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ABSTRACTS

Grande, Francisco; and Prigge, William F. (Jay Phillips Res. Lab., Mount Sinai Hosp., and Lab. of Physiol. Hygiene, Univ. of Minnesota, Minneapolis, Minn.): GLUCAGON INFUSION, PLASMA FFA AND TRIGLYCERIDES, BLOOD SUGAR, AND LIVER LIPIDS IN BIRDS. *Amer. J. Physiol.* 218:1406-11, May 1970.

Verbatim summary. Glucagon infusion produced elevations of plasma free fatty acids (FFA), triglycerides (TGL), and blood sugar in geese and ducks. Free fatty acids rose promptly after the beginning of the infusion, reaching a level which was maintained constant until the end of infusion. Blood-sugar rose continuously throughout the infusion. The effect of doses between 0.05 and 0.5 ug./kg. per min. on the plasma FFA of geese showed significant correlation ($r = + 0.74$, $P < 0.01$) with the logarithm of the glucagon-infusion rate. In ducks, glucagon infusion (0.5 ug./kg. per min. for 2 hr.) caused significant elevation of the TGL content of the liver, but epinephrine and norepinephrine, infused at the same rate as glucagon, failed to elevate plasma FFA and caused no significant change of liver TGL. The results demonstrate that glucagon has a marked adipokinetic effect in birds, which is associated with elevations of plasma TGL and deposition of TGL in the liver. By contrast, catecholamines, which elevate plasma FFA and produce elevations of liver TGL in mammals, have no such effects in ducks.

Greene, Harry L.; Schubert, William K.; and Hug, George (Dept. of Pediat., Univ. of Cincinnati Coll. of Med., Cincinnati, Ohio): CHRONIC LACTIC ACIDOSIS OF INFANCY. *J. Pediat.* 76:853-60, June 1970.

Chronic metabolic acidosis in a six-month-old girl resulted in three hospital admissions and eventual death eight months later despite vigorous therapy. Lactic acidosis was established and lactate and pyruvate serum levels exceeded normal levels as much as ten-fold. Chronic lactic acidosis of infancy was reviewed, since many features of this rare disorder existed in the patient: convulsions, tetany, tachypnea, muscular hypotonia, and recurrent acidosis. Central nervous system lesions are also common and at postmortem examination, dilated ventricles, necrotizing encephalopathy and brain degeneration were noted. Of interest were the new findings of cataracts and anemia in this subject. The authors speculate that this condition may result from defective decarboxylation of pyruvate as a consequence of abnormal thiamine metabolism. R.K.K.

Huttenlocher, Peter R.; Hillman, Richard E.; and Hsia, Yujen E. (Sect. of Neurol. and Div. of Med. Genetics of the Depts. of Med. and Pediat., Yale Univ. Sch. of Med., New Haven, Conn.): PSEUDOTUMOR CEREBRI IN GALACTOSEMIA.

J. Pediat. 76:902-05, June 1970.

Three infants presented with histories of poor feeding and development and signs of increased intracranial pressure with bulging fontanelles. These findings obscured underlying galactosemia and initially central nervous disease was primarily suspected. Following documentation of galactosemia, galactose-free diets led to prompt improvement in each case. Fontanelles were less full and head circumference diminished with amelioration of cataracts and reduction of hepatomegaly. It was suggested that cerebral edema may result from abnormal accumulations in brain of a metabolite of galactose, dulcitol. Since this sugar-alcohol derivative is not metabolized further and does not freely diffuse out of cells, its osmotic action may draw water into brain tissue and lead to edema. R.K.K.

James, W. P. T.; and Coore, H. G. (Tropical Metabolism Res. Unit and Dept. of Physiol., Univ. of West Indies, Mona, Kingston, Jamaica): PERSISTENT IMPAIRMENT OF INSULIN SECRETION AND GLUCOSE TOLERANCE AFTER MALNUTRITION. *Amer. J. Clin. Nutr.* 23:386-89, April 1970.

Insulin secretion and glucose tolerance were studied in three groups of Jamaican children. Twenty-six children with malnutrition aged six to eighteen months were tested an average of twelve days after admission. Patients received a milk diet (100 kcal./kg. body wt.) with additional glucose for at least forty-eight hours prior to testing. A group of twenty-eight malnourished children underwent glucose tolerance testing after a prolonged period (average twelve weeks) of dietary treatment. A third group of five well nourished children served as control group.

All tests were performed after a six-hour fast. Blood glucose was measured by the glucose-oxidase method and plasma insulin by the double antibody method of Hales and Randle. All insulin assays were performed in triplicate using pork insulin standards for calibration. Results indicated impaired glucose tolerance after oral glucose (2 gm./kg. body wt.) and intravenous glucose (0.5 gm./kg. body wt.) in the children with malnutrition, even in those treated for three months with an adequate protein and calorie intake.

