# ABSTRACTS

*Abramson, Eugene A.; and Arky, Ronald A.* (Thorndike Memorial Lab. and 2nd and 4th (Harvard) Med. Serv. and Diabetes Clin., Boston City Hosp., and Dept. of Med., Harvard Med. Sch., Boston, Mass.): COEXISTENT DIABETES MELLITUS AND ACTH DEFICIENCY: REPORT OF A CASE. Metabolism 17:492-95, June 1968.

Adrenal insufficiency secondary to an isolated defect in adrenocorticotrophin secretion was demonstrated in a patient with diabetes mellitus. Withdrawal of steroid therapy resulted in improvement in fasting hyperglycemia and glycosuria although an abnormal glucose tolerance persisted. An episode of hypoglycemia followed a period of semistarvation and excessive alcohol intake. It is suggested that hypoglycemia following alcohol ingestion and brief starvation warrants investigation of the functional integrity of the pituitary-adrenal axis. C.R.S.

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*Alexander, D. Pauline; Britton, H. G.; Cohen, N. M.; Nixon, D. A.; and Parker, R. A.* (Depts. of Physiol. and Path. St. Mary's Hosp. Med. Sch., London, and Dept. of Med., Guy's Hosp. Med. Sch., London, England): INSULIN CONCENTRATIONS IN THE FOETAL PLASMA AND FOETAL FLUIDS OF THE SHEEP. J. Endocr. 40:389-90, March 1968.

Ewes were delivered of fetuses by cesarean section at 42 to 144 days of gestation (term: 148 days). Blood samples were obtained from the umbilical artery and from the dorsalis pedis artery of the mother when the fetus was exposed, and insulin concentration was measured by immunoassay. Insulin was detectable in fetal plasma from early fetal life; the level was correlated with the concentration of glucose and fructose in plasma, but was not proportional to maternal plasma insulin levels. Insulin could be extracted from fetal pancreas as early as seventy days of gestation. H.T.N.

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*Balasse, E.; and Ooms, H. A.* (Medical Clin. and Depts. of Experimental Med. and Clin. Chem., Univ. of Brussels, Brussels, Belgium): CHANGES IN THE CONCENTRATIONS OF GLUCOSE, FREE FATTY ACIDS, INSULIN AND KETONE BODIES IN THE BLOOD DURING SODIUM β-HYDROXYBUTYRATE INFUSIONS IN MAN. Diabetologia 4:133-35, 1968.

*Verbatim summary.* Sodium β-hydroxybutyrate was infused for 1.5 hr. in eight normal subjects, at a constant rate of 5 mmoles/kg./hr. Equimolar amounts of sodium chloride were infused in five control subjects. The induced hyperketonemia provoked the following changes in peripheral blood: a fall in glycemia (15 mg./100 ml.) and in plasma NEFA concentration (50 per cent) without concomitant modifications of insulin concentrations. These results indicate that the glucose and NEFA changes observed are not mediated by a pancreatic stimulation.

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*Bowers, Cyril Y.; and Hawley, William D.* (Dept. of Med., Tulane Univ. Sch. of Med., New Orleans, La.): THE TREATMENT OF CHEMICAL DIABETES MELLITUS. Geriatrics 23:146-53, June 1968.

Twenty-eight patients with slightly abnormal glucose tolerance tests, but normal fasting blood sugar levels, were treated with chlorpropamide for periods up to two years. It was possible to maintain their carbohydrate tolerance unchanged. The theoretical possibilities of preventing diabetes are extensively discussed. O.V.S.

*Breitbach, A.* (2. Med. Klinik and Poliklinik der Univer. Düsseldorf, Düsseldorf, Germany): THE DETERMINATION BY A NOMOGRAMME OF THE COEFFICIENT OF ASSIMILATION, *K*, OF CONARD FOR AN INTRAVENOUS GLUCOSE LOAD. Diabetologia 4:167-68, 1968.

*Verbatim summary.* The determination of the coefficient of glucose assimilation, *k*, of Conard, is very useful for evaluating the test using intravenous glucose load. In order to calculate the factor *k* according to the formula given by Conard, one has to know the logarithmic values of the results of the test. To this end, Conard has already described a graphical method plotted on semilogarithmic paper. The calculation of *k* is facilitated by the nomogramme described here for it directly gives the appropriate values of *k* for blood glucose levels measured after 20 and 40 min.

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*Burditt, Anne F.; Caird, F. I.; and Draper, G. J.* (The Nuffield Dept. of Med. and Dept. of Biomathematics, Univ. of Oxford, Oxford, England): THE NATURAL HISTORY OF DIABETIC RETINOPATHY. Q. J. Med. 37:303-17, April 1968.

*Verbatim summary.* Over a fifteen-year period, 3,907 observations made by ophthalmologists on the eyes of 2,184 diabetics have been analysed.

