Its application to the measurement of rate of insulin disappearance. Diabetologia 6:581-85, 1970.

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ABSTRACTS

Antar, M. A.; Little, J. A.; Lucas, C.; Buckley, G. C.; and Csima, A. (Dept. of Med., Dietetics, Biochem., Epidemiology, and Biometrics, St. Michael's Hosp., Univ. of Toronto, Toronto, Ontario, Canada): INTERRELATIONSHIP BETWEEN THE KINDS OF DIETARY CARBOHYDRATE AND FAT IN HYPERLIPOPROTEINEMIC PATIENTS. 3. SYNERGISTIC EFFECT OF SUCROSE AND ANIMAL FAT ON SERUM LIPIDS. Atherosclerosis 11:191-201, March-April 1970.

Verbatim summary. Fifteen hyperlipoproteinemic patients (9 type II, 4 type III or IV, and 2 type V) were fed formula diets which simulated a typical North American diet for two, twenty-eight day periods. Total carbohydrate, fat and protein constituted 50, 35 and 15 per cent of calories respectively. The diets were high in saturated fat (P:S = 0.1) and cholesterol (310 mg./1000 calories). Substitution of 40 per cent of calories as sucrose for starch resulted in higher serum cholesterol, phospholipid and triglyceride levels in all patients. The mean increases were highly significant ($P < 0.001$, < 0.001 and < 0.01, respectively). The differences in serum lipids, especially triglyceride, were more marked for type III, IV or V than for type II patients. In view of our previous results (Parts 1 and 2 of this series) with diets high in polyunsaturated fat and low in cholesterol which showed no uniform hyperlipidemic effect for sucrose, the present findings suggest that there is a synergistic effect between dietary sucrose and animal fat. An explanatory hypothesis is discussed.

Bell, W. E.; Samaan, N. A.; and Longnecker, D. S. (Depts. of Pediat. and Neurol., University Hosp. and V. A. Hosp., Iowa City, Iowa): HYPOGLYCEMIA DUE TO ORGANIC HYPERINSULINISM IN INFANCY. Arch. Neur. 23:330-39, October 1970.

Two cases are presented with onset of hypoglycemia in infancy due to hyperinsulinism. The first child was found to have islet cell hyperplasia and remained hypoglycemic after subtotal pancreatectomy. Diazoxide restored the blood glucose to normal levels and was associated with a reduction in serum insulin content. The second case was found to be markedly leucine-sensitive and operation at age six months revealed an islet cell adenoma. Both children sustained severe brain disease secondary to persistently low blood glucose levels.

Differentiation by laboratory methods of infants with "idiopathic" hypoglycemia from those with islet cell hyperplasia or adenoma remains difficult, if not impossible. Inability to maintain an adequate blood glucose level after a brief trial of medical therapy should warrant surgery, if brain damage is to be prevented. If an adenoma is not identified, subtotal pancreatectomy should be performed. P.M.F.

Curry, Donald L.; and Curry, Katherine P. (Dept. of Physiological Sciences, Sch. of Veterinary Med., Univ. of California, Davis, Calif.): HYPOTHERMIA AND INSULIN SECRETION. Endocrinology 87:750-55, October 1970.

Isolated perfused rat pancreas was used to observe the effect of decreased body temperature on insulin secretion. A direct relationship was found between tissue temperature and the total quantity of insulin release in response to glucose or tolbutamide. By subjecting the pancreas to extreme cold and rewarming to body temperature, it was shown that partial inhibition of insulin release persists for thirty minutes after which normal secretory activity is regained. Hypothermic inhibition occurred in the presence of phentolamine, an alpha adrenergic inhibitor, excluding catecholamine suppression of insulin release as the explanation for this phenomenon. C.R.S.

Debons, Albert F.; Krimsky, Isidore; and From, Annette (Nuclear Med., Veterans Administration Hosp.; and Dept. of Surg., State Univ. of New York, Downstate Med. Center, Brooklyn, N.Y.): A DIRECT ACTION OF INSULIN ON THE HYPOTHALAMIC SATIETY CENTER. Amer. J. Physiol. 219:938-43, October 1970.

Verbatim summary. Diabetic mice, unlike normal mice, do not develop necrosis of the hypothalamic satiety center after administration of gold thioglucose. In previous studies, the rapid action of intravenously administered insulin in restoring the sensitivity of the satiety center of diabetic mice to gold thioglucose suggested that insulin might act directly on the satiety center. In the present studies, the effect of intrahypothalamic injection of insulin on the restoration of the sensitivity of the center to gold thioglucose necrosis was investigated

in diabetic mice. Intrahypothalamic injection of insulin restored the sensitivity of the center. Insulin given by this route does not act by entering the circulatory system, since the effect was obtained in the presence of anti-insulin serum which prevented circulating insulin from acting. It is concluded that insulin can act directly on cells of the satiety center. An important physiological role of insulin in regulation of the satiety center in its control of feeding behavior is indicated.

