies adrenaline (100  $\mu$ M.) and phentolamine (100  $\mu$ g. per milliliter) stimulated glycerol release has been compared in adipose tissue from groups of nondiabetic, nonobese, diabetic and obese subjects. Adipose tissue from obese diabetics showed a highly significant ( $p < 0.001$ ) diminution in stimulated lipolysis when compared with nondiabetic, nonobese adipose tissue. The conditions of obesity and diabetes are required to be present simultaneously to maintain this difference in lipolysis. Diabetes or obesity per se are responsible for only marginally significant differences in stimulated glycerol release. The possible reasons for this defect in lipolysis in obese elderly diabetics, pertaining to fat cell receptors, the adenylyl cyclase system and the hormone sensitive lipase, have been discussed.

*Block, Marshall B.; Mako, Mary E.; Steiner, Donald F.; and Rubenstein, Arthur H.* (Depts. of Med. and Biochem., Pritzker Sch. of Med., Univ. of Chicago, Chicago, Ill.): DIABETIC KETOACIDOSIS: EVIDENCE FOR C-PEPTIDE AND PROINSULIN SECRETION FOLLOWING RECOVERY. *J. Clin. Endocrinol. Metab.* 35:402-06, September 1972.

During episodes of ketoacidosis, seven diabetics had very low or unmeasurable circulating insulin, proinsulin, and C-peptide levels. Two to twenty weeks later, while still receiving insulin therapy, all patients had evidence of beta cell secretory activity as assessed by C-peptide immunoreactivity

(CPR). Subsequently, three patients were managed by diet alone, while the dosage of insulin was substantially reduced for two. The authors conclude that the occurrence of ketoacidosis does not necessarily indicate irreversible beta cell failure. Possible reasons for temporary cessation and recovery of beta cell secretory function in these cases are discussed, but no evidence is cited to substantiate the various mechanisms considered. T.J.M.

*Bottger, Ingolf; Faloona, Gerald R.; and Unger, Roger H.* (Dept. of Int. Med., Univ. of Texas Southwestern Med. Sch. at Dallas; and V.A. Hosp., Dallas, Tex.): THE EFFECT OF CALCIUM AND OTHER SALTS UPON THE RELEASE OF GLUCAGON-LIKE IMMUNOREACTIVITY FROM THE GUT. *J. Clin. Invest.* 51:831-36, April 1972.

A calcium-lowering effect of the gut glucagon-like immunoreactive material (GGLI) has been suggested. The effect of calcium absorption upon caval venous plasma levels of GGLI was investigated in dogs. A large intraduodenal dose of calcium chloride or calcium lactate resulted in significant increases in plasma GGLI (as measured using an antiglucagon serum which strongly cross-reacts with GGLI); levels of pancreatic glucagon, insulin, or glucose did not change. Intraduodenal administration of magnesium chloride or sodium chloride was associated with a significant though modest increase in GGLI. When GGLI release was induced by intraduodenally administered glucose, plasma calcium decreased by only 9 per cent. These experiments do not define the physiologic significance of the increases in plasma GGLI induced by the absorption of calcium salts. However, a possible role of the GGLI as a regulator of the electrolyte homeostasis should be considered. S.P.

*Burghen, George A.; Kitabchi, Abbas E.; and Brush, James S.* (Labs. of Endocr. and Metabolism Res. Serv., V.A. Hosp., and Depts. of Biochem., Pediat. and Med., Univ. of Tennessee, Memphis, Tenn.): CHARACTERIZATION OF A RAT LIVER PROTEASE WITH SPECIFICITY FOR INSULIN. *Endocrinology* 91: 633-42, September 1972

A soluble hepatic enzyme isolated from the supernatant of rat liver possesses 96 per cent of the total insulin degrading activity in fractionated liver homogenates. The remaining 4 per cent is located in the debris, mitochondrial and microsomal fractions. The enzyme, estimated to have a molecular weight of 80,000, was shown to be proteolytic with optimal activity at pH 7.6 and was independent of glutathione (GSH) for enzymatic activity. Its specificity for insulin is indicated by a rate of insulin destruction fifteenfold greater than for proinsulin. Other proteolytic hormones showed no specificity for insulin degradation over proinsulin. Human growth hormone was not degraded by the purified enzyme. Data are presented to support the concept that a sulfhydryl group in the enzyme molecule is necessary for its activity. Tolbutamide and phenformin were found to inhibit the enzyme by noncompetitive inhibition. These studies demonstrate the presence in the liver of an insulin protease which may represent the major route of insulin catabolism in the body. C.R.S.