Age at diagnosis and duration of diabetes are the main determinants of the frequency of retinopathy. Progression is commoner and regression less common with advancing age at diagnosis, except that the development of "malignant retinopathy" (new vessel formation, glial proliferation or vitreous hemorrhage) is rare in patients over sixty at diagnosis.

A lower "glycosuria percentage" (proportion of routine clinic urine tests showing glycosuria of 2 per cent or more) is associated with a lower frequency of retinopathy in patients under sixty at diagnosis, but not with any difference in the behavior of established retinopathy.

Evidence is presented that reduction in the subsequent chance of development of retinopathy is especially associated with a lower "glycosuria percentage" in the first five years after diagnosis of diabetes.

The pathogenesis of diabetic retinopathy is briefly reviewed in the light of these findings.

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*DeChatelet, Lawrence R.; and McDonald, Hugh J.* (Dept. of Biochem. and Biophysics, Loyola Univ., Stritch Sch. of Med., Chicago, Ill.): EFFECT OF IN VIVO ADMINISTRATION OF VARIOUS ORAL HYPOGLYCEMIC AGENTS ON HEPATIC PROTEIN SYNTHESIS. Proc. Soc. Exp. Biol. Med. 127:415-18, February 1968.

*Verbatim summary.* The effects of the in vivo injection of two oral hypoglycemic agents (tolbutamide and phenethylbiguanide) upon the in vitro incorporation of leucine-C-14 into hepatic protein were measured. The acute injection of a large amount of either agent impaired the ability of animal liver to synthesize protein. This impairment was seen to occur at the level of the cell sap and was not associated with the microsomes. The daily injection of smaller amounts of these compounds resulted in no significant effect on protein metabolism. The data appear to indicate that these agents may, under certain circumstances, have a deleterious effect on the protein balance of the organism.

*Donaldson, Charles L.; Wegienka, Laurence C.; Miller, Daniel; and Forsham, Peter H.* (Metabolic Res. Unit and Dept. of Med., Univ. of California Med. Center, San Francisco, Calif.): GROWTH HORMONE STUDIES IN TURNER'S SYNDROME. J. Clin. Endocr. *28*:383-85, March 1968.

*Verbatim summary.* Fourteen subjects with Turner's syndrome were studied before and after insulin hypoglycemia: eleven had brisk growth hormone responses as measured by radioimmunoassay, and three had limited responses with maximum values below 10 mμg./ml. Twelve healthy female control subjects of normal stature were studied in the same manner, and eleven had brisk responses, with one showing a limited response. No one in either group had complete absence of growth hormone. Thus, some defect other than growth hormone deficit must be implicated in the short stature of patients with Turner's syndrome.

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*Everson, Gladys J.; and Shrader, Ruth E.* (Dept. of Nutrition, Univ. of California, Davis, Calif.): ABNORMAL GLUCOSE TOLERANCE IN MANGANESE-DEFICIENT GUINEA PIGS. J. Nutr. *94*:89-94, January 1968.

Both oral and intravenous glucose tolerances were impaired in guinea pigs after two months on a manganese-deficient diet. The defect was corrected by manganese supplementation. The metal may cause hypoglycemia in diabetic patients, also in rabbits or dogs. Whether this is due to excessive insulin secretion or reduced glucose utilization is unknown. A.R.C., JR.

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*Fernandes, J.; and Huijing, F.* (Wilhelmina Kinderziekenhuis, Univ. of Utrecht; and Dept. of Med. Enzymology, Lab. of Biochem., Univ. of Amsterdam, Netherlands): BRANCHING ENZYME-DEFICIENCY GLYCOGENOSIS: STUDIES IN THERAPY. Arch. Dis. Child. *43*:347-52, June 1968.

Another rare case of type IV glycogen storage disease is reported in a male infant. Deficiency of branching enzyme (α-1,4-glucan:α1,4-glucan 6-glucosyl transferase) was found in the patient's leukocytes whereas phosphorylase and debranching enzyme activities were normal. Analysis of liver glycogen was consistent with an abnormal structure containing long outer branches. Because it has been reported previously that the parenteral administration of α-glucosidase reduces glycogen content of tissues in both human and animal subjects, therapy was initiated in this case. Purified α-glucosidase was given intravenously for a period of six days. Liver glycogen content was successfully reduced from 10.7 per cent to 1.0 per cent but began reaccumulating after therapy was discontinued despite subsequent daily injections of zinc-glucagon. The authors feel, however, that this kind of approach to treatment of glycogen storage disease has great potential usefulness. R.K.K.

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*Findlay, J. A.; Gill, J. R.; Irvine, G.; Lever, J. D.; and Randle, P. J.* (Dept. of Anat., Univ. College, Cardiff, Cardiff, and Dept. of Biochem., Univ. of Bristol, Bristol, England): CYTOLOGY OF β-CELLS IN RABBIT PANCREAS PIECES INCUBATED IN VITRO; EFFECTS OF GLUCOSE AND TOLBUTAMIDE. Diabetologia *4*:150-60, 1968.