The malnourished children exhibited practically no increase in plasma immunoreactive insulin levels and the rise in plasma insulin was less in the treated than the control group, even after three months treatment.

Persisting reduction in the rate of glucose uptake by the periphery in the treated group was thought to be partly due at least to defective insulin production or release by the pancreas, or both. It was further suggested that malnutrition may pro-

duce a permanent reduction in insulin secretion ability. B.R.B.

Johnson, Brian F.; and Wolff, Frederick W. (Res. Foundation of Washington Hosp. Center & Div. of Clin. Pharmacol., Dept. of Med., George Washington Univ. Sch. of Med., Washington, D.C.): TRIAL OF MANNOHEPTULOSE IN MAN. *Metabolism* 19:354-62, May 1970.

Ingestion of the 7-carbon sugar mannoheptulose (MH) resulted in minor elevations of blood glucose without significant changes in plasma insulin levels. Intravenous glucose tolerance tests performed two hours after MH ingestion resulted in the reduction of K values when compared with controlled studies. Nausea and diarrhea occurred at dose levels of 20 gm. but no side effects were noted at lower doses. In one patient with islet cell carcinoma the ingestion of 15 gm. of MH produced no change in the clinical course and hypoglycemia occurred at the time of the peak blood MH concentration. Although MH is not a likely therapeutic agent in man it remains of interest as an experimental agent because of its inhibitory action upon the insulin release. C.R.S.

Kaneto, Akio; Mizuno, Yoshiatsu; Tasaka, Yoshimasa; and Kosaka, Kimori (Dept. of Intern. Med., Tokyo Women's Med. Coll., Shinjuku-ku, Tokyo, Japan): STIMULATION OF GLUCAGON SECRETION BY TETRAGASTRIN. *Endocrinology* 86:1175-80, May 1970.

A synthetic C-terminal tetrapeptide amide of gastrin (tetragastrin) injected into dogs caused the prompt elevation of plasma immunoreactive glucagon (IRG) and insulin (IRI) in the pancreatic duodenal vein followed by significant hyperglycemia. The administration of a gastrin antagonist, SC-15396, prior to tetragastrin was associated with inhibition in the response of pancreatic vein IRG but did not abolish the IRI response to tetragastrin. These findings indicate the possibility of the presence of a primary betacytrotrophic action combined with an alphacytrotrophic activity of tetragastrin in the pancreatic endocrine gland. C.R.S.

Kreisberg, R. A.; and Pennington, L. F. (Univ. of Alabama Med. Center, Birmingham, Ala.): TUMOR HYPOGLYCEMIA: A HETEROGENEOUS DISORDER. *Metabolism* 19:445-52, June 1970.

Glucose and lactate kinetics were studied in a patient with hypoglycemia attributed to a primary hepatoma utilizing C-14 labeled substrates. Lactate conversion to glucose and endogenous glucose production were markedly reduced while glucose utilization was minimally elevated demonstrating that hypoglycemia in this patient was due to defective hepatic glucose synthesis. These studies and others cited from the literature support the concept that the causes of tumor hypoglycemia are multiple and that various tumors will differ in the mechanism by which they produce hypoglycemia. C.R.S.

Kroeger, A.; Heisig, N.; and Harders, H. (I. Medizinische Universitätsklinik Hamburg, Hamburg, Germany): RHEOLOGICAL ASPECTS OF BLOOD FLOW IN LIPEMIC CAPILLARIES. *Klin. Wschr.* 48:723-28, June 15, 1970.

Verbatim summary. The capillary blood flow in the pancreas and mesenteric fatty tissue of rabbits was observed by means of a pancreas chamber technic. The influence of intravenously infused cottonseed oil emulsions (Lipo-fundin) on the corpuscular blood flow in capillaries was measured. The corpuscular velocity was decreased in every case of oil injection but no change could be registered after the infusion of the pure emulsifying agent. The most important parameters of

the flow (arterial and venous blood pressure, body and object temperature, hematocrit and heart rate) were found to be constant during the time of observation. Only a short and low decrease of the heart frequency was recorded after the maximal fat intake (2 gm. fat/kg. body weight). Big changes of the hematocrit had a significant influence on the corpuscular flow velocity.

During hyperlipemia the capillary bed was overcrowded of fat droplets. The intensity and frequency of the rhythmically alternating capillary flow was changed. The resting of erythrocytes in some capillaries during the whole hyperlipemic phase or flow phenomena during the decrease and increase of the microcirculatory flow velocity are discussed under the viewpoint of fluid mechanics.

There was a correlation between the corpuscular flow velocity and the thickness of the marginal plasma layer. The decrease of corpuscular velocity after fat injection was larger in capillaries with a big plasma zone than in capillaries with a small one. This "inversion phenomenon" is interpreted rheologically and its possible physiological importance is pointed out.