Caspary, W. F.; Rhein, A. M.; and Creutzfeldt, W. (Div. of Gastroenterol. and Metab., Depart. Med. Univ. of Goettingen, GFR): INCREASE OF INTESTINAL BRUSH BORDER HYDROLASES IN MUCOSA OF STREPTOZOTOCIN-DIABETIC RATS. *Diabetologia* 8:412-14, December 1972.

*Verbatim summary.* Experimental diabetes mellitus in rats was induced by streptozotocin. Five days after administration of streptozotocin intestinal brush border hydrolases (maltase, sucrase, trehalase, lactase) and alkaline phosphatase were markedly elevated at all levels of the small intestine as measured in the total homogenate and in the isolated brush border preparation. Insulin treatment beginning fifteen hours after administration of streptozotocin was able to decrease the increased disaccharidase activity due to streptozotocin diabetes. In experimental diabetes mellitus of rats transport as well as digestive functions of the intestinal mucosa are stimulated.

Deconinck, J. F.; Van Assche, F. A.; Potwielge, P. R., and Gepts, W. (Dept. of Pathol., Brugmann Univ. Hosp. and Queen Elisabeth Foundation, Vrije Universiteit Brussel, Brussels, and Dept. of Obster. and Gynec., Sint Rafael's Hosp., Katholieke Universiteit Leuven, Louvain, Belgium): THE ULTRASTRUCTURE OF THE HUMAN PANCREATIC ISLETS. II. THE ISLETS OF NEONATES. *Diabetologia* 8:326-33, November 1972.

*Verbatim summary.* The ultrastructure of the islets of Langerhans was studied in seven human neonates. Out of the five cell types described by the same authors in the islets of adults, four were also found in the islets of neonates: B cells, A cells, type III cells and type IV cells. Type III cells were far more numerous in the newborn in contrast with type V cells which were not found. In comparison with the islets of adults those of neonates showed a considerably higher number of pale granules in the B cells and a complete absence of fat vacuoles in all four cell types.

Evans, Nigel; Robinson, V. P.; and Lister, J. (Wexham Park Hosp., Slough; King Edward VII Hosp., Windsor, England; and St. Mary's Hospital, London, England): GROWTH AND BONE AGE OF JUVENILE DIABETICS. *Arch. Dis. Child.* 47: 589-93, August 1972.

*Verbatim summary.* The growth of a group of juvenile diabetics on restricted carbohydrate diets has been studied using standardized technics. Most patients were distributed between the tenth and ninetieth percentiles for height, weight, age, and subscapular skinfold thickness. There was, however, a statistically significant tendency for females to be above average in weight and for both sexes to have thicker than normal skinfolds. A duration of diabetes of over six years led to significant underheight in boys and girls in the presence of normally distributed bone ages. Boys who had diabetes for less than six years were found to have advanced bone ages.

Frenkel, G.; Kraicer, P. F.; and Shani, J. (Dept. of Zool., Tel-Aviv Univ., and Dept. of Appl. Pharmacol., Sch. of Pharmacy, Hebrew Univ., Jerusalem, Israel): DIABETES IN THE SAND-RAT: DIABETOGENESIS, RESPONSES TO MANNOHEPTULOSE AND ATRIPLEX ASH. *Diabetologia* 8:313-18, November 1972.

*Verbatim summary.* Diabetes was induced in sand rats by increasing the dietary intake of calories. The development of diabetes was followed by progressively greater hyperglycemic levels in the glucose tolerance test and the appearance of cataract, glucosuria and obesity. Ketonuria was never seen. Diabetic sand rats had a slightly elevated BMR and an RQ

of approximately 1. They responded to D-mannoheptulose with hyperglycemia but not with reduced RQ. *Atriplex halimus* ash did not reduce the hyperglycemic response to glucose, though it has been reported to do so in alloxanized rats. Alloxanized rats were shown to retain responsiveness to D-mannoheptulose and it is speculated that response to D-mannoheptulose may be dependent on secretion of glucagon.

