concentration on Ca-45 uptake in frog sartorius muscle. J. Cell. Comp. Physiol. 65:385, 1965.

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EDITORIAL

CHANGE IN EDITORS

The Journal DIABETES salutes Dr. Irving Graef in this final issue published under his Editorship. Dr. Graef became Associate Editor in 1956, and succeeded Dr. William C. Stadie as Editor in 1960. During his tenure as Editor, the Journal DIABETES has enjoyed unusual growth for a periodical devoted to a single disorder and its related metabolic problems.

There have been remarkable changes in DIABETES during this period. The number of manuscripts received annually has been ever increasing thus allowing representation of many interests. Of particular note is the acquisition of papers reporting new work in the basic sciences. Dr. Graef has consistently encouraged new ideas and has striven for literary excellence. He has been alert to new developments, particularly abroad, and has featured them in "Brief Notes and Comments" and in editorials.

The Journal thanks Dr. Graef for his untold hours of work, conscientious correspondence with authors, encouragement of the young writer, and development of DIABETES to its present status. The new Editor, Dr. Harvey C. Knowles, Jr., with Dr. David M. Kipnis and Dr. Henry T. Ricketts as Associate Editors, will endeavor to continue publication at the same levels of enthusiasm and excellence set by Dr. Irving Graef.

ABSTRACTS

Angervall, L.; and Säve-Söderbergh, J. (Patholog. Institute and Sahlgrenska Sjukhuset, Univ. of Göteborg, Sweden): MICROANGIOPATHY IN THE DIGESTIVE TRACT IN SUBJECTS WITH DIABETES OF EARLY ONSET AND LONG DURATION. Diabetologia 2:117-22, 1966.

Verbatim Summary. The digestive tract has been examined by light microscopy in seventeen subjects with diabetes of early onset, long duration and with various causes of death, in six "normal" controls and ten controls with uremia and/or hypertension. In the diabetics grave lesions were demonstrated to a large extent in the capillaries and venules of the oral mucosa, and in small arteries and arterioles in the gastrointestinal tract (from the oesophagus to rectum). The capillary and venular lesions were similar to those earlier described in the skin of diabetics. The arterial lesion was characterized by a hyalin, strongly PAS-positive, picrinophilic (eosinophilic), richly fat-containing (sudanophilic) wall thickening accompanied by heavy reduction of the lumen, endothelial atrophy and medial degeneration. Similar arterial lesions were demonstrated in the kidneys, pancreas, liver, spleen, adrenal glands, testes, prostate and ovaries. The study suggests that hypertension was not of essential importance to the development of the arterial lesions. It is assumed that the grave arterial lesion accentuates terminally in the course of diabetes, where final complications such as ischemia and adrenocortical overactivity are of pathogenetic significance.

Anselmino, K. J.; and Hoffmann, F. (Rheinische Landesfrauenklinik Wuppertal, and Evangelisches Krankenhaus, Essen-Werden, W. Germany): THE PANCREATROPHIC (INSULOTROPHIC) PRINCIPLE OF THE ANTERIOR PITUITARY GLAND. Deutsch. Med. Wschr. 91:1401-05, August 1966.

A review of the authors' early experiments regarding the existence of an insulotropic hormone supposedly elaborated by the anterior pituitary gland. They suggest, and quote some circumstantial evidence from the literature, that the active principle is not identical with growth hormone. O.V.S.

Benjamin, Fred; and Casper, Donald J. (Depts. Obstet. and Gynec., Queens Hosp. Center Affiliation and Long Island Jewish Hosp., Jamaica, N.Y.): ALTERATIONS IN CARBOHYDRATE METABOLISM INDUCED BY PROGESTERONE IN CASES OF ENDOMETRIAL CARCINOMA AND HYPERPLASIA. Amer. J. Obst. Gynec. 94:991-96, April 1, 1966.

The effect of a long-acting progestational compound, Dela-

lutin, on eighteen patients with endometrial hyperplasia or carcinoma who had a previously established impaired glucose tolerance curve was studied. In ten out of the eighteen cases, glucose tolerance was improved. The authors postulated that Delalutin increased the peripheral use of the glucose and thus improved the glucose tolerance. E.A.W.

Bleicher, Sheldon J.; Farber, Leonard; Lewis, Arthur; and Goldner, Martin, G. (Metabolic Res. Unit, Dept. of Med., Jewish Hosp. of Brooklyn, and the Dept. of Med., Downstate Med. Center, State Univ. of New York, Brooklyn, N.Y.): ELECTROLYTE-ACTIVATED LIPOLYSIS IN VITRO: MODIFYING EFFECT OF CALCIUM. Metabolism *15*:742-48, August 1966.