Kuo, Peter T.; and Feng, Louise Y. (Cardiac Sect., Dept. of Med., Robinette Foundation for Cardiovascular Res., & Geo. S. Klump Lab., Hosp. of Univ. of Pennsylvania, Phila., Pa.): STUDY OF SERUM INSULIN IN ATHEROSCLEROTIC PATIENTS WITH ENDOGENOUS HYPERTRIGLYCERIDEMIA (TYPES III AND IV HYPERLIPOPROTEINEMIA). *Metabolism* 19:372-80, May 1970.

Atherosclerotic patients with type III and IV hyperlipoproteinemia were studied to determine the relationship between insulin and endogenous hypertriglyceridemia. After stabilization of the serum lipid on a 60 per cent carbohydrate diet oral sucrose and starch tests were performed during which blood glucose, serum immunoreactive insulin (IRI) and serum insulin-like activity (ILA) were determined serially. The mean blood glucose levels of the patients did not differ from normolipemic control. However, serum IRI and ILA responses were markedly elevated above the corresponding values of healthy controls. The hyperlipoproteinemia and ILA elevations responded promptly to a carbohydrate restricted low calorie diet while the IRI levels were reduced slowly towards normal. These data support other observations that hyperinsulinemia and exaggerated postprandial insulin response may play an important role in endogenous hypertriglyceridemia. C.R.S.

Misugi, Kazuaki; Misugi, Nobuko; Sotos, Juan; and Smith, Blanca (Depts. of Path., Pediat., and Surg., Ohio State Univ., Columbus, Ohio): THE PANCREATIC ISLET OF INFANTS WITH SEVERE HYPOGLYCEMIA. *Arch. Path.* 89:208-20, March 1970.

Verbatim summary. The pancreatic tissues from three infants with severe hypoglycemia were studied by light and electron microscopy. Leucine sensitivity and hyperinsulinism were demonstrated in those tested. Histological examination demonstrated varying degrees of hyperplasia and hypertrophy of islet cells in all cases. A large proportion of the cells (over 30 per cent) failed to color satisfactorily by special granule stains.

Electron microscopic study demonstrated two types of granular cells which were different from the usual alpha and beta cells. We have tentatively named them type 3 and type 4 cells. They permit ready distinction from alpha and beta cells. Type

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3 cells were found more frequently in these specimens than in the control.

Najjar, Samir S.; and Stephan, Leila (Dept. of Pediat., Sch. of Med., American Univ. of Beirut, Beirut, Lebanon): URINARY INSULIN II. EXCRETION IN CHILDREN AND ADULTS. *Metabolism* 19:301-08, April 1970.

The overnight urinary excretion of insulin measured in normal children and adults revealed mean values of 149.3 uU./hr. for ages one to five years, 172uU./hr. for those six to fifteen years and 225 uU./hr. for adults. More IRI was excreted hourly and per milligram of creatinine during the day than during the night. There was no correlation between body weight and urinary IRI excretion except in children weighing less than 40 kg. Marked variation was noted in the day to day excretion of urinary IRI which limits the comparative use of this determination. Elevated levels may be useful in detecting individuals with high levels of plasma IRI. Four such examples were found in seventy-eight offspring of diabetic parents, two of which manifested plasma IRI responses to oral glucose similar to that found in pre-diabetic patients. C.R.S.

Packer, J. T.; Kraner, K. L.; Rose, S. D.; Stuhlman, R. A.; and Nelson, L. R. (Depts. of Path. and Lab. Animal Med., Univ. of Missouri Med. Center, Columbia, Mo.): DIABETES MELLITUS IN MYSTROMYS ALBICAUDATUS. *Arch. Path.* 89: 410-15, May 1970.

Verbatim summary. Spontaneous diabetes mellitus has developed in a colony of South African hamsters or white-tailed rats, *Mystromys albicaudatus*. Diabetes in this species is characterized by hyperglycemia, polyuria, glycosuria, ketonuria, and severe degenerative changes in the pancreatic islets of Langerhans. Obesity is not associated with hyperglycemia in *Mystromys*. No relationship to laboratory dietary influence has been detected. Hyperglycemia is well established in many animals by the age of four months and appears to shorten the life expectancy of this normally long-lived rodent. A strong predilection for the disease in males suggests that in this species the disorder may be sex-linked.

Pagliari, Anthony S.; and Goodman, A. David (Div. of Endocr. and Metabolism, Dept. of Med., Albany Med. Coll., Albany, New York): EFFECT OF 3',5' AMP G and C',E'-IMP ON PRODUCTION OF GLUCOSE AND AMMONIA BY RENAL CORTEX. *Amer. J. Physiol.* 218:1301-06, May 1970.