Frohman, Lawrence A.; Goldman, Jack K.; and Bernardis, Lee L. (Depts. of Med. and Path., State Univ. of New York at Buffalo, and V.A. Hosp., Buffalo, N.Y.): METABOLISM OF INTRAVENOUSLY INJECTED 14-C-GLUCOSE IN WEANLING RATS WITH HYPOTHALAMIC OBESITY. *Metabolism* 21:799-805, September 1972.

Removal of labeled glucose from plasma was more than twice as rapid in VMN rats as in control rats despite comparable glucose levels. Incorporation of the labeled glucose into lipid was augmented in liver, diaphragm and epididymal fat tissue in the VMN rats due to an increase in the rates of fatty acid synthesis. Incorporation of label into glycogen by VMN rats was enhanced in adipose tissue but unaltered in muscle and liver. These results indicate that weanling VMN rats exhibit increased glucose utilization in vivo directed primarily toward lipogenesis, not only in adipose tissue but in muscle and liver as well. C.R.S.

Gates, Ronald J.; Hunt, M. I.; Smith, R.; and Lazarus, Norman R. (Diabetes Res. Unit, Wellcome Foundation, Dartford, Kent, England): RETURN TO NORMAL OF BLOOD-GLUCOSE, PLASMA-INSULIN, AND WEIGHT GAIN IN NEW ZEALAND OBESE MICE AFTER IMPLANTATION OF ISLETS OF LANGERHANS. *Lancet* 2:567-70, September 16, 1972.

New Zealand obese mice (NZO) have a genetic lesion which is characterized by hyperglycemia, hyperinsulinemia, and obesity. In 1970 Strautz reported that when obese mice (obob) were implanted with islets isolated from their lean litter mates, their weight gain, blood glucose, and plasma insulin returned to normal. In this study a similar procedure was carried out in NZO mice. At age five to eight weeks NZO mice were implanted with about 200 islets obtained from either normal mice or NZO mice using a millipore chamber. Serial observations were made of weight and insulin and glucose response to oral glucose. The results showed that NZO mice implanted with normal islets gained significantly less weight than those given no islets or NZO islets. The blood glucose, oral glucose tolerance, and plasma insulin values in NZO mice given normal islets changed toward normal. The authors conclude that the defect responsible for obesity, hyperglycemia, and hyperinsulinemia in NZO mice is due to a lesion in the islets. They report that studies are in progress to determine if an islet cell factor may influence the binding of insulin to cell membranes. T.G.S.

Hadfield, M. Gary; Vennart, George P.; and Rosenblum, William I. (Dept. of Path., Med. Coll. of Virginia, Richmond, Va.): HYPOGLYCEMIA: INVASION OF THE HYPOTHALAMUS BY LYMPHOSARCOMA. *Arch. Path.* 94:317-21, October 1972.

*Verbatim summary.* Hypoglycemia was accompanied by lymphosarcoma that had metastasized to the ventral and medial portions of the hypothalamus and to the brain tissue dorsal to the hypothalamus. The affected brain areas are known, from animal experiments, to participate in the control of peripheral glucose levels. In part, this control appears to be mediated by alterations in insulin levels. Thus, in rats, ablation of the ventro-

median nucleus of the hypothalamus or of the adjacent nerve tracts, may result in hyperinsulinemia. After careful consideration of alternate possibilities, the present case appears best interpreted as an "experiment of nature" which confirms, in man, the existence of hypothalamic centers and of efferent pathways from the hypothalamus, which control peripheral glucose or insulin levels or both. We are unaware of any previous report in man of hypoglycemia associated with ventromedial hypothalamic lesions or with lesions in efferent pathways from the hypothalamus.

*Karp, M.; Brown, M.; and Laron, Z.* (Pediat. Metab. and Endocrine Service, Rogoff-Wellcome Med. Res. Inst., Beilinson Hosp., Petah Tiqva, and Dept. of Statistics, Tel Aviv Univ., Israel): A CONTRIBUTION TO THE INTERPRETATION OF THE ORAL GLUCOSE TOLERANCE (OGTT). *Diabetologia* 8:381-84, December 1972.