*Verbatim summary.* The electron microscopic appearances of rabbit pancreas β-cells taken in vivo and after in vitro incubation have been compared and the effects of high glucose and tolbutamide stimulation of insulin release in vitro on β-cell cytomorphology investigated. Normal structure was maintained on in vitro incubation in a proportion of β-cells; this varied in different samples from 35-100 per cent. The cause of this variation was not apparent but it was not influenced by the time of incubation, medium glucose concentration or tolbutamide. Quantitative measurements have been made of the proportion of β-cell profiles showing marginal distribution of granules, of the number of contacts between granule sac membranes and the plasma membrane, of the number of granule sacs showing perforations, of the population density of specific secretion granules, lysosomes and autophagic bodies, and estimates have been made of the extent of the Golgi apparatus in cross-section. No consistent change in these parameters was observed following stimulation of insulin release with glucose or tolbutamide. There was no evidence in any of the specimens examined of continuity between the interior of a granule sac and the outside of a β-cell. Calculations based on the rate of release of insulin and the insulin content of the pancreas indicate that the chance of visualizing granule extrusion by electron microscopy is small. The significance of these results in relation to the emiocytosis theory of insulin release (Lacy and Hartroft) is discussed.

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*Grant, D. B.* (Inst. of Child Health, London, England): SERUM-INSULIN CHANGES FOLLOWING ADMINISTRATION OF L-LEUCINE TO CHILDREN. Arch. Dis. Child. *43*:69-72, February 1968.

*Verbatim summary.* Serum immunoreactive insulin was measured during leucine tolerance tests in twenty-eight children with mental retardation or hypoglycemia. Little change in serum-insulin was found in twenty-five leucine-insensitive children. Insulin increments of 23-57 μU./ml. were observed in three children with leucine-sensitive hypoglycemia. The relevance of serum-insulin measurement in the diagnosis of leucine-sensitive hypoglycemia is discussed.

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*Hazlewood, Carlton F.; and Zierler, Kenneth L.* (Dept. of Med., The Johns Hopkins Univ. Sch. of Med., Baltimore, Md.): INSULIN-INDUCED HYPERPOLARIZATION OF SKELETAL MUSCLE FROM NORMAL AND FROM HYPOPHYSECTOMIZED RATS. Johns Hopkins Med. J. *121*:188-93, September 1967.

Resting membrane potentials (RMP) were measured in muscle fibers of the extensor digitorum longus of normal and hypophysectomized rats in the presence and absence of insulin from the incubation medium. In the presence of insulin, cell membranes were hyperpolarized, the RMP rose from 71.4 mV to 74.2 mV in normal muscle, and from 73.1 mV to 77.7 mV in muscles from hypophysectomized animals. The rise in intracellular $K^+$ and fall in $Na^+$ concentrations were too small to account for the changes in RMP. It was concluded that hyperpolarization of cell membranes was a primary effect of insulin. O.V.S.

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*Hazelwood, Robert L.* (Dept. of Biol., Univ. of Houston, Houston, Texas): GROWTH HORMONE, PLASMA GLUCOSE, AND KETONE BODIES AS DETERMINANTS OF CARDIAC GLYCOGEN IN NORMAL AND DIABETIC RATS. Proc. Soc. Exp. Biol. Med. *127*:450-58, February 1968.

*Verbatim summary.* The influence of growth hormone, plasma glucose and plasma ketone bodies on cardiac glycogen deposition was studied in fasted intact rats and both nonfasted and fasted alloxan-diabetic rats. The results indicate a close positive correlation between plasma ketones (but not plasma

glucose) and cardiac glycogen. Fasting does not increase diabetic myocardial glycogen levels and, unlike normal intact rats, growth hormone did not influence myocardial polysaccharide levels in diabetic rats, indicating a possible tissue refractoriness to the hormone or the need for "permissive" amounts of insulin to be present.

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*Hildebrand, J.; Joffroy, A.; Graff, G.; and Coërs, C.* (Med. Biochem. Dept., Brussels Univ.; Inst. Bordet; and Neurol. Dept. Brugmann Hosp., Brussels, Belgium): NEUROMUSCULAR CHANGES WITH ALLOXAN HYPERGLYCEMIA. Arch. Neurol. *18*:633-41, 1968.

The electrophysiological, histological and chemical study of neuromuscular apparatus was performed in rats with alloxan-induced diabetes. After four months of hyperglycemia segmental demyelination occurred in some nerve fibers with shortening of internodal length in medium and large fibers. An abnormal collateral and ultraterminal branching of motor nerve fibers was observed in ten of twenty-four animals. A reduction of maximal afferent conduction velocity was noted with no decrease in efferent conduction velocity. There was abnormal dispersion of conduction velocity in individual motor fibers. Hyperglycemia did not impair the metabolic activity of Schwann cells of incorporating inorganic phosphorus from the blood stream in the sciatic nerve undergoing Wallerian degeneration after proximal section or in the nonoperated nerve. The defect in nerve transmission is due to segmental demyelination and is compensated by distal sprouting of motor nerve fibers. C.R.S.