Verbatim summary. In studies employing rat renal cortical slices, guanosine 3',5'-monophosphate (cyclic GMP) substantially decreased production of glucose from glutamine and glutamate but not from α -ketoglutarate. Further, cyclic GMP increased the concentration of glutamate but not of α -ketoglutarate in cortex incubated in the presence of glutamine. These studies suggest that cyclic GMP inhibits the conversion of glutamate to α -ketoglutarate. Inosine 3',5'-monophosphate (cyclic IMP) and inosine monophosphate (5'-IMP) increased production of glucose from glutamine, glutamate, α -ketoglutarate, fumarate, and oxalacetate but not from glycerol or fructose, suggesting that these nucleotides accelerate a rate-limiting gluconeogenic reaction between oxalacetate and the triose phosphates. The present observations constitute the first demonstration that cyclic nucleotides other than adenosine 3',5'-monophosphate can affect metabolic processes. In the presence of glutamine, cyclic GMP, which inhibits gluconeogenesis and increases cor-

tical glutamate content, decreased ammonia production, whereas cyclic IMP and 5'-IMP, which enhance gluconeogenesis, decreased cortical glutamate content and increased ammonia production. These observations are consistent with a previously advanced hypothesis that cortical gluconeogenesis, glutamate concentration, and ammonia production may be interdependent.

Peluffo, Raul O.; Ayala, Sixta; and Brenner, Rodolfo R. (Catedra Bioquímica, Inst. Fisiología, Facultad Ciencias Médicas, Univers. Nacional de La Plata, La Plata, Argentina): METABOLISM OF FATTY ACIDS OF THE LINOLEIC ACID SERIES IN TESTICLES OF DIABETIC RATS. *Amer. J. Physiol.* 218:669-73, March 1970.

Verbatim summary. The capacity of testicular microsomes to desaturate linoleic acid-C-14 into gamma-linolenic acid in vitro was investigated. The highest conversion was found in the rats when the maturation of germinal tissue was just defining and decreased with the age. However, a significant increase of docosa-4,7,10,13,16-pentaenoic acid was found simultaneously. When linoleic acid-1-C-14 was injected into the testis it was converted into arachidonic and docosa-4,7,10,13,16-pentaenoic acids. In the alloxan diabetic rat the atrophy of the testes was coincident with a pronounced decrease of this conversion. Daily administration of 100 mg. ethyl arachidonate to alloxan diabetic rats for three months was not capable of curing their advanced testicular atrophy but it cured the scales of the tail.

Persson, B.; Sterky, G.; and Strandvik, B. (Dept. of Pediat. at Crown Princess Lovisa's Children's Hosp., Karolinska Inst., Stockholm, Sweden): INTRAVENOUS GLUCOSE TOLERANCE IN OVERWEIGHT NEWBORN INFANTS AND THEIR MOTHERS. *Pediatrics* 45:589-97, April 1970.

Gestational diabetes mellitus is frequently associated with births of large infants. In the present study intravenous glucose tolerance tests were performed on 129 infants weighing in excess of 4,500 grams. Similar studies were done on seventy-eight mothers of some infants during the first few weeks after parturition.

Twenty-six neonates (20.9 per cent) had glucose disappearance rates (k_G) that were greater than 2.0. These values were within the range of accelerated k_G among infants of mothers with overt or subclinical diabetes during pregnancy.

Postpartum investigations of mothers whose infants had k_G less than 2.0 were compared with those whose neonates had k_G above 2.0. No significant differences were found.

The authors conclude that since most gestational diabetic women revert to normal carbohydrate tolerance postpartum, a satisfactory way to enhance suspicion of the disease may be to perform intravenous glucose tolerance tests in the newborn infants of these mothers. R.K.K.

Podolsky, Stephen; and Sheremata, William A. (Med. and Neurol. Serv., Boston Univ. Sch. of Med., and Veterans Admin. Hosp., Boston, Mass.): INSULIN-DEPENDENT DIABETES MELLITUS AND FRIEDREICH'S ATAXIA IN SIBLINGS. *Metabolism* 19:555-61, August 1970.

Two sisters with Friedreich's ataxia developed insulin-dependent diabetes at ages fifteen and twenty-one years. Both exhibited ECG changes of precordial T wave inversion attributed to myocardial fibrosis. The younger sister had a myocardial infarction at age forty-three and died of pulmonary embolism after thirty-one years of diabetes. The older sister is fifty-nine

years of age and seriously handicapped after thirty-eight years of diabetes. These diseases have occurred concomitantly in seventy-two previously reported cases, most of whom were insulin-dependent. In thirteen instances the association occurred in two or more members of a family; females have predominated although Friedreich's ataxia is more common in males. Consanguinity was present in four of fourteen families. The relationship between juvenile diabetes and Friedreich's ataxia may be due to pleiotropic effects of an abnormal gene in homozygous form. C.R.S.