*Verbatim summary.* An oral glucose tolerance test was performed in ninety subjects aged eight to twenty years. Fifty subjects were normal controls. Twenty subjects had juvenile diabetes. These subjects were subdivided into two subgroups according to their insulin response: A group of ten patients with no insulin response who subsequently required insulin treatment, and another group of ten patients with delayed insulin response who subsequently were treated with diet and/or oral hypoglycemic agents. Twenty subjects were obese, ten of whom had normal glucose tolerance and ten had glucose intolerance. It was found that the area under the glucose curve as calculated by fitting a quadratic function to the recorded values can discriminate between the glucose intolerance of the four groups of patients as compared to the normal controls. As to the insulin response, it was found that the area under the insulin curve is not sufficient to express the delayed insulin response found in the juvenile diabetics who subsequently did not need treatment with insulin.

*Mabry, C. Charlton; and Hollingsworth, Dorothy R.* (Depts. of Pediat. and Path. Univ. of Kentucky, Lexington, Ky.): FAILURE OF HYPOPHYSECTOMY IN GENERALIZED LIPODYSTROPHY. *J. Pediat.* 81:990-92, November 1972.

Pituitary irradiation has been reported to be beneficial in patients with generalized lipodystrophy. Surgical hypophysectomy was performed on a thirteen year old girl with progressive disfiguring generalized lipodystrophy. Improvement was noted after surgery in that the liver became smaller, skin pigmentation decreased, and sensitivity to insulin increased. By twelve months after surgery, her condition had worsened and was comparable to that prior to hypophysectomy. It is suggested on the basis of this single case that hypophysectomy does not seem promising for patients with generalized lipodystrophy. P.S.R.

*Pekar, Allen H.; and Frank, Bruce H.* (Lilly Res. Lab., Indianapolis, Ind.): CONFORMATION OF PROINSULIN. A COMPARISON OF INSULIN AND PROINSULIN SELF-ASSOCIATION AT NEUTRAL PH. *Biochemistry* 11:4013-16, October 24, 1972.

*Verbatim summary.* The self-association of porcine insulin and proinsulin at pH 7.00 and 24.5° has been studied using sedimentation equilibrium technics. We found that the apparent weight-average molecular weight of insulin in solution was less than 11,550 at a protein concentration of about 0.17 mg. per milliliter. This finding indicates that the aggregates of insulin are in equilibrium with the 5,775 molecular weight

monomer of insulin. The molecular weight data can be fit with a model involving monomers, dimers, hexamers, and polymers of the hexamer units. Calculations based on the equilibrium constant for dimer formation show that the mole ratio of monomer to dimer would be about 800,000 to 1 at physiologic concentrations (about 0.1 ng. per milliliter of serum). We found the self-association of proinsulin to be essentially identical to that of insulin. This suggests that the same sites of association are involved for both proinsulin and insulin, and that the connecting peptide does not interfere with the process of self-association. These data are also consistent with the earlier proposal that the insulin moiety of proinsulin exists in the same conformation as does insulin itself.

*Quabbe, Hans-Jurgen; Bratzke, Hans-Jurgen; Siegers, Ulrike; and Elban, Kadip* (Med. Clin. and Policlinic, Klinikum Steglitz, Free Univ., Berlin, Germany): STUDIES ON THE RELATIONSHIP BETWEEN PLASMA FREE FATTY ACIDS AND GROWTH HORMONE SECRETION IN MAN. *J. Clin. Invest.* 51:2388-98, September 1972.

The influence of plasma levels of free fatty acids (FFA) upon the release of human growth hormone (HGH) was investigated in healthy subjects. Decreases in plasma FFA evoked by intravenous infusion of nicotinic acid resulted in significant increases in plasma HGH, which occurred approximately two hours after the beginning of the infusion. Hyperglycemia induced by infusion of dextrose failed to modify these increases in plasma HGH. When the reduction in plasma FFA resulting from administered nicotinic acid was reversed by infusion of a lipid emulsion together with heparin shortly before the expected rise in plasma HGH, the increase failed to occur. Plasma HGH augmentations occurring with insulin-induced hypoglycemia were attenuated when plasma FFA had been raised by infusion of the lipid-heparin mixture or of norepinephrine. These findings suggest the presence of a negative-feedback relationship between plasma levels of FFA and HGH release. Despite the lag period between the decreases in plasma FFA and increases in HGH, the plasma concentration of FFA itself appears to be the signal for HGH release. The abundance of glucose or of FFA appears to have little or no effect upon the release of HGH evoked by lowered plasma levels of FFA or glucose, respectively. S.P.