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*Humbel, R. E.; Derron, R.; and Neumann, P.* (Inst. of Biochem., Univ. of Zürich, Zürich, Switzerland): CHROMATOGRAPHIC SEPARATION OF AMINOETHYLATED INSULIN A AND B CHAINS. Biochemistry 7:621-23, February 1968.

Aminoethylation of cysteine residues in proteins with ethyleneimine introduces additional sites where cleavage by trypsin can occur. In the case of insulin, after reduction of the disulfide bridges and aminoethylation of the resulting sulfhydryl groups, the A- and B-chain derivatives that are formed are difficult to separate by ion-exchange chromatography because they have the same net charge at neutral pH. The present paper describes a method of separating aminoethylated insulin chains on IRC-50 resin columns with linear gradients of acetic or formic acid. H.T.N.

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*Jackson, W. P. U.; Marine, N.; and Vinik, A. I.* (Groote Schuur Hosp., Univ. of Cape Town, South Africa): THE SIGNIFICANCE OF GLYCOSURIA. Lancet 1:933-36, May 4, 1968.

Glycosuria often indicates diabetes but, because renal glycosuria is common, the predictive value of glycosuria is uncertain. In this study a systematic survey of the relationship of glucose in the blood to glucose in urine was made in three nonwhite racial groups living in South Africa. Glycosuria was estimated by Tes-Tape and screening for diabetes was made by measuring glycosuria after either a heavy carbohydrate meal or oral administration of 50 gm. glucose. Diabetes mellitus was diagnosed by using blood sugar value in excess of 120 mg. per 100 ml. fasting, 200 mg. per 100 ml. one hour, and 140 mg. per 100 ml., two hours, after a 50 gm. oral glucose load. Glycosuria was rare (0.1 per cent) in children but in adults nondiabetic glycosuria was found in 4.4 per cent of men and 2.7 per cent of women. The highest rates of glycosuria were in older people but, since renal glycosuria did not increase in prevalence after age fifty-five, an increasing incidence of glycosuria with age was found to be due to diabetes. Data analysis indicated that the probability that glycosuria was due to diabetes was 53 per cent in women and 30 per cent in men. It was 78 per cent in those with 4+ glycosuria. Just 50 per cent of those eventually diagnosed as diabetics had glycosuria after a screening meal and after glucose screening 66 per cent had glycosuria. In about a quarter of the patients diagnosed as diabetics there was no glycosuria during OGTT. T.G.S.

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*Javier, Zenaida; Gershberg, Herbert; and Hulse, Mildred* (Dept. of Med., New York Univ. Sch. of Med., and Bellevue Hosp., New York, N. Y.): OVULATORY SUPPRESSANTS, ESTROGENS, AND CARBOHYDRATE METABOLISM. Metabolism *17*:443-56, May 1968.

Many women taking oral contraceptives manifest impaired tolerance to a glucose load and most promptly develop abnormal cortisone glucose tolerance. The administration of estrogen alone produces these changes. Early in the course of treatment, insulin secretion increases as the blood glucose rises. With prolonged treatment, glucose tolerance becomes impaired and the levels of insulin secretion decrease in certain women, suggesting failure of the pancreas to respond to hyperglycemia. The results may be attributed to alterations in liver function, elevation of triglyceride and free fatty acid levels or corticosteroid activity during administration of ovulatory suppressants. C.R.S.

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*Jensen, V. A.; and Lundbæk, K.* (Dept. of Ophthalmol. and the II Clinic of Internal Med., Kommunehospitalet, Aarhus Univ. Sch. of Med., Aarhus, Denmark): FLUOROSCENCE ANGIOGRAPHY OF THE IRIS IN RECENT AND LONG-TERM DIABETES. Diabetologia *4*:161-63, 1968.

*Verbatim summary.* Fluorescence angiographic studies have been carried out on a series of nondiabetics, young recent diabetics and long-term diabetic patients with retinopathy. The time of appearance was 9-21 sec., the arterial phase lasted 3-5 sec., not significantly different in the three groups of patients. In the nondiabetics and the young patients with recent juvenile diabetes, tiny fluorescent dots along the pupillary seam were observed for a short interval of time. In long-term diabetic patients a characteristic pattern was observed, consisting of the development of coarse, irregular dots along the pupillary border, showing confluence and culminating in a glow which lasted for the entire period of observation (50 sec). This pattern is interpreted as the expression of an abnormal capillary permeability of the vascular arcades of the annulus minor. The abnormal pattern of confluence and glow was observed in long-term diabetic patients before the development of visible rubeosis iridis. The rubeosis vessels filled after the appearance of the confluent dots and emptied into the veins.