Goldman, Jack K.; Schnatz, J. David; Bernardis, Lee L.; and Frohman, Lawrence A. (Dept. of Med. State Univ. of New York; and the Veterans Administration Hosp., Buffalo, N.Y.): ADIPOSE TISSUE METABOLISM OF WEANLING RATS AFTER DESTRUCTION OF VENTROMEDIAL HYPOTHALAMIC NUCLEI: EFFECTS OF HYPOPHYSECTOMY AND GROWTH HORMONE. Metabolism *19*:995-1005, November 1970.

Destruction of the ventromedial nuclei in weanling rats results in increased body fat, hyperinsulinemia, decreased growth hormone levels and hypertriglyceridemia with normoglycemia and normal food intake. In these animals glucose oxidation and incorporation into lipid were markedly elevated, while palmitate oxidation was decreased in the adipose tissue. Neither hypophysectomy nor treatment with growth hormone in rats with VMN lesions modified the characteristic changes observed, the origins of which remain a subject for speculation. C.R.S.

Hall, Knowlton, W.; Cravey, Eugene C.; Chen, Ping Tuan; Ostendorff, Martha E.; Hollowell, Joseph G., Jr.; and Thevaos, Theo. G. (Dept. of Biochem. and Pediat., Med. Coll. of Georgia, Augusta, and Gracewood State Sch. and Hosp., Gracewood, Ga.): AN EVALUATION OF GALACTOSURIA. J. Pediat. 77:625-30, October 1970.

Screening tests for galactosuria were performed on 1,200 mentally retarded children after breakfast. Fifty-nine routinely excreted excessive amounts of this sugar on repeated examinations. When the dietary habits of twenty-four of these patients were compared to thirteen with negative excretion, the differences could be attributed mostly to a greater milk intake in the positive group. In another study known galactose loads were administered orally to three subjects with negative tests and to five galactose excreters after an overnight fasting. The correlation of these results with the screening tests performed after breakfast was poor.

Measurements of erythrocyte galactose-1-phosphate uridyl transferase in thirty-seven patients fed controlled amounts of galactose also did not correlate very well with degrees of galactosuria.

It was suggested that screening tests should be performed only after controlled galactose loading in a fasting state followed by more specific assays in suspicious patients. R.K.K.

Little, J. A.; Birchwood, B. L.; Simmons, D. A.; Antar, M. A.; Kallos, A.; Buckley, G. C.; and Csima, A. (Dept. of Med., Dietetics, Biochem., Epidemiology, and Biometrics, St. Michael's Hosp., Univ. of Toronto, Toronto, Ontario, Canada): INTERRELATIONSHIP BETWEEN THE KINDS OF DIETARY CARBOHYDRATE AND FAT IN HYPERLIPOPROTEINEMIC PATIENTS. 1. SUCROSE AND STARCH WITH POLYUNSATURATED FAT. Atherosclerosis *11*:173-81, March-April 1970.

Verbatim summary. Nine hyperlipoproteinemic patients (4 type II, 3 type III-IV and 2 type V) were maintained on various ideal dietary regimens to test the effect of sucrose and starch on serum lipids. In the 4 type II patients, 20 per cent of calories as sucrose was exchanged for starch in cholesterol-free diets containing 65 per cent of calories as corn oil during two, twenty-eight-day periods. This resulted in significantly lower serum cholesterol and phospholipid but no change in triglyceride levels. Using similar diets in two, fifteen-day periods for the type III-IV patients, serum cholesterol and phospholipid were approximately equal while serum triglyceride tended to be slightly higher on sucrose as compared to starch. The two type V patients were fed diets with high carbohydrate (70 per cent of calories) and low fat (10 per cent of calories), partly of animal origin, for two, fifteen-day periods. Substituting sucrose for starch (57 per cent of calories) resulted in higher levels of all serum lipids in one patient and only higher triglyceride in the other. Thus, under the conditions of these experiments sucrose was not definitely hyperlipidemic. However, it is suggested that the effect of sucrose on serum lipids may depend on patient type and on the relative proportions of sucrose and polysaccharide and the kind and amount of accompanying fat in the diet. Indeed, the studies reported in Part 2 and 3 of this series of papers indicate that sucrose in comparison with starch is uniformly hyperlipidemic in diets having large amounts of saturated fat and cholesterol.

Little, John R.; Goto, Masahiro; and Spitzer, John J. (Dept. of Physiol. and Biophysics, Hahnemann Med. Coll. and Hosp., Philadelphia, Pa.): EFFECT OF KETONES ON METABOLISM OF FFA BY DOG MYOCARDIUM AND SKELETAL MUSCLE IN VIVO. Amer. J. Physiol. *219*:1458-63, November 1970.