A reciprocal effect of sodium and potassium upon spontaneous lipolysis in rat epididymal fat tissue was demonstrated in vitro. Lipolysis was maximal in all K media and decreased with decreasing K and increasing Na concentrations. A biphasic response to K was induced as calcium was added to the media. While Ca did not affect lipolysis in all Na it potentiated the lipolytic effect of small amounts of K in the medium. Neither magnesium nor buffer anions were found to play any role in regulating the basal state of adipose tissue and in directing its response in generally anabolic or catabolic directions. C.R.S.

Buchler, Dolores; and Warren, James C. (Dept. Obstet. and Gynec., Kansas Univ. Sch. of Med., Kansas City, Kan.): EFFECTS OF ESTROGEN ON GLUCOSE TOLERANCE. Amer. J. Obst. Gynec. *95*:479-83, June 15, 1966.

Verbatim Summary. Fourteen women were treated with diethylstilbestrol or norethynodrel with mestranol for thirty days. The oral and intravenous glucose tolerance test was done before and after treatment. Eleven patients had a diabetic oral glucose tolerance curve following treatment. Because the intravenous glucose tolerance curves were normal, it is suggested that the diabetic oral curves may be due to delayed gastrointestinal absorption, although direct data on this point are not available. Patients who display diabetic oral glucose tolerance curves while taking estrogens should be re-examined either with the intravenous test or after discontinuance of estrogen therapy. E.A.W.

Cameron, J. S.; Boyns, D. R.; Jarrett, R. J.; and Keen, H. (Dept. Med., Guy's Hosp., London, England): THE PROPERTIES OF TRICHLORACETIC ACID-ETHANOL EXTRACTS OF HUMAN PLASMA. 1. BIOASSAY AND IMMUNOASSAY OF PLASMA AND EXTRACTS. Diabetologia *2*:86-90, 1966.

Verbatim Summary. Bioassay, using the rat hemidiaphragm and epididymal fat pad preparations, has been performed upon the plasma and upon a TCA-ethanol extract of the plasma of fourteen newly diagnosed diabetics. Immunoassay of the extracts was also carried out. Both bioassay and immunoassay of three pooled TCA-ethanol extracts were performed. Five of thirteen plasmas tested showed insulin-like activity (ILA) on the hemidiaphragm, while all of fourteen tested on the fat pad showed ILA. In contrast, eleven of fourteen extracts revealed considerable amounts of ILA on the hemidiaphragm. Again, all the extracts revealed ILA upon the fat pad. Immunoreactive insulin was found in all extracts, but the levels of "insulin" measured by this method were much lower than those measured by the fat pad assay. No extract showed significant antagonism to the effects of added insulin (1 mu/ml. on the hemidiaphragm. Two of the pooled extracts contained very large amounts of both bioassayable and immunoreactive insulin. No one of the three, however, in our experiments, showed any significant antagonism to the effects of added insulin on the hemidiaphragm.

Cameron, J. S.; Boyns, D. R.; Jarrett, R. J.; and Keen, H. (Dept. Med., Guy's Hospital, London, England): THE PROPERTIES OF TRICHLORACETIC ACID-ETHANOL EXTRACTS OF HUMAN PLASMA. 2. PHYSICAL, CHEMICAL AND IMMUNOLOGICAL PROPERTIES OF THE EXTRACTS. Diabetologia *2*: 91-95, 1966.

Verbatim Summary. The insulin-like activity (ILA) of TCA-ethanol extracts, prepared from the plasma of normal subjects was compared with that of crystalline insulin. Dose-response curves were obtained for the glucose uptake and C-14-glucose incorporation into lipid of the epididymal fat pad and the glucose uptake of the rat hemidiaphragm. For each of these, the dose-response relationship of the ILA of the extract approximated to that of crystalline insulin. The stimulation of C-14-glucose incorporation into lipid by the extracts and by crystalline insulin was suppressed by 10^{-4}M n-ethylmaleimide. Antiserum to ox-insulin from guinea pigs, which completely suppressed the effect of human and bovine crystalline insulin, had no effect upon the ILA of eight extracts and induced a small but statistically significant reduction in the ILA of four extracts. Studies were also performed, using gel filtration by Sephadex G. 200, on extracts prepared from the plasma of both normal and diabetic individuals, and upon three pooled TCA-ethanol extracts. In each case, the extract showed two peaks of elution of protein, the second being identical with that of I-125-labeled human albumin. The first peak corresponded to an apparent molecular weight of 300,000-1,000,000. Despite the difference in molecular weight, the properties of the two eluates were similar when compared by electrophoresis and by immuno-electrophoresis. Assay of the column eluate showed that both nonsuppressible ILA and immunoreactive insulin were nonsuppressible. ILA and immunoreactive insulin were present throughout the whole range of elution. The findings are discussed with reference to the phenomenon of insulin-like activity and of synalbumin antagonism.