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*Knowles, Harvey C., Jr.* (Dept. of Med., Univ. of Cincinnati, Cincinnati, O.): PREVALENCE AND DEVELOPMENT OF DIABETES. Fed. Proc. *27*:945-48, May-June 1968.

In a review of reports by many investigators, the prevalence of diabetes in various groups and populations was found to range from none in some groups to a very high prevalence

in others. The reasons for this great discrepancy may be actual differences. The possibility cannot be excluded, however, that the differences depend on the constitution of the groups, the methods and criteria employed for diagnosis, the age of the persons studied, etc.

In the development of diabetes the genetic factor is generally accepted, although the exact mode of inheritance is still disputed. Other factors, acquired or environmental, may influence the development of diabetes. Besides age, urban life, various hormonal and endocrine factors, obesity, nutrition and individual food substrates have been implicated. Lipid levels and arteriosclerosis have a connection to blood glucose elevation.

The chronic diabetic syndrome characterized by vascular disease may be a consequence of the insulin inefficiency; alternatively both the acute manifestations of insulin insufficiency and the chronic complications of the diabetic syndrome may stem from common sources. Both theories have supporting but inconclusive evidence.

It was concluded from this review that the actual prevalence of diabetes in different population groups has to be established by using uniform methods. When differences between two groups can be shown, further studies will help delineate the environmental influences leading to hyperglycemia and vascular disease. M.C.B.

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*Konikova, S. A.; Morenkova, S. A.; Kritzman, M. G.; and Perova, N. V.* (A. V. Vishnersky's Inst. of Surg., and Inst. of Therapy, Academy of Med. Sciences, Moscow, U.S.S.R.): UTILIZATION OF PARENTERALLY INJECTED C-14-POLYPEPTIDE CHAINS OF INSULIN BY PROTEINS OF ORGANS AND TISSUES. Metabolism *17*:411-19, May 1968.

Preparations of A and B chains of insulin labeled with C-14 amino acids were injected into rats. Radioactivity was found in all organs and tissues investigated. Treatment of the organ proteins with NaOH did not alter the radioactivity indicating strong bonds between labeled compound and protein. Similarity in distribution of radioactivity suggests that intact polypeptide chains may enter into protein structure. These similarities were observed in the case of injection of three variously labeled preparations of A chain indicating that injected A chain made complexes with tissue protein before decomposition. After injection of variously labeled B chain differences in the distribution of the labels indicated that fragmentation into peptide fragments occurred with their subsequent utilization in formation of organ and tissue protein. These results suggest the possibility of incorporation of polypeptide chains or peptide fragments of the insulin molecule into organ proteins. C.R.S.

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*Lestradet, H.; and Billaud, L.* (Hôpital Hérold, Paris, France): DEGENERATIVE COMPLICATIONS AFTER 15 YEARS INFANTILE DIABETES. La Presse Médicale 76:303-06, Feb. 10, 1968.

Eighty-six juvenile diabetic patients with a mean duration of the disease of 17.7 yrs. were followed continuously. They were treated with an unrestricted diet and with insulin injections adjusted exactly to their needs. Twenty-six achieved good chemical and clinical control of diabetes, fifty-two had fair, and eight poor, control. Degenerative complications (retinopathy, albuminuria, hypertension, cataracts, or absent reflexes) occurred in thirty-nine of the eighty-six patients; their frequency was progressively greater in those with fair and poor control; those with good control had the smallest frequency. All patients with poor control had complications. M.C.B.

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*Liebermeister, H.; Daweke, H.; Gries, F. A.; Schilling, W. H.; Grüneklee, D.; Probst, G.; and Jahnke, K.* (2. Medizinische Universitätsklinik and Diabetes-Forschungsinstitut, Universität Düsseldorf, Düsseldorf, Germany): INFLUENCE OF WEIGHT REDUCTION ON CARBOHYDRATE AND FAT METABOLISM AND ON SERUM INSULIN RESPONSE IN OBESITY. Diabetologia *4*:123-32, 1968.