Verbatim summary. The uptake of β-hydroxybutyrate (β-OHB), acetoacetate (AcAc), and free fatty acids (FFA) by the myocardium and the thigh skeletal muscle of mongrel dogs was measured under control conditions and during the infusion of Na dl-β-hydroxybutyrate. Oxidation of FFA was also determined by continuously infusing palmitate-1-C-14 complexed to human albumin during each experiment and measuring the FFA-C-14 uptake and the CO_2 and C-14-O_2 production. Infusion of the exogenous ketone caused an elevation in the blood levels of both β-OHB and AcAc. A marked uptake of β-OHB and AcAc by myocardium and skeletal muscle was observed, and this was accompanied by a decrease in the rate of FFA uptake and oxidation by both tissues. The specific activity of FFA-C-14 was lower in the venous blood from both tissues than in the arterial blood, indicating release of unlabeled FFA. A small but significant uptake of triglyceride-C-14 by both tissues was observed. Under the present experimental conditions ketones appeared to be the major substrate for the myocardium; if completely oxidized they could have accounted for 83 per cent of the myocardial CO_2 production.

Otsuka, Masanori; and Ohtsuki, Iwao (Dept. of Pharmacol., Faculty of Med., Tokyo Med. and Dental Univ.; Dept. of Pharmacol., Faculty of Med., Univ. of Tokyo, Tokyo, Japan): MECHANISM OF MUSCULAR PARALYSIS BY INSULIN WITH SPECIAL REFERENCE TO PERIODIC PARALYSIS. Amer. J. Physiol. *219*:1178-82, November 1970.

Insulin in a concentration of 0.1-1.1 IU./ml. depressed the twitch contraction of the isolated diaphragm of K-deficient rats with low-K Krebs solution (0-1.2 mM.). The contraction was restored by raising the K concentration in the extracellular fluid $[K]_0$. (Offerijns et al., 1958). The muscle fibers of the diaphragm from K-deficient rats were depolarized by the addition of insulin in low $[K]_0$, and this depolarization was shown to be the cause of the mechanical failure. Resting potential

was restored when $[K]_0$ was raised to normal concentration. The depolarization produced by insulin was abolished when Na in the external medium was replaced by choline. This result suggests that insulin increases the permeability of the muscle membrane to Na under the present experimental condition. There are close similarities between the contraction failure induced by insulin in the K-deficient rat and the paralytic attack in the patients with hypokalemic periodic paralysis. The underlying mechanism of the contraction failure in this disease was discussed. T.J.M.

Pepin, Juan; Singh, Hira; Pairent, Frederick; Appert, Hubert; and Howard, John (Depts. of Surg., Biological Chem., and Physiol., Hahnemann Med. Coll., Philadelphia, Pa.): A STUDY OF INSULIN SECRETION IN THORACIC DUCT LYMPH OF THE DOG. Ann. Surg. 172:56-60, July 1970.

Verbatim summary. Glucose, epinephrine, and glucagon increased slightly the flow of thoracic duct lymph. ACTH had no such effect.

Glucose concentrations during control periods were higher in lymph than in serum. There was a parallel rise in glucose concentration in lymph and serum following glucose, epinephrine and glucagon injection.

Following glucose and glucagon administration, the serum and lymph insulin levels rose. This rise in insulin level synchronized with that of glucose. Insulin levels appeared to be higher in serum than in lymph, which indicates that the pathway of insulin secretion by the pancreas is chiefly via blood.

Neither glucose, epinephrine, glucagon nor ACTH caused any change in amylase and lipase concentration of thoracic duct lymph or of peripheral blood.

Poffenbarger, Phillip L.; Espinosa de los Monteros Mena, Antonio; and Steinke, Jurgen (Dept. of Med., Harvard Univ. Med. Sch. and Peter Bent Brigham Hosp.; the Elliott P. Joslin Res. Labs. and the Joslin Diabetes Foundation, Inc., Boston, Mass.): NONSUPPRESSIBLE INSULIN-LIKE ACTIVITY: IMMUNOCHEMICAL AND PHYSIOCHEMICAL EVIDENCE AGAINST ITS PANCREATIC ORIGIN. Metabolism 19:509-17, July 1970.

Isolated rat pancreatic islets were incubated and the resulting insulin-like activity (ILA) in the medium measured by fat-pad bioassay. Guinea pig anti-insulin serum suppressed ILA activity of the medium. Physiochemical studies and immunochemical characterization of the medium ILA, pancreatic homogenates and extracts failed to demonstrate the presence of any large molecular weight nonsuppressible insulin-like activity (NSILA). Based on these findings it is concluded that the pancreas gland and islets are not sources of circulatory NSILA in the rat. C.R.S.