Carlson, L. A.; and Östman, J.: PLASMA B-HYDROXYBUTYRIC ACID RESPONSE TO NICOTINIC ACID-INDUCED PLASMA FREE FATTY ACID DECREASE IN MAN. Diabetologia *2*:127-29, 1966.

Verbatim Summary. Nicotinic acid was in acute studies administered to four patients with untreated juvenile diabetes and to four obese fasting patients. In all cases the plasma level of FFA decreased. This was soon followed by a decrease in plasma B-hydroxybutyric acid. The effects were less prompt and pronounced in the obese fasting subjects. There were lesser changes in the concentration of blood glucose.

Dettwyler, W. (Dept. Exper. Med., Guy's Hospital, London, England): SOME ASPECTS OF ZINC METABOLISM IN DIABETICS. Diabetologia *2*:75-81, 1966.

Verbatim Summary. Gel filtration offers new possibilities for studying labeled zinc fixation on plasma proteins. This heavy metal has a great affinity to protein, but its binding is reversible under the effect of *p*H and chelating substances (Versenate, Penicillamine). The existence of endogenous chelating substances as well as the chelating effect of alloxan are

not confirmed. Owing to an appropriate dose of Versenate, it is possible to obtain a chelating effect of 50 per cent of labeled zinc, which defines a zinc fixation index on plasma proteins. Comparing plasma of normal and diabetic subjects decompensated and not yet treated, it is possible to show evidence of a higher fixation in diabetics. This higher fixation capacity is probably the result of an increase in globulin fractions fixing zinc strongly, but it is not possible to assess whether it is a primary or a secondary phenomenon to diabetes. It is known that proteinuria appears very early, even contemporary to the onset of diabetes and its importance seems quite sufficient to explain zincuria which is increased in diabetics badly decompensated.

Drachman, Robert H.; Root, Richard K.; and Wood, W. Barry, Jr. (Dept. of Microbiology, The Johns Hopkins Univ. Sch. of Med., Baltimore, Md.): STUDIES ON THE EFFECT OF EXPERIMENTAL NONKETOTIC DIABETES MELLITUS ON ANTIBACTERIAL DEFENSE. I. DEMONSTRATION OF A DEFECT IN PHAGOCYTOSIS. J. Exp. Med. *124*:227-40, August 1966.

Alloxan diabetic rats injected intrabronchially with Type 25 pneumococci suspended in mucin exhibited a greater mortality than nondiabetic animals. Alveolar exudates showed increased numbers of bacteria and depressed phagocytosis due to the osmotic action of glucose on leukocytes. Other sugars produced a similar effect when added in equivalent concentration to pooled normal rat serum. Since no immunological disturbance has been demonstrated in nonacidotic diabetics, it is concluded that chronic hyperglycemia impairs resistance to bacterial infection and should therefore be controlled. A.R.C., JR.

Editorial. THE WHERE AND HOW OF INSULIN. Lancet *2*: 427-28, August 20, 1966.

Two concepts regarding the role of insulin action at the molecular level are discussed. S. P. Bessman hypothesizes that insulin is anabolic, is not indispensable, acts intracellularly and does not need a membrane for its effect. He proposes that the insulin molecule forms a mechanical bond between the mitochondrion and muscle hexokinase or liver glucokinase. By doing so, it brings the enzyme into closer juxtaposition to the site of generation of adenosine triphosphate. This arrangement could thus promote both the phosphorylation of glucose and prevent the mitochondrial electron-transport chain from being choked by accumulating adenosine triphosphate. The Bessman hypothesis emphasizes that the spatial arrangement of enzymes and substrates is crucial to hormonal action. A different approach to insulin action is advanced by Dormandy and Zarday. They showed that when insulin was added to suspensions of red blood cells in simple electrolyte solutions it brought about immediate extracellular *p*H and redo-potential swings and ion shifts between cells and media. This response points to a change in the cell-extracellular interface rather than an interference with intracellular activity. Accordingly, insulin may act as a metabolic regulator whose prime function is to set the redox-potential gradient of interfaces. T.G.S.

Fineberg, S. K. (Diabetes and Obesity-Diabetes Clinics, Harlem Hosp., New York, N.Y.): APPLICATION OF NEWER CONCEPTS IN DIABETES. J. Amer. Geriat. Soc. *14*:463-71, May 1966.

The author defines diabetes mellitus as being due to lack of effective insulin action and discusses possible causes of the ineffective insulin in three theories: (1) Excessive binding of free insulin into inactive complexes by an antagonistic substance. (2) An upset in the homeostatic mechanism normally regulating the balance between active free insulin and inactive bound form of circulating insulin. (3) An enzymatic defect in the biosynthesis of insulin with the compensatory overproduction of an abnormal form which is biochemically less active.