Rastogi, Krishna Sudha; and Campbell, James (Dept. of Physiol., Univ. of Toronto, Toronto, Ontario, Canada): EFFECT OF GROWTH HORMONE ON CORTISONE-INDUCED HYPERINSULINEMIA AND REDUCTION IN PANCREATIC INSULIN IN THE MOUSE. *Endocrinology* 87:226-32, August 1970.

Cortisone injections into mice resulted in enhancement of insulin secretion with the rate of secretion closely correlated to the rate of synthesis. Daily injection of bovine growth hormone (GH) had no effect upon serum insulin levels or pancreatic insulin content. When both hormones were injected simultaneously GH depressed the rise in insulin produced by cortisone during three days. Aldosterone, estradiol and testosterone had little or no effect on serum or pancreatic insulin while hydroxyprogesterone slightly increased insulin levels in serum and pancreas. There were marked and obvious differences between species in the metabolic responses to growth hormone and cortisol as well as to other hormones studied in animals and humans. C.R.S.

Rathgeb, I.; Winkler, B.; Steele, R.; and Altszuler, N. (Dept. of Pharmacol., New York Univ. Sch. of Med., N.Y., & Biology Dept., Brookhaven National Lab., Upton, N.Y.): EFFECT OF CANINE GROWTH HORMONE ON THE METABOLISM OF PLASMA GLUCOSE AND FREE FATTY ACIDS IN THE DOG. *Endocrinology* 87:628-32, September 1970.

The intravenous injection of canine growth hormone had no immediate effect on plasma glucose or insulin concentrations but plasma FFA and glycerol fell initially with a significant rise above control levels at four hours. Daily administration of canine growth hormone resulted in a rise in plasma levels of glucose and insulin with increased rates of glucose production and uptake. The data indicated that transient diabetes resulted from growth hormone treatment with a simultaneous increase in the turnover of labeled palmitate. The rise in plasma FFA was transient despite continuation of the canine growth hormone and diabetes abated upon cessation of the brief regimen. All of the metabolic effects observed with canine growth hormone were similar to those produced by bovine growth hormone. C.R.S.

Rebfeld, Jens F.; Jubl, Erik; and Quaade, Flemming (Dept. Clin. Chem. & Med. Dept. B, Bispebjerg Hosp., Copenhagen, Denmark): EFFECT OF JEJUNOILEOSTOMY ON GLUCOSE AND INSULIN METABOLISM IN TEN OBESE PATIENTS. *Metabolism* 19:529-38, July 1970.

Jejunostomy performed for the correction of obesity resulted in a significant lowering of blood sugar for prolonged periods but with gradual recovery. Glucose tolerance improved and serum insulin levels became normal. During oral glucose tolerance tests the serum insulin levels rose despite relatively flat glucose responses suggesting that the entero-insulin axis may remain intact following the intestinal

shunt procedure. C.R.S.

Root, Allen W.; Bongiovanni, Alfred M.; and Eberlein, Walter R. (Div. of Endocr., Children's Hosp. of Philadelphia, and Dept. of Pediat., Univ. of Pennsylvania Sch. of Med., Philadelphia, Pa.): INHIBITION OF THYROIDAL RADIOIODINE UPTAKE BY HUMAN GROWTH HORMONE. *J. Pediat.* 76:422-29, March 1970.

Verbatim summary. Thyroidal twenty-four-hour uptake of I-131 declined by 25 per cent or more of the control value following the short-term administration of human growth hormone in eight of fifteen children with hypopituitarism and in one of five subjects with growth retardation of other etiology, an effect which was reversed by giving exogenous thyrotropin. The plasma concentration of thyrotropin decreased 20 to 40 per cent in two boys with acquired hypothyroidism following administration of human growth hormone. It is hypothesized that growth hormone inhibits the pituitary synthesis and/or release of thyrotropin.

Rosenbloom, Arlan L. (Dept. of Pediat., Univ. of Florida, Coll. of Med., Gainesville, Fla. 32601): INSULIN RESPONSES OF CHILDREN WITH CHEMICAL DIABETES MELLITUS. *New England J. Med.* 282:1228-31, May 28, 1970.

Eight children with mild intermittent symptoms suggestive of hypoglycemia were studied to determine insulin and glucose responses after oral glucose loading. After loading three patients exhibited insulin hypoactivity which was corrected by treatment with tolbutamide. The remaining children demonstrated normal or increased plasma immunoreactive insulin responses to oral glucose loading. All children were chemical diabetics.

The authors suggest these findings may indicate a stage of diabetes mellitus in certain children when normal or elevated levels of immunoreactive insulin are circulating but glucose tolerance is abnormal. Detection, prognosis and treatment of children before progression into insulin-dependent overt diabetes is recommended. B.R.B.