Rabkin, Ralph; Simon, Norman M.; Steiner, Sheldon; and Colwell, John A. (Dept. of Med., V.A. Research Hosp.; Passavant Memorial Hosp.; Chicago Wesley Memorial Hosp., and Northwestern Univ. Med. Sch., Chicago, Ill.): EFFECT OF RENAL DISEASE ON RENAL UPTAKE AND EXCRETION OF INSULIN IN MAN. New Eng. J. Med. 282:182-87, Jan. 22, 1970.

The authors report on the quantitative uptake and excretion of endogenously secreted insulin by normal and diseased kidney in man at various steady-state plasma glucose and insulin concentrations.

Twenty-one kidneys were studied in thirteen patients nineteen to sixty-two years of age (mean age forty years). Two noninsulin dependent diabetics had biopsy-proved nodular glomerulosclerosis. Nine patients were suspected to have unilateral renal disease and two had undergone diagnostic cardiac catheterization for mitral and aortic valvular disease.

Insulin was assayed using pork insulin standards by the double antibody technic of Morgan and Lazarow except that iodoinsulin I-125 was used in place of I-131. The normal functioning kidney was shown to have a considerable capacity for removing insulin from the blood stream. No significant difference between percentage uptake of insulin in the fasted and glucose-loaded state was observed.

In the mild to moderately diseased kidney, the percentage uptake of insulin and the relation between insulin uptake and arterial insulin concentration was of the same order as that of the relatively normal kidney. The kidney in normal subjects and seven patients with moderate renal insufficiency removed approximately 39 ± 4 per cent of the arterial insulin.

The total amount of insulin uptake by diseased kidneys was reduced because the load carried to the kidneys was smaller owing to impaired renal plasma flow. Reduced insulin uptake of 9 per cent occurred in four patients with severe renal insufficiency, including the two diabetic patients.

In the severely diseased kidney relatively little insulin was removed. No relation between the type of renal disease and the ability of the kidney to extract insulin was noted. It was concluded that not all renal uptake of insulin could be explained by glomerular filtration rate alone. B.R.B.

Reske-Nielsen, Edith; Lundbaek, Knud; Gregersen, Gunnar; and Harmsen, Aage (Dept. of Neuropathology, Second Clinic of Intern. Med. and Dept. G of Neurosurgery, Kommunehospitalet, Aarhus Univ. Sch. of Med., Aarhus, Denmark): PATHOLOGICAL CHANGES IN THE CENTRAL AND PERIPHERAL NERVOUS SYSTEM OF YOUNG LONG-TERM DIABETICS. Diabetologia 6:98-103, 1970.

Verbatim summary. Muscle biopsies were studied from sixteen juvenile, long-term diabetics. Most of the patients had severe retinopathy, but clinical signs of other forms of angiopathy and neuropathy were either absent or mild. The biopsies revealed severe degeneration as well as ineffective regenerative changes of the terminal nerve fibers and endorgans.

Roberts, William C.; Levy, Robert I.; and Frederickson, Donald S. (Sect. of Path. and Molecular Disease Branch, National Heart and Lung Inst. N.I.H., Bethesda, Md.): HYPERLIPOPROTEINEMIA. Arch. Path. 90:46-56, July 1970.

Verbatim summary. The five types of hyperlipoproteinemia (HLP) are reviewed, and autopsy findings in a patient with type 3 are presented for the first time. Atherosclerosis of the coronary arteries and aorta is accelerated in patients with types 2, 3, 4 and possibly 5. The atherosclerosis plaques in the coronary arteries in patients with types 2 and 4 are usually of the complicated variety, but may consist predominantly of foam cells and fibrous tissue in type 3. Type 2 and 4 patients respond poorly to therapy, whereas type 3 patients respond favorably; this difference may be due to the types of atherosclerotic plaques. Nonspecific foam cells may occur in the spleen, liver, lymph nodes, and bone marrow in any patient with hypertriglyceridemia which includes types 1, 3, 4, or 5.

Sperling, Mark A.; Kenny, Frederic M.; and Drash, Allan L. (The Children's Hosp. of Pittsburgh and The Dept. of Pediat. of The Univ. of Pittsburgh School of Medicine, Pittsburgh, Pa.): ARGININE-INDUCED GROWTH HORMONE RESPONSES IN CHILDREN: EFFECT OF AGE AND PUBERTY. J. Pediat. 77:462-65, September 1970.

Plasma immunoreactive growth hormone (HGH) responses to intravenous arginine infusion were assessed in three studies of pediatric patients. In the first investigation, fifty-six children of both sexes were subdivided into five groups according to age. The entire age range was between three months and sixteen years. No significant differences existed among the five groups with respect to HGH responses measured during a sixty minute period after completion of the infusion.

However, in a second investigation, HGH responses of six pubertal boys and six pubertal girls were compared to those of thirteen prepubertal children selected from the same group. In this instance no differences existed between HGH levels of pubertal boys and prepubertal children, but pubertal girls had significantly higher responses.