He asserts that the obese diabetic becomes obese because he is diabetic rather than becoming diabetic because he is obese and states that the circulating insulin in the obese subject is an abnormal insulin in that its effect on the transfer of glucose into the cell is impaired but is quite normal in its effect on the conversion of carbohydrate into fat and the enhancement of fat storage. He suggests that the obese diabetic patient be treated first of all with a basic reducing diet and nutrition education, followed if necessary by anorexigenic agents and later by phenformin and then phenformin plus chlorpropamide, if earlier regulation has not been established. Chlorpropamide plus phenformin is further advised as a good therapeutic combination for use in insulin resistance and it is suggested that steroids should be added if these agents prove to be more successful than insulin but not totally satisfactory in the treatment of the patient with insulin resistance.

Comment. Proof that the insulin found in the obese subject is an abnormal molecule is not available, thus one should hesitate to draw this conclusion. Furthermore, it is important to distinguish the obese insulin-resistant patient from the nonobese in that the former is far more likely to respond to caloric restriction than to any agent, whereas the nonobese individual with a high insulin antibody titer will frequently respond to a change from beef to pork or dealanated pork insulin rather than requiring steroid therapy. B.R.B.

Franckson, J. R. M.; Malaise, W.; Arnould, Y.; Rasio, E.; Ooms, H. A.; Balasse, E.; Conard, V.; and Bastenie, P. A. (Med. Clin. Lab. of Exper. Med., Univ. of Brussels, Belgium): GLUCOSE KINETICS IN HUMAN OBESITY. Diabetologia *2*:96-103, 1966.

Verbatim Summary. The kinetics of glucose utilization have been studied in 325 normal subjects, and 150 obese patients free from diabetes or other endocrine diseases. The investigation included measurements in the basal state by isotope dilution technic, determinations of glucose utilization rate induced by endogenous insulinic response (intravenous glucose load and tolbutamide) and by administration of various doses of exogenous insulin. Results showed that whatever the test used, the disappearance rate constants (slope values or fractional disappearance rate) and the total uptakes (absolute value) of the obese patients were systematically lower than the corresponding values in the normal subjects. This metabolic abnormality is not favored by aging, but is not due to a diminished ability of the pancreas to release insulin: basal levels of plasma insulin and rises induced by glucose and by tolbutamide were significantly higher in obese patients. The deficiency is better revealed by increasing the utilization rate by insulinic stimulation: the greater the slope value, the larger the impairment. In fact, there is a straight line relationship showing direct proportionality between the impairment of the glucose utilization rate constant and the velocity of the process,

irrespective of the amount of insulin present or added. This feature strongly suggests in human obesity that the metabolic disturbance primarily affects the glucose uptake process itself rather than the action of insulin.

Gelb, Alvin M. (Div. of Gastroenterology, Dept. of Med., The Mount Sinai Hosp., New York, N.Y.): EFFECT OF HYPOPHYSECTOMY, THYROIDECTOMY, ADRENALECTOMY AND ALLOXAN DIABETES ON INCORPORATION OF FATTY ACIDS INTO ESTERS BY THE SMALL INTESTINE IN VITRO. Metabolism 15:707-13, August 1966.

The influence of various hormones upon incorporation of C-14 myristic acid into esters by the small intestine of rats or hamsters was investigated in vitro. Alloxan diabetes produced a slight increase in incorporation of fatty acid to ester unrelated to the height of blood sugar. Glucose and insulin added to the incubation medium did not affect the incorporation in alloxan diabetic animals. Hypophysectomy and thyroidectomy produced an increase in incorporation. These alterations were reversed by cortisone and/or thyroid hormone but not by growth hormone in the hypophysectomized animals. Desiccated thyroid given to intact hamsters caused a slight decrease in incorporation while adrenalectomy, cortisone and epinephrine had no effect. C.R.S.

Gomez-Acero, José; Lopez-Quijada, Clemente; and R-Candela, José Luis (Instituto G. Marañon, Consejo Superior de Investigaciones Científicas, Madrid, Spain): FINE STRUCTURE OF B CELL FROM PANCREAS PIECES INCUBATED IN VITRO. Diabetologia 2:110-16, 1966.