*Verbatim summary.* To find out which of the metabolic changes observed in obesity are reversible by a reducing diet, we examined thirty-seven obese out-patients with a mean overweight of 71 per cent BROCA. A manifest diabetes mellitus and endocrine diseases were excluded by clinical means. Twenty subjects showed disturbances of carbohydrate tolerance. Oral intravenous glucose tolerance tests gave normal results in seventeen. Both subgroups were put on a 1000 cal. mixed diet and had mean weight losses of 21.2, vs. 17.5 kg. corresponding to 34 per cent vs. 28 per cent BROCA, i.e., less than half of their overweight. The following changes were observed in the subgroup with impaired carbohydrate tolerance: 1. Significant improvement of glucose-tolerance with beginning normalization of fasting blood sugar, 120′ value after oral glucose and the *k*-values for intravenous and oral glucose-tolerance tests. 2. Highly significant reduction of the elevated fasting values for free serum glycerol with normalization of the quotient: free fatty acids/glycerol in fasting serum. 3. Significant fall of the high levels for insulin-like activity and for immunologically reacting insulin. Under identical conditions the subgroup with normal carbohydrate tolerance showed only a moderate increase of free fatty acids 90′ and 120′ after glucose. In the obese group as a whole, we found a reduction of serum esterified fatty acids under low calorie diet. The changes described under 1-3 were more pronounced with this dietary treatment than in fasting periods generally described until now, and occurred predominantly in the subgroup with impaired carbohydrate tolerance. Our findings indicate that hyperinsulinism held responsible for obesity up to now by some authors is probably adaptive.

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*Louis, L. H.; and Conn, J. W.* (Dept. of Int. Med., Univ. of Mich. Med. Sch., Ann Arbor, Mich.): A DIABETOGENIC POLYPEPTIDE FROM HOG AND SHEEP ADENOHYPOPHYSIS SIMILAR TO THAT FOUND IN LIPOATROPHIC DIABETES. Metabolism *17*:475-84, June 1968.

A polypeptide with physical and biological properties similar to that excreted in urine of patients with lipoatrophic diabetes was previously isolated from bovine adenohypophysis. The same isolation procedures applied to the anterior pituitary glands of hogs and sheep yielded a similar principle which induced hyperglycemia and insulin resistance in humans and dogs. There are no similarities between the polypeptide and growth hormone or prolactin. The presence of this substance in the pituitary glands of the three species studied suggests that it is normally occurring material with unknown physiological significance. It is assumed that the diabetogenic polypeptide isolated from the urine of lipoatrophic diabetic patients may be of pituitary origin. C.R.S.

*Mansford, K. R. L.; and Opie, Lionel* (Med. Res. Council, Dept. of Biochem., Imperial Coll. of Science and Technology, London, England): COMPARISON OF METABOLIC ABNORMALITIES IN DIABETES MELLITUS INDUCED BY STREPTOZOTOCIN OR BY ALLOXAN. Lancet 1:670-71, March 30, 1968.

In 1963 it was reported that the intravenous injection of the antibiotic streptozotocin resulted in specific damage to the insulin-secreting cells of the pancreas and caused a new type of experimental diabetes mellitus in animals. In this study rats were given 65 mg./kg. and one week later changes in their blood sugar, plasma FFA, and heart glycogen content were compared to values obtained in normal and alloxan diabetic rats.

Alloxan diabetes was characterized by striking elevations of glucose, FFA, ketones and glycogen. Streptozotocin administration caused hyperglycemia but FFA and ketones were not elevated and cardiac glycogen was decreased. In studies of the isolated perfused heart, alloxan was associated with increases in glucose-6-phosphate, fructose-6-phosphate, and citrate but decreases in fructose-1, 6 diphosphate. Streptozotocin decreased citrate but resulted in concentrations of glucose-6-phosphate, fructose-6-phosphate, and fructose 1, 6 diphosphate. The results suggest that the metabolic pattern of streptozotocin diabetes may resemble maturity onset diabetes more than alloxan diabetes. T.G.S.

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*Missmahl, H. P.; and Riemann, J.* (Med. Universitätsklinik Tübingen, Germany): SIMPLE PROOF OF CAPILLARY MICROANGIOPATHY OF THE RECTAL MUCOSA IN DIABETIC PATIENTS. Klin. Wschr. 46:374-76, April 1, 1968.

Thickening of capillary basement membranes of the rectum was found in sixteen patients with manifest and twenty patients with latent diabetes. Microscopy under polarized light indicated accumulation of material with double refraction. O.V.S.

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*Penchev, I.; Andrew, D.; and Ditzov, S.* (Diabetic Research Group, Bulgarian Acad. of Sci., Sofia, Bulgaria): INSULIN-PRECIPITATING ANTIBODIES IN INSULIN-TREATED AND UNTREATED DIABETIC PATIENTS. Diabetologia 4:164-66, 1968.

*Verbatim summary.* Although the existence of precipitating insulin antibodies (PIA) has been questioned by many authors, others have shown that such antibodies can really be found in insulin-treated animals. The authors have studied the problem in insulin-treated and untreated diabetic patients, using the agar-precipitation test of Oudin. It has been possible to demonstrate PIA in 20 per cent of the 276 unselected diabetics studied. All control examinations were negative. Unexpectedly, the precipitation reaction was more often positive in the group of diabetics not treated with insulin. The data of the authors disclose systematically for the first time the existence of PIA in man, and the prevalence of such antibodies in diabetic patients that have never been treated with insulin and in prediabetic subjects. These findings raise the question of an autoimmune pathogenesis of some types of diabetes.