In a third study HGH responses of pubertal menstruating girls were compared to pubertal nonmenstruating girls. The latter group had significantly lower plasma HGH concentrations thirty minutes after completion of the arginine infusion.

These studies indicate that age has little influence on arginine-stimulated HGH release from the hypophysis in pediatric patients. Sexual maturity of girls, in contrast to boys, enhances HGH release and is apparently related to greater estrogen effects in this group. R.K.K.

Spitz, I. M.; Rubenstein A. H.; Bersohn, I.; and Van, As. M. (Dept. Med. Renal Unit, Witwatersrand Med. Sch., Johannesburg; The South African Inst. for Med. Res., Johannesburg, South Africa; and Dept. of Med. Univ. of Chicago, Chicago, Ill.): THE BLOOD SUGAR AND SERUM INSULIN RESPONSE TO INTRAVENOUS GLUCAGON IN CHRONIC RENAL FAILURE. Proc. Soc. Exp. Biol. Med. *134*:142-45, May 1970.

Verbatim summary. The blood sugar and serum insulin response to glucagon was evaluated in eight patients with chronic renal disease and six control subjects. When compared to the controls, the patients demonstrated a normal blood sugar rise together with an exaggerated response of serum insulin. These observations indicate that hepatic glycogen stores are adequate and that impaired insulin secretion is not a major factor in the pathogenesis of the glucose intolerance of chronic renal failure.

Stoll, R. W.; Touber, J. L.; Menahan, L. A.; and Williams, R. H. (Div. of Endocr., Dept. of Med., Univ. of Washington Hosp., Seattle, Wash.): CLEARANCE OF PORCINE INSULIN, PROINSULIN, AND CONNECTING PEPTIDE BY THE ISOLATED RAT LIVER. Proc. Soc. Exp. Biol. Med. *133*:894-96, March 1970.

Verbatim summary. In the isolated rat liver perfusion system, the immunological half-life of crystalline single-component insulin was seventeen minutes. In contrast, there was no significant clearance of either proinsulin or the connecting peptide that links the A and B chain of insulin in the proinsulin molecule. There was also no evidence of conversion of proinsulin to insulin. This may, in part, explain the prolonged in vivo half-life of proinsulin relative to insulin.

Sulway, M. J.; and Malins, J. M. (Diabetic Clin., General Hosp., Birmingham, England): ACETONE IN DIABETIC KETOACIDOSIS. Lancet 2:736-40, Oct. 10, 1970.

Heretofore it has been assumed that the plasma of diabetics with ketoacidosis contains acetoacetic acid and beta hydroxybutyric acid but little or no acetone. In this study blood acetoacetate and hydroxybutyrate were measured by chemical methods and plasma acetone was measured by gas chromatography in twenty-seven patients admitted to the hospital with ketoacidosis. Plasma acetone values were found to range from 2.5 to 12.9 m moles per liter and were always greater than acetoacetate levels. In patients studied during treatment, hydroxybutyrate and acetoacetate levels fell rather rapidly but acetone levels declined slowly. Since acetone is both hydrophilic and lipophilic and can be metabolized in only a limited fashion, its chief routes of exit from the body are the kidney and lung. However, the kidney cannot concentrate acetone so its chief egress is via the lung by diffusion. The toxicity of acetone is low and no good relationship between levels of consciousness and acetone concentration are found. T.G.S.

Swynghedaw, B.; and Hatt, P. Y. (Hôpital Léon-Bernard, F-94-Limeil-Brévannes, France): METABOLISM OF CARBOHYDRATES IN THE MYOCARDIUM. Presse Med. *78*:211-16, Jan. 28, 1970; and *78*:459-66, Feb. 25, 1970.

In a series of two articles the authors discuss the biochemical steps in the utilization of carbohydrates in the myocardium in contrast to other tissues. The enzymatic and hormonal factors which influence it and the effects of work, anoxia, digitalis and cardiac insufficiency on the metabolism are presented. M.C.B.

Unger, R. H. (Veterans Administration Hosp., Dallas, Tex.): THE ORGAN OF LANGERHANS IN NEW PERSPECTIVE. Amer. J. Med. Sci. *260*:79-81, August 1970.

In this editorial Dr. Unger develops the thesis that the organ of Langerhans should not be considered an anatomical repository for alpha and beta cells with uncoordinated divergent functions, but rather as a single functional unit designed to direct the flow of the principal nutrients into or out of cells in accordance with the needs of the various tissues and availability of exogenous nutrients. He develops the concept of the coordinated physiology of glucagon and insulin from feast to famine with evidence from studies of his own and other laboratories. This reciprocal relationship of insulin and glucagon is further supported by the reciprocal nature of the response of the target enzymes or tissues to the two hormones. Dr. Unger points out that genetic diabetes is not a unihormonal problem, that is, a pure and simple deficiency of insulin, but rather is accompanied by an exaggeration of the glucagon response. D.R.C.