*Rocha, Dalva Marreiro; Faloona, Gerald R.; and Unger, Roger H.* (Dept. of Int. Med., Univ. of Texas Southwestern Med. Sch. at Dallas, and V.A. Hosp., Dallas, Tex.): GLUCAGON-STIMULATING ACTIVITY OF 20 AMINO ACIDS IN DOGS. *J. Clin. Invest.* 51:2346-51, September 1972

*Verbatim summary.* The effect of twenty L-amino acids upon pancreatic glucagon secretion has been studied in conscious dogs. Each amino acid was administered intravenously over a fifteen-minute period in a dose of 1 mmole per kilogram of body weight to a group of four or five dogs. Pancreatic glucagon and insulin were measured by radioimmunoassay. Seventeen of the twenty amino acids caused a substantial increase in plasma glucagon. Asparagine had the most glucagon-stimulating activity (GSA), followed by glycine, phenylalanine, serine, aspartate, cysteine, tryptophan, alanine, glutamate, threonine, glutamine, arginine, ornithine, proline, methionine, lysine, and histidine. Only valine, leucine, and isoleucine failed to stimulate glucagon secretion, and isoleucine may have reduced it. No relationship between glucagon-stimulating activity

and insulin-stimulating activity was observed. The amino acids which enter the gluconeogenic pathway as pyruvate and which are believed to provide most of the amino acid-derived glucose, had a significantly greater GSA than the amino acids which enter as succinyl CoA or as  $\alpha$ -ketoglutarate. However, pyruvate itself did not stimulate glucagon secretion. The R-chain structure of the amino acid did not appear to be related to its GSA, except that the aliphatic branched chain amino acids, valine, leucine, and isoleucine, were devoid of GSA.

Simon, E.; Frenkel, G.; and Kraicer, P. F. (Inst. of Science, Dept. of Zoology, Tel Aviv Univ., Israel): BLOCKADE OF INSULIN SECRETION BY MANNOHEPTULOSE. *Israel J. of Med. Sci.* 8:743-52, 1972.

The authors have reviewed new information reported since 1967 on mannoheptulose. The substance undergoes practically no catabolism in the body, for after injections of C-14-labeled mannoheptulose, 98 per cent of the injected dose can be recovered from the urine. It inhibits glucose-stimulated insulin secretion but does not inhibit the insulin secretion stimulated by tolbutamide or xylitol. Mannoheptulose infusion results in a rise in glucagon in dogs. The compound has been used to reduce the insulin levels in a glucose- and leucine-sensitive hypoglycemic child. Thus, mannoheptulose (in the form of avocado pears) or one of its homologs may be of future therapeutic value in the treatment of subjects with hyperinsulinemic states. J.M.F.

Spellacy, W. N.; Bubi, W. C.; and Birk, S. A. (Dept. of Obstet. and Gynec. of Univ. of Miami Sch. of Med., Miami, Fla.): THE EFFECT OF THE PROGESTOGEN ETHYNODIOL DIACETATE ON GLUCOSE, INSULIN, AND GROWTH HORMONE AFTER SIX MONTHS TREATMENT. *Acta Endocr.* 70:373-84, June 1972.

Oral glucose tolerance tests were performed in seventy-one women before and after uninterrupted daily oral administration of a small, contraceptive dose (0.25 mg.) of the progestogen, ethynodiol, for six months. With progestogen pretreatment, blood levels of glucose were elevated significantly in the fasting state and during the first two hours after ingestion of glucose. Carbohydrate tolerance had deteriorated in 12.6 per cent of the women who had normal tolerance before administration of ethynodiol. In the fasting state and during the entire three hour period of the tolerance test, mean plasma levels of insulin were significantly higher after ethynodiol therapy than in the control period. Fasting ambulatory plasma levels of growth hormone were not altered significantly. These results indicate that the progestogen component of oral contraceptives may contribute to the development of metabolic abnormalities observed with these drugs. With the advent of fertility control using "mini-pills" containing progestogens but no estrogens, such metabolic effects of the progestogens should be investigated carefully. S.P.