Roxe, David M.; Disalvo, Joseph; and Balagura-Baruch Sulamita (Dept. of Physiol., Cornell Univ. Med. Coll., New York, N.Y.): RENAL GLUCOSE PRODUCTION IN THE INTACT DOG. *Amer. J. Physiol.* 218:1676-81, June 1970.

Verbatim summary. Renal glucose production was studied in anesthetized fasting (eighteen hour) dogs, in various states of acid-base balance, by two procedures: (a) by measuring the difference of glucose concentration in renal venous and arterial plasma, using the standard glucose oxidase method; (b) by measuring simultaneously the rates of renal release of C-14-labeled glucose during renal intra-arterial infusion of C-14-labeled a-ketoglutaric acid, malic acid, or glutamine. No net renal glucose production was detected by chemical means in the normal state, nor in chronic metabolic acidosis, acute metabolic alkalosis, and acute respiratory acidosis or alkalosis. In contrast, in all cases renal gluconeogenesis was detected from the appearance of C-14-labeled glucose in renal venous blood during renal intra-arterial infusion of C-14-labeled precursor. With this procedure, renal gluconeogenesis was detected even in the instances in which there was net extraction of glucose from arterial blood. Acute changes of acid-base balance altered the rates of renal release of C-14-labeled glucose but did not affect renal arteriovenous concentrations measured chemically. This study indicates that renal gluconeogenesis is a process

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occurring continuously at extremely low rates which fail detection by chemical means and that its contribution to the economy of the body is negligible. If changes in rates of renal gluconeogenesis occur during changes of acid-base balance, as suggested by the isotopic measurements, their magnitude is below the sensitivity of the standard glucose oxidase method.

Ryan, Jerome R.; Balodimos, Marios C.; Chazan, Bernard I.; Root, Howard F.; Marble, Alexander; White, Priscilla; and Joslin, Allen P. (Joslin Diabetes Foundation, Inc.; New Eng. Deaconess Hosp.; & Dept. of Med., Harvard Med. Sch., Boston, Mass.): QUARTER CENTURY VICTORY MEDAL FOR DIABETES: A FOLLOW-UP OF PATIENTS ONE TO TWENTY YEARS LATER. *Metabolism* 19:493-01, July 1970.

Recipients of the Joslin Quarter Century Victory Medal were evaluated by means of a questionnaire to determine their conditions regarding complications of diabetes, results of treatment, laboratory studies and other relevant observations. There were 105 responders of 124 patients receiving the Medal after twenty-five years of diabetes unassociated with vascular complications. The average elapsed time of twelve years after the medal award found one third of them with evidence of vascular or microvascular complications indicating that the appearance of angiopathy was considerably postponed but not entirely eliminated. Among the factors of significance in the low rates of diabetic complications are near ideal weight, favorable heredity, and good control of diabetes. C.R.S.

Sadeghi-Nejad, Abdollah; Loridan, Liliane; and Senior, Boris (Dept. of Pediat., Tufts Univ. Sch. of Med., and Pediat. Endocr.-Metabolic Serv., New England Med. Center Hosps., Boston Floating Hosp. for Infants and Children, Boston, Mass.): STUDIES OF FACTORS AFFECTING GLUCONEOGENESIS AND GLYCOLYSIS IN GLYCOGENOSIS OF THE LIVER. *J. Pediat.* 76:561-70, April 1970.

Three classes of glycogen storage disease in which impaired ability to convert glycogen to glucose is characteristic are Types I, III and VI. The deficient enzymes are glucose-6-phosphatase, amylo-1, 6-glucosidase and the phosphorylase system, respectively. To assess the ability of liver to synthesize glucose by means other than from glycogen break-down in these disorders, the authors measured a major gluconeogenic enzyme, fructose-1, 6-diphosphatase, and a major glycolytic enzyme, phosphofructokinase, in liver biopsies obtained from a small group of patients with these diseases. In addition, plasma insulin, growth hormone, cortisol and free fatty acids were determined.

Compared to a control group of patients, hepatic fructose-1, 6-diphosphatase activity was significantly greater in subjects with any one of the three glycogen storage diseases. Mean phosphofructokinase activity did not differ from control values, however. Fasting plasma human growth hormone and cortisol levels were also similar to those of control patients, but fasting insulin concentrations were lower in afflicted individuals even when related to glucose levels. Plasma free fatty acids were increased above normal concentrations. The authors concluded that liver adaptation to impaired glycogen breakdown involves an increase of unidirectional gluconeogenic enzymes. This is consistent with previous reports of more rapid plasma disappearance of gluconeogenic substrates such as glycerol when administered parenterally to these patients. The lowering of plasma insulin out of proportion to the depressed levels of glucose may represent another protective mechanism against

the development of a more intense hypoglycemia. Increased plasma free fatty acid concentrations provide an alternative fuel in this instance. R.K.K.

