

ABSTRACTS

Blumenthal, Herman T.; Probst, J. G.; and Berns, A. W. (Clinical Research Program on Aging, Veterans Hospital, Jefferson Barracks, and the Departments of Surgery, Jewish Hospital, Washington Univ. School of Med., St. Louis, Mo.): INTERRELATIONSHIP OF DIABETES MELLITUS AND PANCREATITIS. Arch. Surg. 87:844-50, November 1963.

In a study of 184 cases of pancreatitis, in comparable diabetic and nondiabetic patients, the authors found a 1.5 to 2.6 times greater frequency of myocardial, cerebral, renal and pancreatic infarcts in the diabetics. They speculate that the initiating event in these lesions is vascular thrombosis. There is a fivefold increase in the frequency of proliferative lesions of small vessels in diabetes. The lesions do not contain a significant quantity of lipid and have characteristics similar to those observed in hyperimmune disease states. The demonstration of insulin binding by vascular lesions in diabetes suggests that this hormone may be the responsible antigenic agent. While the relatively greater occurrence of pancreatitis in diabetics is usually regarded as a complication of the latter, another possibility is that the vascular manifestations may antedate the clinical manifestations of both diabetes and pancreatitis. The association of pancreatitis and diabetic acidosis may represent a concomitant onset of both diseases linked with the presence of an associated vascular phenomenon. L.S.S.

Bolinger, Robert E.; Morris, J. Harold; McKnight, Frank G.; and Diederich, Dennis A. (Clin. Res. Center, Dept. of Med., Univ. of Kansas Med. Center, Kansas City, Kans.): DISAPPEARANCE OF I-131-LABELED INSULIN FROM PLASMA AS A GUIDE TO MANAGEMENT OF DIABETES. New England J. Med. 270:767-70, April 9, 1964.

The characteristics of the rapid phase (10-20 min.) of the plasma disappearance of I-131-labeled insulin was studied in forty-five diabetic patients. The half life was 14.6 min. for diabetic patients not treated with insulin, 23.5 min. for stable insulin treated patients, and 58.6 min. for patients with brittle diabetes. It was found that patients with the longest half life or disappearance of labeled insulin obtained optimal regulation on Regular Insulin whereas those with a half life in the range of 20-40 min. were best regulated with mixtures of Isophane and Regular Insulin. Those with an insulin half life of less than 20 min. were best regulated on Isophane insulin alone. *Comment:* It is likely that measurements of insulin binding capacity would have demonstrated that antibodies accounted for the prolonged disappearance of the insulin, rather than complexing of the insulin, as intimated by the authors. B.R.B.

Bosbell, Buris R.; Kirschenfeld, J. J.; and Soteres, Pete S. (Veterans Administration Hosp. and Med. College of Alabama, Depts. of Med., Birmingham, Ala.): EXTRAPANCREATIC INSULIN-SECRETING TUMOR. New England J. Med. 270:338-41, February 13, 1964.

A patient with severe bouts of hypoglycemia associated with a retroperitoneal fibrosarcoma was evaluated via glucose tolerance, tolbutamide tolerance, and leucine tolerance tests. The patient exhibited no unusual sensitivity to any of these agents.

In vitro studies of the tumor revealed a high level of insulin-like activity which could be suppressed with specific anti-insulin antibody and with a sulfhydryl inhibitor, N-ethylmaleimide. This appears to provide direct evidence that one mechanism for the hypoglycemia in the extrapancreatic tumor is the secretion of insulin. B.R.B.

Bottiger, L. E.; and Holmstrom, A. (Dept. of Med., Karolinska Institutet of Serafimer-Casarefted and King Gustav Vth Research Institute, Stockholm, Sweden): SERUM PROTEIN-BOUND CARBOHYDRATES IN NORMAL WOMEN. J. Lab. Clin. Med. 63:772-75, May 1964.

Because of the increasing emphasis placed on serum values of protein-bound carbohydrates in investigation of disease states, data for levels of serum hexoses, hexosamines and sialic acids in a large series of normal adults is presented. Blood samples from ninety healthy women aged 26-80 yrs. were randomly selected from a larger group and analyzed for hexoses by an anthrone reagent, hexosamines by the Elson-Morgan procedure and sialic acids by a Resorcinol-Copper method. Mean values were: hexoses, 112.9 ± 1.4 mg. per cent hexosamines, 89.8 ± 0.9 mg. per cent; sialic acids, 62.4 ± 0.7 mg. per cent. When compared to values previously obtained in a group of normal men, no essential differences were found. An increase in values of sialic acid (but not other acids) with increasing age was found. T.G.S.

Bowers, C. Y.; Muldrey, J. E.; and Hamilton, J. G. (Dept. of Med., Tulane Univ. Sch. of Med., New Orleans, La.): BLOOD LIPID AND GLUCOSE LEVELS OF PATIENTS WITH DIABETES MELLITUS TREATED WITH CHLORPROPAMIDE. Amer. J. Med. Sci. 247:676-81, June 1964.

A comparison of the fasting blood cholesterol, free fatty acid and cholesteryl ester (palmitate, oleate, linoleate and arachidonate) levels in a group of ten maturity onset diabetic patients with and without treatment with chlorpropamide. The treatment was pursued to the point of fasting blood sugar levels of 102-121 (mg. per 100 ml. Folin-Wu versus 150-223 mg. per 100 ml. untreated), but not to the point of complete (postprandial) normoglycemia. No differences in lipid levels were detected between these two treatment levels, although it had previously been shown that postprandial free fatty acid level elevations were restored to normal under similar circumstances. S.B.B.