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*Pfeiffer, E. F.; and Raptis, S.* (Dept. of Endocr. and Metabolism, Center for Intern. Med., Univ. of Ulm, Germany): INTESTINAL HORMONES AND INSULIN SECRETION. Klin. Wschr. 46:337-42, April 1, 1968.

A review article of the stimulating effects of secretin, pancreozymin, and glucagon on insulin. Serotonin and gastrin, when applied to slices of pancreas in vitro, stimulated insulin secretion. O.V.S.

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*Roy, Claude, C.; Shapcott, Dennis, J.; and O'Brien, Donough* (Dept. of Pediatrics, Univ. of Colorado Medical Center, Denver, Colo.): THE CASE FOR AN "ABNORMAL" INSULIN IN DIABETES MELLITUS. Diabetologia 4:111-17, 1968.

*Verbatim summary.* Understanding of diabetes in molecular terms has advanced very little. The possibility that a structural difference exists in the circulating and pancreatic insulin moiety of diabetics is supported by three lines of evidence obtained in the authors' laboratory. Immunologically purified circulating insulin from diabetic subjects untreated with insulin was noted to be relatively resistant to degradation by a crude muscle insulinase preparation. The pancreatic insulin of five diabetic pancreases was found to have a decreased biological activity in its ability to enhance glycogen synthesis in vivo and in its capacity to stimulate RNA turnover in tissue culture. The nature of this "abnormal insulin" and its hypothetical role in the physiopathology of diabetes are discussed in the light of the need for a specific definition of the precise molecular change.

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*Settle, Harold P., Jr.; Munsie, William J.; and Owen, John A., Jr.* (Div. of Clin. Pharmacol., Dept. of Internal Med., and the Dept. of Pathol., Sch. of Med., Univ. of Virginia, Charlottesville, Virginia): TOXIC EFFECTS OF A CHLOROTHIAZIDE-DIAZOXIDE COMBINATION ON ADIPOSE TISSUE AND KIDNEYS OF INTACT RATS. Diabetologia 4:136-40, 1968.

*Verbatim summary.* In order to explore effects of chlorothiazide (CTZ) and diazoxide (DZX) on rat adipose tissue, as being possibly related to previously reported hyperglycemia in man, intact rats fed ad libitum were given daily injections of CTZ (200 mg./kg.), DZX (50 mg./kg.), or both for fourteen days. They were then killed and their fat pads were incubated in buffer with and without insulin (250 μU./ml.), DZX (but not CTZ) and the combination significantly decreased baseline glucose oxidation and incorporation into lipids; response to insulin was significantly impaired by either drug alone and especially by the CTZ-DZX combination. An unexpected effect of the drug combination was severe renal disease with azotemia and death as early as the fourth day. Histologically, the primary change seemed to be epithelial hyperplasia in the collecting tubules suggestive of the effect of potassium depletion. This in turn produced tubular obstruction with proximal dilatation and focal, acute, interstitial inflammation in both cortex and medulla.

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*Spellacy, William N.; Carlson, Karen L.; Birk, Sharon A.; and Schade, Sandra L.* (Dept. of Obstet. and Gynec., Univ. of Miami Sch. of Med., Miami, Fla.): GLUCOSE AND INSULIN ALTERATIONS AFTER ONE YEAR OF COMBINATION-TYPE ORAL CONTRACEPTIVE TREATMENT. Metabolism 17:496-501, June 1968.

Intravenous glucose tolerance tests were performed in ninety-three normal subjects before and after one year of treatment with a combination-type oral contraceptive. A slight rise was observed in blood glucose and a significant rise in plasma insulin was noted at the end of the period. The greatest changes occurred in those of older age, those with infants of birth weight greater than nine pounds and those with excessive weight gain while taking the drug. C.R.S.

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*Spergel, Gabriel; Bleicher, Sheldon J.; and Ertel, Norman H.* (Dept. of Med. and Clin. Metabolic Res. Unit of the Jewish Hosp. and Med. Center of Brooklyn, and Dept. of Med., State Univ. of New York Downstate Med. Center, Brooklyn, N.Y.):

CARBOHYDRATE AND FAT METABOLISM IN PATIENTS WITH PHEOCHROMOCYTOMA. New Eng. J. Med. *278*:803-09, April 11, 1968.

Detailed studies of carbohydrate and fat metabolism in two patients with pheochromocytoma are presented. Both patients demonstrated insulin release suppression and resistance to the hypoglycemic action of endogenous or exogenous insulin. Surgical removal of the tumors resulted in exaggerated response of plasma insulin levels to glucose and tolbutamide. Resistance to insulin hypoglycemic effects was not diminished. Carbohydrate metabolism returned toward normal after surgery. Before surgery, free fatty acid levels fell after oral glucose but plasma glycerol levels did not. Exogenous insulin caused decrease in both free fatty acid and glycerol levels. After surgery, both levels decreased after oral glucose administration. Those observations suggest that, before surgery, plasma insulin levels were suppressed after oral glucose loading. Re-esterification accelerated by hyperglycemia was suggested as modifying free fatty acid concentrations probably averting ketoacidosis. B.R.B.