Verbatim Summary. Pieces of the tail of the rabbit pancreas were incubated in a shaking incubator with Ringer solution supplemented with glucose (0.6 mg./ml.), pyruvate, fumarate and glutamate (5 mM each), in a gas phase of 95 per cent O_2:5 per cent CO_2 at 38° C. There were no significant changes in the fine structure of the islet cells attributable to the incubation. Combined glutaraldehyde and osmium fixation of such incubated slices gave good preservation of the secretory products of the B cells. The mechanisms of degranulation and regranulation of the B cells were observed to be the same as those reported for the animal in vivo. The intensity of secretion differed depending upon whether the animals were killed after being knocked unconscious or after being injected with a lethal dose of anesthesia. B-cell secretion was more prominent in the former case. The method is considered to be valid for further studies on the mechanism of granule release and synthesis in the pancreas of rabbits.

Jackson, Ivor M. D.; Hassan, Tarek H. A.; Prentice, Colin R. M.; and Browning, Margaret C. K. (Depts. of Endocr. and Steroid Biochem., Royal Infirmary, Glasgow, C.4, Scotland): INSULIN-INDUCED HYPOGLYCEMIA AS A TEST OF PITUITARY-ADRENAL FUNCTION IN THYROTOXICOSIS. J. Clin. Endocr. 26:545-49, May 1966.

Verbatim Summary. The insulin tolerance test was performed in ten patients before and after treatment of thyrotoxicosis. Plasma cortisol was measured in response to the insulin-induced hypoglycemia. As a group, no definite abnormality of pituitary-adrenal function was found, but some individual cases demonstrated impaired cortisol responses, suggesting that in severe stress steroid therapy may be necessary in certain hyperthyroid patients. Although fasting blood sugar levels were significantly elevated prior to treatment, following the onset of euthyroidism there was no alteration in the insulin sensitivity, which was normal. O.V.S.

Julkunen, Heljo; Kärävä, Risto; and Viljanen, Veikko (Second Med. Clin., and Roentgen Diagnostic Inst., Univ. of Helsinki, Helsinki, Finland): HYPEROSTOSIS OF THE SPINE IN DIABETES MELLITUS AND ACROMEGALY. Diabetologia 2:123-26, 1966.

Verbatim Summary. A series of 658 patients routinely examined in a medical clinic was studied for senile ankylosing hyperostosis of the spine. The disease was diagnosed from lateral views of the thorax, typical bridges between the vertebrae being regarded as the criterion. A total of 510 patients had diabetes mellitus, and hyperostosis was detected in 13 per cent of these. In the range 60-69 yrs. there was a very significant difference between 122 diabetics and 148 nondiabetics in regard to the occurrence of hyperostosis. In a series of twenty-one patients with acromegaly hyperostosis was detected in six cases. Eight patients were over 50 yrs. old. Of these, four showed hyperostosis and two of the latter had diabetes. The results seem to indicate that the growth hormone may play a part in the development of hyperostosis. This observation is significant also from the standpoint of clinical practice.

Klein, Joseph P. (Dept. of Pediat., Univ. of Oregon Med. Sch., Portland, Ore.): DIPHENYLHYDANTOIN INTOXICATION ASSOCIATED WITH HYPERGLYCEMIA. J. Pediat. 69:463-65, September 1966.

This case report describes a twenty-month old male infant suffering from pharyngitis and febrile grand mal seizures who inadvertently was given at least 800 mg. of diphenylhydantoin elixir over a twenty-four hour period at home. Lethargy progressing to coma with additional seizures during the next three days led to hospitalization and discovery of the error.

Admission laboratory studies of note were a cerebrospinal fluid glucose level of 185 mg. per 100 ml. and a moderate depression of the serum potassium and bicarbonate. A blood glucose level determined eighteen hours later was 726 mg. per 100 ml., and the hyperglycemia responded promptly to a single dose of 20 U. insulin. A week later, after the child had recovered, both standard and cortisone glucose tolerance tests were normal.

Although the case is complicated by seizures and administration of other medications and parenteral fluids containing glucose before the first specimen for blood glucose level was obtained, the author gives reasons for believing the hyperglycemia was due to diphenylhydantoin toxicity. R.K.K.

Kopetz, K.; Bürgi, H.; Froesch, E. R.; and Schwarz, K. (II. Medizinische Klinik der Universität München und Stoffwechselabteilung der Medizinischen Klinik der Universität Zürich): THE DEGRADATION OF INSULIN BY THE ISOLATED RAT LIVER PERFUSED WITH RAT SERUM AND LEUCINE. Diabetologia 2: 104-09, 1966.

Verbatim Summary. (1) Isolated rat livers were perfused with a semisynthetic medium containing diluted rat serum to see whether or not the rat liver can convert crystalline rat insulin into nonsuppressible insulin-like activity. The influence of L-leucine on the clearance of insulin by the perfused liver was studied in the same perfusion system. (2) Nonsuppressible ILA was not found in the perfusion fluid, even after prolonged perfusion of the liver with crystalline rat insulin. (3) The clearance of insulin by the liver was not changed by the addition of L-leucine (approximately 60 mg. per cent) to the perfusion fluid. (4) The specific liver clearances for crystalline insulin were almost identical under the

three experimental conditions studied. The perfused isolated rat liver appears to be a good model for the study of the hepatic degradation of insulin.