Stephan, F.; Reville, Ph.; Thierry, R.; and Schlienger, J. L. (Clinique Endocrinologique, C. H. V. Strasbourg, France): CORRELATIONS BETWEEN PLASMA INSULIN AND BODY WEIGHT IN OBESITY, ANOREXIA NERVOSA AND DIABETES MELLITUS. *Diabetologia* 8:196-201, June 1972.

*Verbatim summary.* Determinations of plasma insulin levels (IRI) were performed in seventy-nine patients before and after a quick intravenous glucose load (0.33 gm./kg. body weight). The patients were divided into normal (N), under-

weight patients (M), obese (O), latent diabetics (D<sub>1</sub>) and overt diabetics (D<sub>2</sub>), obese latent diabetics (OD<sub>1</sub>) and obese diabetics (OD<sub>2</sub>). The body weights varied from 59 to 290 per cent of ideal body weight and the ages from fourteen to seventy-five years. We were unable to find any significant correlation between basal IRI values and body weight. We found significant correlations between IRI values obtained after glucose administration and body weight. The insulinogenic index rises with increasing body weight in all subjects, in nondiabetics (N-M-O) as well as in diabetics (D<sub>1</sub>-D<sub>2</sub>-OD<sub>1</sub>-OD<sub>2</sub>). In undernutrition due to anorexia nervosa, the basal plasma IRI and the plasma IRI increase after the glucose load, are normal in the studied patients. Overt diabetic patients (D<sub>2</sub> and OD<sub>2</sub>) were significantly older than nondiabetic patients having the same body weight (N-O). The insulinogenic index fell with increasing age in obese and in diabetic patients. The correlations between plasma IRI and blood sugar are discussed.

Strohfeldt, P.; Meissner, H. P.; and Weinges, K. F. (Dept. of Med., Univ. of Saarland, Homburg/Saar, Germany): THE EFFECT OF BUFORMIN UPON BLOOD GLUCOSE LEVEL OF NORMAL RATS AND CARBOHYDRATE METABOLISM OF THE ISOLATED RAT DIAPHRAGM. *Diabetologia* 8:377-80, December 1972.

*Verbatim summary.* 1. Two hours after a single oral dose of 25 mg. of buformin per normal rat, the blood glucose level was significantly lower when compared to the control group ( $78.9 \pm 1.4$  mg./100 ml. to  $67.1 \pm 5.2$  mg./100 ml.,  $p < 0.05$ ). The incubated diaphragms of these animals showed no differences with regard to glucose uptake, lactate production and glucose oxidation in comparison to the control. 2. When treated for seven days with identical dosages of buformin the blood glucose level of the treated rats was lowered to a greater extent ( $80.5 \pm 3.7$  mg./100 ml. to  $51.6 \pm 5.7$  mg./100 ml.,  $p < 0.01$ ) and the incubated diaphragms showed a significantly increased glucose uptake, lactate production and decreased glucose oxidation. 3. As a result of these findings and supported by reports in literature it is suggested that the drug may accumulate in the skeletal muscle of normal rats. 4. No insulin potentiating effect could be detected. 5. With regard to previous reported results from our laboratory we suggest that biguanides may increase Cori cycle activity in the rat.

Taton, J.; Malczewski, B.; and Wisniewska, A. (Third Dept. of Int. Med., Warsaw Med. Sch., Prof. A. Czyzyk Diabetol. Clin. Res. Center): STUDIES ON THE PATHOGENESIS OF LIPOATROPHIC DIABETES: A CASE OF CONGENITAL SYSTEMIC ABSENCE OF ADIPOSE TISSUE ASSOCIATED WITH INSULIN-RESISTANT DIABETES MELLITUS AND HEPATOSPLENOMEGALY. *Diabetologia* 8:319-25, November 1972.

*Verbatim summary.* A case of coexisting lipotrophy, hyperlipemia, insulin-resistant diabetes mellitus and hepatosplenomegaly (fatty liver and early cirrhosis, as shown by biopsy) is described. Investigations attempting to explain the pathogenesis of these disturbances are presented. From the urine of the patient both the insulin antagonizing (Louis' factor) and lipid mobilizing substance (Chalmers' factor) were extracted. Injection of these extracts obtained from the patient's urine induced 1) insulin resistance, 2) hyperlipemia and 3) fatty infiltration of the liver in mice. The pathogenetic hypothesis that humoral factors cause a constant increase in lipolysis and therefore prevent triglyceride storage in the adipocytes is discussed.