Varsano-Aharon, Nora; Echemendia, Elsa; Yalow, Rosalyn S.; and Berson, Solomon A. (Radioisotope Serv., Vets. Admin. Hosp., Bronx, N. Y.; and Dept. of Med., Mt. Sinai Sch. Med., N. Y., N. Y.): EARLY INSULIN RESPONSES TO GLUCOSE AND TO TOLBUTAMIDE IN MATURITY-ONSET DIABETES. Metabolism *19*:409-17, June 1970.

Intravenous glucose injection elicited a sharp and immediate rise in plasma insulin levels in normal control subjects whereas in maturity-onset diabetic patients a very slight and delayed rise occurred in plasma insulin following the glucose injection. In contrast both groups manifested a prompt and significant secretory insulin response following the injection of tolbutamide intravenously. A biphasic response was observed in the diabetics with sustained insulin release for over thirty minutes. A patient with pancreatogenous diabetes responded poorly to both glucose and tolbutamide. The disappearance rates for crystalline beef insulin from plasma of control subjects, maturity-onset diabetes and pancreatogenous diabetes were

similar, with half-times ranging from nine to eleven minutes after the initial distribution phase. Plasma insulin concentrations therefore appear to reflect alterations in secretory rates rather than differences in metabolic turnover. The evidence indicates that the disturbance in beta cell function in maturity-onset diabetes is expressed as a failure of insulin release to be triggered by glucose rather than a defective mechanism for synthesizing and storing insulin. C.R.S.

Vinik, A.; Seftel, H.; and Joffe, B. I. (Subdepartment of Chem. Path., Univ. of Natal, Durban, South Africa): METABOLIC FINDINGS IN HYPEROSOMOLAR, NON-KETOTIC DIABETIC STUPOR. Lancet 2:797-98, Oct. 17, 1970.

The authors studied the clinical and laboratory findings of three women and four men aged sixteen to seventy years who were admitted to the hospital with hyperosmolar diabetic stupor. Chemical findings on admission showed the following ranges: blood glucose 616-1,415 mg./100 ml.; serum Na 125-154, K 2.6-5.8, CO_2 content 9-22 mEq./L.; osmolarity 310-439. The sera of six of the seven patients contained immunoreactive insulin in a concentration which ranged from 12 to 50 uU./ml. but in the seventh patient no insulin was detectable. Plasma growth hormone was suppressed to zero in five and below 4.4 mug./ml. in the other two. Plasma cortisol was above 25 ug. per cent in all. Curiously plasma FFA was above 1,400 uEq./L. in all but one subject; acetone was not present in significant quantities in the plasma of any. Serum triglyceride levels were elevated. These data are interpreted as indicative that patients presenting with the syndrome have enhanced rather than inhibited lipolysis and that resynthesis of mobilized FFA by the liver is active. The reason for the absence of ketosis is not apparent. T.G.S.

Vost, A.; and Hollenberg, C. H. (McGill Univ. Med. Clin., Montreal Gen. Hosp., Montreal, Quebec, Canada): EFFECTS OF DIABETES AND INSULIN ON DNA SYNTHESIS IN RAT ADIPOSE TISSUE. Endocrinology 87:606-10, September 1970.

Incorporation of thymidine into the cellular elements of the adipose tissue of rats was investigated. In alloxan diabetic animals insulin deprivation resulted in a significant decrease in thymidine incorporation into the DNA of stromal elements and fat cells. In rats treated with insulin, the DNA synthesis was completely restored in stromal cells and was partially restored in fat cells. The effect of insulin upon DNA synthesis of normal animals demonstrated a marked augmentation of thymidine incorporation into stromal DNA but insignificant changes in cells destined to become adipocytes. Prolonged insulin administration increased the lipid content of adipose tissue, the lipid/DNA ratio of fat cells and the stromal DNA content but did not alter the DNA content of the fat cell pool. The results indicate that insulin is necessary for DNA synthesis in both stromal and primitive fat cells and that hyperinsulinism increases stromal DNA synthesis but does not accelerate new fat cell formation. C.R.S.

Wessels, M.; Gries, F. A.; Irmscher, K.; Liebermeister, H.; Buchenau, H.; and Viehweger, I. (II. Medizinische Klinik, Diabetes-Forschungsinstitut und Fortbildungsinstitut fur Ernahrungsberatung und Diatetik der Deutschen Gesellschaft fur Ernahrung, Universitat Dusseldorf, Dusseldorf, Germany): METABOLIC CONSEQUENCES OF A LOW CARBOHYDRATE DIET ("POINT DIET") IN NORMAL SUBJECTS. Deutsch. Med. Wschr. 95:382-86, March 1970.