Souadjiian, Jacques V.; Molnar, George D.; Silverstein, Murray N.; and Titus, Jack L. (Mayo Clin. & Mayo Foundation, Rochester, Minn.): MORPHOLOGIC STUDIES OF THE THYMUS IN ACROMEGALY, DIABETES MELLITUS, AND CUSHING'S SYNDROME. *Metabolism* 19:401-05, June 1970.

Morphologic features of thymus glands obtained at autopsy in three groups of patients with endocrinologic disorders, acromegaly, diabetes and Cushing's Syndrome, were compared with those of normal subjects. Thymuses from acromegalic and juvenile-onset diabetic patients displayed an increase in the number and the diameters of Hassall's corpuscles. There were no significant thymic changes in patients with adult-onset diabetes or Cushing's Syndrome when compared to normals. C.R.S.

Spring, Maxwell; Fleck, Henry; and Cohen, Burton D. (Depts. of Med. and Rehabilitation Med., Bronx-Lebanon Hosp. Center, Bronx, N.Y.): DUPUYTREN'S CONTRACTURE. WARNING OF DIABETES? *New York J. Med.* 70:1037-41, May 1, 1970.

The prevalence of Dupuytren's contracture in a group of 400 known diabetics was compared with a group of 500 persons not known to be diabetic. Twenty-one per cent of the diabetics were found to have palmar thickening or contractures compared to 5 per cent in the nondiabetic group. Another group of fifty-four individuals without manifest diabetes but with all stages of Dupuytren's contracture was studied using intravenous glucose tolerance tests. Results were compared to a control group of thirty-three without known diabetes or contracture. The mean rate disappearance constant of glucose for the group with Dupuytren's contracture showed a statistically significant difference from that of the control group. Additional oral glucose tolerance tests were done on ten patients, and in each instance there was an abnormal response. In twenty-five nondiabetic patients with contracture who underwent electrodiagnostic studies, there was no evidence of generalized muscular atrophy, but in twenty-four out of twenty-five patients studied, there was evidence of peripheral denervation.

The authors conclude that the results indicate a remarkable relationship between altered glucose tolerance and the changes in the palmar fascia attributable to peripheral neuropathies common to both diabetes and Dupuytren's contracture. P.S.E.

X Steinke, Jurgen (Elliott P. Joslin Res. Lab., 170 Pilgrim Road, Boston, Mass.): MANAGEMENT OF DIABETES MELLITUS AND SURGERY. *New Eng. J. Med.* 282:1472-74, June 25, 1970.

The author presents recommendations for the management of diabetes pre- and post-operatively. Included are treatment of the known diabetic on oral hypoglycemic agents and the insulin-dependent patient. Special consideration is indicated in the pre- and post-partum care of the pregnant diabetic patient, the possible diabetic with glycosuria and the ketoacidosis prone diabetic. In the glycosuric patient the severity or mildness of diabetes must be first established and the diagnosis of renal glycosuria ruled out. Vigorous treatment with insulin and intravenous fluids should be monitored every two to four hours in the ketoacidotic diabetic. The importance in recognizing "pseudoappendicitis" of early diabetic ketoacidosis is emphasized. Failure to recognize this abdominal emergency could be fatal. B.R.B.

Vernon, R. G.; and Walker, D. G. (Dept. of Biochem., Univ. of Birmingham, Birmingham, England): GLYCEROL METABOLISM IN THE NEONATAL RAT. *Biochem. J.* 118:531-36, July 1970.

Although gluconeogenesis from amino acids is thought to be an important source of glucose in the adult during starvation, the significance of this process is uncertain in the neonatal animal since there is a considerable requirement for amino acids in protein synthesis during this period of rapid growth. In the present work the role of glycerol as a precursor of glucose was investigated in the developing rat. The authors recorded the activities of glycerol kinase and 1-glycerol-3-phosphate dehydrogenase in the liver, kidney and other tissues at birth and during the neonatal period. Blood glycerol concentrations were high in the neonatal rat. Immediately after birth there was a marked increase in the ability of both liver and kidney to convert glycerol to glucose. This increased ability to convert glycerol to glucose correlated well with an increase in glycerol kinase activity. Specific problems relating to this conversion are discussed in detail. T.J.M.

Vogelberg, K. H.; and Gries, F. A. (II. Medizinische Klinik und Poliklinik der Universität Düsseldorf, Düsseldorf, Germany): TRI-, DI- AND MONOGLYCERIDES IN HUMAN SERUM AND THEIR RELATION TO THE LIPOPROTEIN SPECTRUM. *Klin. Wschr.* 48:227-31, Feb. 15, 1970.