Lefebvre, P. (Institute of Med., Univ. of Lieges, Lieges, Belgium): THE PHYSIOLOGICAL EFFECT OF GLUCAGON ON FAT-MOBILISATION. Diabetologia 2:130-32, 1966.

Verbatim Summary. In normal dogs under pentobarbital anesthesia, intraportal infusion of physiological doses (0.002 μg./kg./min.) of cystein-treated glucagon increases markedly the plasma FFA levels in the peripheral blood. This can be considered as an argument for a possible role of glucagon as a physiological regulator of lipid metabolism.

Lynch, Henry T.; Kaplan, Arnold R.; Henn, Mary J.; and Krush, Anne J. (Eppley Inst. for Res. in Cancer and Allied Dis., Univ. of Nebraska Coll. of Med., Omaha, Neb.; Cleveland Psychiatric Inst., Cleveland, O.): FAMILIAL COEXISTENCE OF DIABETES MELLITUS, HYPERLIPEMIA, SHORT STATURE, AND HYPOGONADISM. Amer. J. Med. Sci. 252:323-30, September 1966.

A report of two male patients, ten and fourteen years of age, with juvenile diabetes, dwarfism, hyperlipemia and secondary hypogonadism. The genetic aspects of this syndrome were investigated in thirty-six individuals in three generations of the kindred who showed some of these features and also milder late-onset diabetes in four. The genetic aspects of diabetes mellitus are discussed in general as well as in the light of the present study. S.B.B.

McCann, Michael L.; Adams, Peter A. J.; Likly, Beverly F.; and Schwartz, Robert (Dept. of Pediat., Western Reserve Univ. Sch. of Med. at Cleveland Metropolitan Gen. Hosp., and Babies and Childrens Hosp., Cleveland, Ohio): PREVENTION OF HYPOGLUCOSEMIA BY FRUCTOSE IN INFANTS OF DIABETIC MOTHERS. New Engl. J. Med. 275:8-12, July 7, 1966.

Fructose was administered to infants of diabetic mothers after delivery. Hypoglucosemia and associated symptoms were prevented or alleviated in these infants. A fructose regimen for initial management of infants of diabetic mothers is suggested. Fructose may be preferable to glucose therapy because rebound hypoglucosemia does not occur. B.R.B.

McCann, Michael L.; Chen, Chiung Hui; Katigbak, Edgardo B.; Kotchen, Jane M.; Likly, Beverly F.; and Schwartz, Robert (Depts. of Pediat. and Obstet. and Gynec., Western Reserve Univ. Sch. of Med. at Cleveland Metropolitan Gen. Hosp., and Babies and Childrens Hosp., Cleveland, Ohio): EFFECTS OF FRUCTOSE ON HYPOGLUCOSEMIA IN INFANTS OF DIABETIC MOTHERS. New Engl. J. Med. 275:1-7, July 7, 1966.

Studies of carbohydrate metabolism in fifty-six pregnant diabetic mothers and their infants as compared to sixty normal mothers and their infants indicated a spectrum of carbohydrate intolerance in these mothers directly proportional to the degree of hypoglucosemia in the infant; in infants of mothers with both gestational (noninsulin-dependent) and insulin-dependent diabetes chemical hypoglucosemia might develop. Fructose administration to the mother, and thereby, transplacentally to the baby, significantly altered glucose metabolism and prolonged normoglucosemia in infants of diabetic mothers. Direct administration of fructose to the infant elevated the blood glucose level in infants of diabetic mothers; fructose, as well as glucose, was utilized more rapidly in infants of diabetic mothers than in normal infants. This difference appears to be independent of type of delivery, hypoglucosemia or hyperglucosemia, exogenous insulin and previous administration of fructose to the mother. B.R.B.

Merimee, T. J.; Burgess, J. A.; and Rabinowitz, D. (The Johns Hopkins Univ. Sch. of Med., Baltimore, Md.): SEX-DETERMINED VARIATION IN SERUM INSULIN AND GROWTH HORMONE RESPONSE TO AMINO ACID STIMULATION. J. Clin. Endocr. 26:791-93, July 1966.

Arginine was infused into nine male and nine female subjects. Insulin and growth hormone concentrations were followed in serum by standard radioimmunoassays. The elevation of insulin and growth hormone levels was greater in females than in males. The rise of growth hormone concentration, but not that of insulin concentration, could be enhanced by treating male subjects with Stilbestrol. It is suggested that estrogens may sensitize the pituitary or hypothalamus to normal growth hormone-releasing stimuli. O.V.S.