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*Steiner, H.* (Path. Inst. der Univ. Zürich, Switzerland): INSULITIS AND FULMINATING DIABETES IN CHILDHOOD. Klin. Wschr. *46*:417-21, April 15, 1968.

This is a report of two fatal cases of diabetes in young children. Histological findings suggested an auto-immune disease, since the insulitis was associated with lymphocytic infiltration. O.V.S.

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*Swiatek, Kenneth R.; Kipnis, David M.; Mason, George; Chao, Kuen-Lan; and Cornblath, Marvin* (Dept. of Pediat., Univ. of Illinois Coll. of Med., Chicago, Ill.; and Dept. of Intern. Med., Metabolism Div., Washington Univ. Sch. of Med., St. Louis, Mo.): STARVATION HYPOGLYCEMIA IN NEWBORN PIGS. Amer. J. Physiol. *214*:400-05, February 1968.

In newborn pigs blood glucose, insulin and FFA levels decreased after seventy-two hours of fasting; GH levels increased. Four-day and one, two and three-week-old animals showed an elevation of FFA levels and maintained their blood glucose levels after a similar period of fasting. The increased susceptibility of new-born pigs to hypoglycemia is probably due to a primary deficiency of fat mobilizable stores and fall of FFA, with a failure of gluconeogenesis. M.C.B.

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*Westman, Sighild* (Dept. of Histol., Univ. of Uppsala, Uppsala, Sweden): DEVELOPMENT OF THE OBESE-HYPERGLYCEMIC SYNDROME IN MICE. Diabetologia *4*:141-49, 1968.

*Verbatim summary.* Mice with the recessively inherited, obese-hyperglycemic syndrome were studied at different stages of their development. Homozygous carriers of the syndrome already exhibited an excessive accumulation of fat resulting in overweight at an age of twenty-six days. A few days later the concentration of serum immunoreactive insulin was raised and then continuously increased until about six months of age. Subsequently there was a gradual decline to the levels observed in the lean litter mates. Serum glucose values above those of the lean controls were first observed at about one month of age. There was a subsequent increase of the blood sugar values until the mice were three-months old, when the mean value was above 300 mg. per 100 ml. The level then decreased until in seven-months-old obese mice it did not differ from that in the lean litter mates. The concentration of serum free fatty acids of the obese mice was not significantly different from that of their lean litter mates, a decrease with age being observed for both types. In the old obese mice there was a fall also in the body weight to approximately normal levels. Administration of insulin to the genetically future-obese mice displayed a higher insulin tolerance as reflected in a slower decrease of the blood sugar level at an age of twenty-seven days. The ability of these mice to resist insulin-induced convulsions was tried as a method for an early identification of individual future-obese mice. It was, however, not possible to classify the mice completely into two genetically different groups at twenty-three to twenty-five days of age, although this test turned out to be fairly reliable. Glucose tolerance tests at the same early age were also found to be less useful. Only in four-months-old, obese-hyperglycemic mice did an intraperitoneal glucose load result in a slower return of the blood sugar level to the pre-injection value. The present findings indicate a triphasic development of the obese-hyperglycemic syndrome. After an initial asymptomatic period lasting for the first twenty-three to twenty-six days of life, the various manifestations of the syndrome appear in the course of a few days. The subsequent period is characterized by increasing serum glucose and insulin concentrations and coincides approximately with the time of rapid gain in body weight. After the body growth ceases the abnormalities associated with the syndrome gradually disappear. The pattern of development of the syndrome is compatible with the view that diabetogenic factors are active during a limited period early in the life of the homozygous mice.

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*Yu, Ts'ai-Fan; Berger, Lawrence; and Gutman, Alexander B.* (Dept. of Med., Mt. Sinai Sch. of Med., New York, N. Y.): HYPOGLYCEMIC AND URICOSURIC PROPERTIES OF ACETOHEXAMIDE AND HYDROXYHEXAMIDE. Metabolism *17*:309-16, April 1968.

Acetohexamide and its chief metabolite, hydroxyhexamide, have distinct uricosuric as well as hypoglycemic effects. The latter action is attributed to its metabolic influence on the beta cells of the pancreas while the uricosuria properties depend upon a renal tubular effect described as inhibition of tubular absorption of uric acid. Dissociation of these properties of the agent is manifested in patients with renal impairment in whom hypoglycemia is not associated with uricosuria. Other sulfonylurea agents were devoid of an uricosuric effect. The enhanced excretion rates of uric acid were promoted by both the levo and racemic forms of 1-hydroxyhexamide. The dual action of acetohexamide on both blood sugar and uric acid makes the drug useful in subjects with coexisting diabetes and gout. C.R.S.