Verbatim summary. 1. The calculation of serum triglycerides usually is carried out by measuring the glyceride-glycerol disregarding the presence of di- and monoglycerides. The separation of these glycerides by thin layer chromatography and the quantitative determination with hydroxamic acid demonstrates in fasting and postprandial serum of normolipemic patients a changeable partial glyceride concentration which was found to fluctuate from a 8.5 per cent in the fasting specimen to 18.3 per cent (max. to 28.6 per cent) two hrs. p.c. In patients with essential hyperlipemia (type V according to Fredrickson et al., 1967) partial glycerides amount to less than 1 per cent of the total glycerides. These results should be considered when triglycerides are calculated from glyceride-glycerol concentrations.

2. The increase of chylomicrons, beta- and pre-beta-lipoproteins, observed in the postprandial serum of normolipemic patients and in the fasting serum of patients with essential hyperlipemia, is accompanied by a decrease of alpha-lipoproteins. The diminution of plasma triglycerides due to peripheral metabolism induces an elevation of alpha-lipoproteins concomitant with a decrease of pre-beta-lipoproteins.

3. Partial glycerides are chiefly transported in alpha-lipoproteins in the fasting state while they are found in chylomicrons in the postabsorptive state.

4. In the calory induced essential hyperlipemia (type V according to Fredrickson) the concentration of alpha-lipoproteins and partial glycerides is decreased. However, injection of heparin into these patients is followed by a marked increase of alpha-lipoproteins and partial glycerides. The activity of lipoprotein-lipase in serum is normal. It may be assumed that in the hyperlipemia the peripheral utilization of triglycerides is disturbed.

Wachman, A.; Hattner, R. S.; George, Barbara; and Bernstein, D. S. (Dept. of Nutrition, Harvard Sch. of Public Health and the Dept. of Med., Harvard Med. Sch. & Peter Bent Brigham Hosp., Boston, Mass.): EFFECTS OF DECAFFEINATED AND NONDECAFFEINATED COFFEE INGESTION ON BLOOD GLUCOSE AND PLASMA RADIOIMMUNOREACTIVE INSULIN RESPONSES TO RAPID INTRAVENOUS INFUSION OF GLUCOSE IN NORMAL MAN. *Metabolism* 19:539-46, July 1970.

Eight normal humans were given intravenous glucose tolerance tests one hour following the ingestion of non-decaffeinated and, on a second occasion, of decaffeinated coffee under identical conditions. Nondecaffeinated coffee raised the fasting blood glucose, impaired glucose tolerance as shown by reduced fractional blood glucose disappearance rate and lowered the insulinogenic response of blood glucose elevation compared to decaffeinated coffee. C.R.S.

Wahl, P.; Krezdorn, W.; and Deppermann, D. (Medizinische Universitätsklinik [Ludolf Krehl-Klinik] Heidelberg, Heidelberg, Germany): INVESTIGATIONS OF THE PATHOGENESIS OF DIABETIC MICROANGIOPATHY I: ISOLATION OF RENAL GLOMERULI AND GLOMERULAR BASEMENT MEMBRANES. DEVELOPMENT AND PRINCIPLE OF METHOD. *Klin. Wschr.* 48:650-53, June 1, 1970.

Verbatim summary. A method is described by which glomeruli can be isolated with the aid of sieves of varying mesh within thirty minutes. The isolated glomeruli are obtained as an almost pure fraction (contamination 5 per cent tubuli) and showed a constant metabolic activity over a period of 2½ hours, which was demonstrated by the linear O₂-consumption, CO₂-14-production, and incorporation rates of C-14 from U-C-14-glucose into the basement membrane. After incubation, the basement membranes can be easily isolated by sonification. The basement membranes were controlled by electron microscopy. This method allows metabolic studies on basement membranes.

Wahl, P.; and Deppermann, D. (Medizinische Universitätsklinik [Ludolf Krehl-Klinik] Heidelberg, Heidelberg, Germany): INVESTIGATIONS OF THE PATHOGENESIS OF DIABETIC MICROANGIOPATHY II: THE CHEMICAL COMPOSITION OF THE GLOMERULAR BASEMENT MEMBRANE OF THE RAT. *Klin. Wschr.* 48:653-58, June 1, 1970.

The glomerular basement membrane of the rat is a glycoprotein with a carbohydrate content of about 10 per cent. The neutral sugars were composed of glucose, galactose, mannose, and fucose in the molar ratio of 1:1:1.5:0.4. Sialic acid and hexosamines consisted of both glucosamine and galactosamine in a ratio of about 1:2 (total amount 2.1 per cent). The lipid content accounted for about 6.5 per cent of the dry weight (62 per cent phospholipids, 26 per cent triglycerides, and 12 per cent cholesterol). The peptide portion of the basement membrane is characterized by the occurrence of large amounts of proline, hydroxy-proline, and hydroxylysine, suggesting a close relationship to collagen. Together with in vitro studies of the metabolic activity of isolated glomeruli a chemical analysis of the basement membrane under various conditions is believed to be a new and promising approach to the elucidation of the pathogenesis of diabetic microangiopathy. J.V.