Miki, Eishi; Like, Arthur A.; Soeldner, J. Stuart; Steinke, Jurgen; and Cahill, George F., Jr. (Elliott P. Joslin Res. Lab., Depts. of Med. and Path., Harvard Med. Sch.; the Peter Bent Brigham Hosp.; and the Diabetes Foundation, Inc., Boston, Mass.): ACUTE KETOTIC-TYPE DIABETIC SYNDROME IN SAND RATS (PSAMMOMYS OBESUS) WITH SPECIAL REFERENCE TO THE PANCREAS. Metabolism 15:749-60, August 1966.

Sand rats, fed Purina laboratory chow and deprived of mixed vegetables, developed an acute ketotic-type diabetic syndrome. Hyperglycemia observed in these animals was associated with elevated serum insulin and reduced extractable pancreatic insulin. A later fall in serum insulin levels was attributed to pancreatic islet cell exhaustion. The beta cells revealed by electron microscopy evidence of degranulation, enhanced protein synthesis and glycogen infiltration prior to a reduction in serum insulin levels. C.R.S.

Niemeyer, Hermann; Pérez, Norma; and Rabajille, Eliana (Instituto de Quimica Fisiologica y Patológica, Borgnoño, Santiago, Chile): INTERRELATION OF ACTIONS OF GLUCOSE, INSULIN, AND GLUCAGON ON INDUCTION OF ADENOSINE TRIPHOSPHATE: D-HEXOSE PHOSPHOTRANSFERASE IN RAT LIVER. J. Biol. Chem. 241:4055-59, Sept. 10, 1966.

The level of this enzyme (glucokinase) in the livers of rats fed on a carbohydrate-free diet is not increased by exogenous insulin which also does not accelerate its induction by glucose. Glucagon, however, prevents induction of glucokinase, an effect which is also not prevented by insulin. Evidence is presented to suggest that glucose and glucagon act as inducer and repressor of the enzyme, insulin acting possibly as a permissive agent. P.H.W.

O'Sullivan, John B.; Gellis, Sydney S.; Dandrow, Robert V.; and Tenney, Benjamin O. (Prenatal Metabolic Clinic and Depts. of Pediat. and Obstet. and Gynec., Boston City Hosp. and Boston Univ. Sch. of Med., Div. of Chronic Diseases, U.S. Public Health Serv., and Dept. of Obstet. and Gynec., Harvard Med. Sch., Boston, Mass.): THE POTENTIAL DIABETIC AND HER TREATMENT IN PREGNANCY. Obst. Gynec. 27:683-89, May 1966.

Verbatim Summary. (1) A total of 615 women shown to have abnormal glucose tolerance in pregnancy were randomly assigned to one of two categories: the positive treated, who received diet and insulin management; and the positive controls, who received routine obstetrical care. Negative controls, 328 patients who were also receiving routine obstetrical care,

were selected at random from the same clinics. Tests indicated that these negative controls had normal glucose tolerance. The evidence that designated the positive groups as potential diabetics is discussed. (2) The outcome of pregnancies revealed a significantly increased number of viable fetal losses in the women who had abnormal glucose tolerance. The lack of significant improvement in the number of viable losses following insulin and diet treatment is discussed in relation to the intensity of this treatment and its failure to effect a meaningful reduction in postprandial blood sugar levels. (3) Among the potential diabetics in the treated group, the number of higher birth weights approximated the normal range. The mechanism effecting this reduction is considered to be related to the significant lowering of postabsorptive blood sugar levels. E.A.W.

Parry, D. G.; and Taylor, K. W. (Dept. of Med. and Diabetic Dept., King's Coll. Hosp., London, England): THE EFFECTS OF SUGARS ON INCORPORATION OF (^{3}H) LEUCINE INTO INSULINS. Biochem. J. *100*:2c-4c, July 1966.

Glucose and mannose, but not galactose, stimulate incorporation of leucine into insulins formed by slices of bovine and rabbit pancreas incubated for three hours in a bicarbonate buffer. Incorporation is increased when the concentrations of these active sugars are raised from 25 to 250 mg. per 100 ml., occurs in the A chain, and is inhibited by mannoheptulose. Insulin synthesis, like insulin secretion, may depend upon further metabolism of glucose phosphates within the islet cells and hence upon energy production from glucose. This stimulant effect of glucose may prevent undue depletion of pancreatic insulin during periods of maximal stimulation of the islet tissue. P.H.W.