The widely used low-carbohydrate, high-fat, and calorically unlimited diet known as "point diet" was evaluated in six normal subjects in a seven-week diet experiment consisting of control, test, and follow-up period. The diet, which can be easily maintained, is satisfying but may lead to aversion. During the test period the caloric intake consisted of 10 per cent carbohydrate, 60 per cent fat, 21 per cent protein and 9 per cent alcohol. Because of the reduced caloric intake, more or less marked weight loss occurred, accompanied by a significant fall in blood pressure. Blood-ketone bodies increased four to eight-fold and were considered to be the cause of the compensated metabolic acidosis which developed. Fasting blood-sugar and serum-insulin levels fell. After meals the blood sugar rose with reduced serum-insulin levels toward the end of the diet period. Serum triglycerides fell, presumably as a result of increased fat catabolism and reduced lipogenesis. The significant increase in BUN while on the diet must be attributed to the increased exogenous protein intake. Serum uric acid and creatinine levels failed to show any systematic rise; there was no indication for significant reduction of body protein. Marked changes in water and electrolyte balance could not be observed. The nutritional changes with this diet lead to far-reaching alterations in fat, carbohydrate and protein metabolism which are tolerated by healthy subjects and, in part, compensated for by adaptation. In patients with latent metabolic disorders, such as occur frequently in obesity, these kinds of diets should only be employed under constant metabolic control. J.E.V.

Whitecar, John P., Jr.; Bodey, Gerald P.; Hill, C. Stratton, Jr.; and Samaan, Naguib A. (Dept. of Development & Therapeutics and Sect. of Endocr., Dept. of Med., Univ. of Texas M. D. Anderson Hosp. and Tumor Inst. at Houston, Houston, Tex.): EFFECTS OF L-ASPARAGINASE ON CARBOHYDRATE METABOLISM. Metabolism 19:581-86, August 1970.

Two of four patients receiving L-asparaginase were found to have impairment of glucose tolerance during therapy. Serum insulin levels were decreased significantly in all patients. An additional patient was found to have low serum insulin levels despite severe hyperglycemia preceding his death. Human growth hormone levels were normal to low in all patients. The degree of hyperglycemia resulting from L-asparagine therapy appears to be dose-dependent and is due to a decrease in insulin synthesis. C.R.S.

Wilcox, Henry G.; and Heimberg, Murray (Dept. of Pharmacol., Vanderbilt Univ. Sch. of Med., Nashville, Tenn.): ISOLATION OF PLASMA LIPOPROTEINS BY ZONAL ULTRACENTRIFUGATION IN THE B14 AND B15 TITANIUM ROTORS. J. Lipid Res. 11:7-22, January 1970.

The authors describe in detail a method for the simultaneous preparative and analytical isolation of lipoprotein by zonal ultracentrifugation. In this system both the VLDL and LDL of human plasma were easily separated from the other plasma proteins, but separation of the HDL from other plasma proteins was unsatisfactory. That the various low density lipoprotein factors were indeed isolated was proved by cross reactions with rabbit anti-human beta-lipoprotein or rabbit anti-human serum, and by paper electrophoresis. When the characteristics of human lipoproteins in this system were compared with those of dog, rabbit, rat and chicken lipoproteins, distinct species differences were observed in the separation of

the high density lipoproteins from the other plasma proteins. P.B.

Wiley, J. H.; and Leveille, G. A. (Lab. of Nutritional Biochem., Dept. of Animal Science, Univ. of Illinois at Urbana-Champaign, Urbana, Ill.): SIGNIFICANCE OF INSULIN IN THE METABOLIC ADAPTATION OF RATS TO MEAL INGESTION. J. Nutr. *100*:1073-80, September 1970.

A meal fed rat which is trained to consume its food in a single daily two-hour meal, must of necessity, become more efficient in converting carbohydrate to storage energy than the "nibbling" rat. The authors present data that insulin plays a major role in this adaptation to a single meal: (1) Greater sensitivity to exogenous insulin was noted in meal fed as compared to nibbling rats, blood glucose being altered in the former group. (2) Maximal rates of fatty acid synthesis by isolated adipose tissue were obtained with lower concentrations of insulin for tissues of meal fed than for nibbling rats. (3) The intravenous administration of tracer amounts of glucose-U-C-14 resulted in a greater insulin-stimulated conversion of glucose to fatty acids by adipose tissue of meal fed rats.

The uptake of glucose in diaphragm muscle, and insulin-stimulated conversion of glucose to glucogen by diaphram muscle were not influenced by meal-feeding. These results suggest that adipose tissue, and not muscle is responsible for the meal fed rat's increased sensitivity to insulin. T.J.M.

Winnick, Sheldon (Dept. of Zoology, California State Coll., Los Angeles, Calif.): RESPONSES OF HEPATIC GLUCOKINASE AND GLUCOSE-6-PHOSPHATASE ACTIVITIES IN JUVENILE AND ADULT HYPERTHYROID MICE. Endocrinology *87*:124-28, July 1970.