Rabinowitz, D.; Merimee, T. J.; Maffezzoli, R.; and Burgess, J. A. (Dept. of Med., Johns Hopkins Sch. of Med., Baltimore, Md.): PATTERNS OF HORMONAL RELEASE AFTER GLUCOSE, PROTEIN, AND GLUCOSE PLUS PROTEIN. Lancet *2*:454-56, Aug. 27, 1966.

The effects of a mixed meal consisting of 0.45 kg. of steak and 100 gm. of glucose on serial concentrations of immunoreactive insulin (IRI) and human growth hormone (HGH) were compared to the effects of the steak or glucose alone in eight healthy women. Steak ingestion alone caused almost no change in glucose, a slight rise in IRI and a moderate rise in HGH. Glucose alone caused an early rise in IRI which peaked at one to two hours and a delayed rise in HGH which peaked at two to five hours. Ingestion of glucose plus protein caused only a modest rise in blood sugar, a marked rise in IRI and an increment in HGH which was less than that seen with either glucose or steak alone. The levels of IRI observed after protein and carbohydrate together suggest that amino acids and glucose act synergistically to stimulate insulin release. The enhancement of insulin probably accounts for the smaller glucose increase. The addition of protein to a glucose load appears to blunt the HGH response seen after carbohydrate alone and could be associated with a metabolic pattern which is associated with increased triglyceride synthesis. T.G.S.

Sharkey, Thomas P. (Ohio State Univ. Coll. of Med., Columbus, Ohio, and Miami Valley Hosp., Dayton, Ohio): RECENT RESEARCH DEVELOPMENTS IN DIABETES MELLITUS—PART I AND PART II. J. Amer. Dietet. Ass. *48*:281-87 and 288-93, April 1966.

A summary of recent research developments related to diabetes mellitus and carbohydrate metabolism presented in two sections. R.F.B.

Vecchio, D.; Luyckx, A.; Zahnd, G. R.; and Renold, A. E. (Institut de Biochimie Clinique, Université de Genève, Geneva, Switzerland; and Laboratoire de Recherche de la Policlinique universitaire médicale Hôpital Cantonal, Geneva, Switzerland): INSULIN RELEASE INDUCED BY GLUCAGON IN ORGAN CULTURES OF FETAL RAT PANCREAS. Metabolism *15*:577-81, July 1966.

The injection of glucagon in man results in an elevation of plasma insulin independent of the rise in arterial blood glucose. This observation was further investigated using pancreatic explants from rats cultivated over four days, then incubated in the presence of various concentrations of glucagon. The latter hormone evoked a clear-cut, dose-dependent release of insulin from the explants. These and other studies point to a new concept of the physiologic interrelations between the two pancreatic hormones. C.R.S.

Whitehouse, Fred W., and Clearly, William J., Jr. (Dept. of Med., Henry Ford Hospital, Detroit, Mich.): DIABETES MELLITUS IN PATIENTS WITH GOUT. JAMA *197*:73-76, July 11, 1966.

Two groups of patients with gout are reported. First, the clinical features of eighty-nine patients with clinical gout, aged thirty to eighty-four years, were analyzed for occurrence of diabetes diagnosed by symptoms (twenty-four patients), screening blood sugar levels (fifty-two patients), or glycosuria (twelve patients). A prevalence of 10 per cent diabetes was found. Of these, 83 per cent were insulin-independent, and 27 per cent were normal or below normal in weight. Secondly, a prospective study of 226 patients with clinical gout was made. The patients were tested two hours after a 100 gm. carbohydrate meal (181 patients) or 100 gm. glucose solution (forty-five patients). Of these, 6 and 33 per cent respectively had abnormally elevated (over 140 mg. per 100 ml., AutoAnalyzer) blood sugar levels. The relationship between diabetes, gout, and obesity is discussed. S.B.B.

Wray, H. Linton; and Winegrad, Albert I. (George S. Cox Med. Inst. and Dept. of Med., Univ. of Pennsylvania, Philadelphia, Pa.): FREE FRUCTOSE IN HUMAN CEREBROSPINAL FLUID. Diabetologia *2*:82-85, 1966.

Verbatim Summary. The presence of free fructose in human cerebrospinal fluid has been demonstrated by enzymatic analysis and high voltage paper electrophoresis. In thirty-nine of forty patients the cerebrospinal fluid fructose concentration exceeded that in plasma. A linear correlation ($r = +0.88$) was observed between cerebrospinal fluid fructose and glucose concentrations. Present evidence suggests that neural tissues are the source of cerebrospinal fluid fructose, and that fluctuations in cerebrospinal fluid fructose concentration mirror fluctuations in the neural concentrations of this hexose. These observations suggest that increased activity of the sorbitol pathway may exist in the neural tissues of patients with diabetes mellitus similar to that recently observed in tissue from animals with experimental diabetes.