The effects of triiodothyronine, (T_3) glucokinase and glucose-6-phosphatase (G-6-pase) activities were measured in mice. Hyperthyroid mice had greater hepatic glucose phosphorylating activity than euthyroid mice corresponding to the increase in glucokinase activity demonstrated in the T_3 treated animals. The use in glucokinase activity was greater following T_3 administration to juvenile than adult animals while the decrease in G-6-Pase activity was the same in both groups. The primary role of thyroid hormone in this study was to increase hepatic glucose utilization which may be correlated with its calorigenic activity. C.R.S.

Wolf, H.; Stubbe, P.; and Sabata, V. (Dept. of Pediat., Univ. of Gottingen, Gottingen, Germany): THE INFLUENCE OF MATERNAL GLUCOSE INFUSIONS ON FETAL GROWTH HORMONE LEVELS. Pediatrics *45*:36-42, January 1970.

Verbatim summary. The alterations in concentration of glucose and GH following maternal glucose and maternal glucose-insulin infusions were studied in three groups of mothers and their infants at delivery. There was a close correlation between maternal and umbilical glucose levels. The maternal and fetal glucose levels were dependent on the duration of infusions. The maternal infusion of glucose (with or without insulin) led to a significant elevation of fetal GH without being dependent on the length of infusion.

Yang, M. M. P. (Dept. of Physiol., Univ. of Hong Kong, Hong Kong, China): EFFECT OF A SINGLE DOSE OF PROGESTERONE ON BLOOD GLUCOSE IN RATS. Endocrinology *86*:929, April 1970.

A large single dose of progesterone given intramuscularly to virgin rats produced hyperglycemia with two peaks at thirty to sixty minutes and five hours. Pretreatment of the animals with ergotamine tartrate abolished the hyperglycemic effect. In adrenalectomized rats a smaller single dose of progesterone caused hypoglycemia with a rise in IRI. In adrenomedullated rats, progesterone did not affect the blood glucose level. It was concluded that the adrenal medulla is involved in the hyperglycemic effect of progesterone. C.R.S.

Yashon, D.; Wagner, F. C.; Demian, Y. K.; and White, R. J. (Div. of Neurosurg., Metropolitan Gen. Hosp., Case-Western Reserve Univ. Sch. of Med., Cleveland, Ohio): CEREBRAL LACTATE ACCUMULATION AND GLUCOSE EXHAUSTION DURING CIRCULATORY ARREST. Proc. Soc. Exp. Biol. Med. *133*:728-30, February 1970.

Verbatim summary. Glucose and lactate content in dog brain were measured before and during arrest of circulation in a standard preparation. Comparison with other studies of the same model allowed the guarded conclusion that the cerebral lactate level in dogs after ten minutes of severe hypoxia may be indicative of an irreversible state. Lactate concentration rose and glucose levels fell during a ten-minute period of ischemia. The increase in lactate concentration was sufficient to account for about one fourth of the decrease in glucose content by way of anerobic glycolysis.

Ylikahri, Reino H. (Dept. of Med. Chem., Univ. of Helsinki, Helsinki, Finland): ETHANOL-INDUCED HYPOGLYCEMIA IN THYROXINE-TREATED RATS. Metabolism *19*:518-28, July 1970.

In normal rats the injection of ethanol results in a marked rise in hepatic lactate/pyruvate ratio and a decrease in the NAD/NADH ratio. In hyperthyroid rats no alteration in these ratios could be demonstrated after ethanol injection. Hyperglycemia occurred with large but not small doses of ethanol in normal rats. Hyperthyroid rats receiving large doses of ethanol became severely hypoglycemic while those given small doses were unaffected. The hypoglycemia seen following large doses of ethanol without any redox changes suggest that thyrotoxicosis induced in the animals had reduced hepatic glycogen stores and increased glucose utilization. A reduction in hepatic lactate and pyruvate concentrations in these animals may inhibit the initial step in gluconeogenesis catalyzed by pyruvate carboxylase without any redox alteration. C.R.S.

Young, Sister John M. and Weser, Elliot (Dept. of Physiol. and Med., Univ. of Texas Med. Sch., San Antonio, Texas): EFFECT OF INSULIN ON THE METABOLISM OF CIRCULATING MALTOSE. Endocrinology *86*:426-29, February 1970.

Nonfasting rats were injected with labeled maltose and glucose to compare the effects of insulin on the utilization of the two sugars in vivo. Intravenously administered maltose and glucose were oxidized to C-14-O_2 and incorporated into epididymal lipids equally. These sugars responded to insulin stimulation in a completely similar manner as manifested by a more rapid oxidation and incorporation into lipids. The findings indicate that circulating glucose and maltose are similarly metabolized and suggest that maltose metabolism proceeds via hydrolysis to glucose. C.R.S.