Butterfield, W. J. H.; Sargeant, B. M.; and Whichelow, M. J. (Dept. of Med., Guy's Hospital, London, S.E. 1, England): THE METABOLISM OF HUMAN FOREARM TISSUES AFTER INGESTION OF GLUCOSE, FRUCTOSE, SUCROSE, OR LIQUID GLUCOSE. Lancet 1:574-77, March 14, 1964.

A comparison of the abilities of orally ingested liquid glucose, glucose, sucrose, and fructose to elevate arterial hexose levels and influence liver and muscle metabolism was made by continuous auto-analysis of hexose levels in three normal men. Ingestion of 45.4 gm. of liquid glucose, or glucose, or sucrose resulted in a rise of arterial hexose of 50-70 mg. per 100 ml. which peaked at 25-40 min. Values for glucose measured by subtracting fructose from total hexose were about the same

after glucose but lower after sucrose. By calculating blood flow and hexose A-V differences in the forearm, cellular uptake of the various hexoses was measured. With the exception of fructose, this value was regarded as an expression of endogenous insulin secretion. Cellular hexose uptake rose sharply after fifteen minutes and peaked within an hour with all sugars except fructose. The rise after fructose largely reflected fructose uptake which was noninsulin dependent and was quantitatively about one third that of the other sugars. The findings indicate that, after administration by mouth, a considerable proportion of fructose is disposed of by the liver, and a considerable portion of glucose and liquid glucose by the periphery, while sucrose occupies an intermediate position. T.G.S.

Dos Reis, Luciano (Instituto de Patologia Geral, University of Coimbra, Coimbra, Portugal): VISCERAL LESIONS IN ACUTE PANCREATITIS. Arch. Surg. 87:604-08, October 1963.

After production of acute bile pancreatitis in twelve dogs, focal degenerative lesions similar to those in humans were found in liver, pancreas, myocardium, and brain. Similar lesions and kidney necrosis were found in dogs either injected with trypsin or manipulated so as to induce the entry of pancreatic enzymes into the circulation by intraductal injection of saline or by the drainage of pancreatic fluid into the peritoneal cavity. It is speculated that circulating pancreatic enzymes, especially trypsin, are causative of the observed lesions. L.S.S.

Doyle, A. P.; Balcerzak, S. P.; and Jeffrey, W. L. (Veterans Administration Hosp.; University of Pittsburgh Sch. of Med., Dept. of Med., and Dept. of Path., Pittsburgh, Pa.): FATAL DIABETIC GLOMERULOSCLEROSIS AFTER TOTAL PANCREATECTOMY. New Eng. J. Med. 270:623-24, March 19, 1964.

A patient who had a total pancreatectomy in 1949 for reticulum cell sarcoma died fourteen years later of diabetic glomerulosclerosis. Evidence of peripheral neuropathy developed within nine months after the total pancreatectomy. Retinopathy and the Kimmelstiel-Wilson syndrome appeared within eleven years. Burton, Kearns and Rynearson described the occurrence of diabetic retinopathy three years after total pancreatectomy but there are no other reports of diabetic nephropathy after this operation. The absence of microangiopathy following pancreatic removal may be due to the limited number of long-term survivors of this procedure. Duncan reported a single instance of diabetic glomerulosclerosis secondary to chronic pancreatitis with hemochromatosis in whom diabetes has been recognized for four years or longer. Retinopathy has been reported as complicating the diabetes due to acromegaly, Cushing's disease, chronic pancreatitis, and hemochromatosis in addition to pancreatectomy. *Comment:* If future reports confirm the presence of the so-called diabetic complications in patients without a family history of diabetes mellitus but with diabetes secondary to pancreatectomy or chronic pancreatitis this will provide strong evidence that the microangiopathies are not necessarily a part of the genetically transmitted diabetic state. B.R.B.

Drash, Allan; and Wolff, Frederick (The Harriet Lane Home, Johns Hopkins Univ. Sch. of Med., Baltimore, Md.; and Div. of Clin. Pharmacol., New York Med. Coll., New York, N.Y.): DRUG THERAPY IN LEUCINE-SENSITIVE HYPOGLYCEMIA. Metabolism 13:487-92, June 1964.

Diazoxide was administered to a child of four years with

leucine-sensitive hypoglycemia. The effect of the drug at a dosage of 4 mg./kg. three times daily was that of promoting postprandial hyperglycemia and marked clinical improvement. The blood sugar fell to hypoglycemia levels 4-5 hrs. after meals but with the absence of symptoms during diazoxide therapy. The serum uric acid was elevated to 8 mg. per cent with a return to normal levels upon discontinuing the drug. No other changes in blood chemistry, aside from hyperglycemia were noted. The blood pressure was unaffected by the drug. C.R.S.

Felts, P. W.; Crofford, O. B.; and Park, C. R. (Depts. of Med. and Physiol., Vanderbilt Univ., Nashville, Tenn.): EFFECT OF INFUSED KETONE BODIES ON GLUCOSE UTILIZATION IN THE DOG. J. Clin. Invest. 43:638-46, April 1964.

Ketone body infusions into intact fasting dogs produced hypoglycemia and improved glucose tolerance. In the same animals made hyperglycemic by constant infusion of glucose, acetoacetate and beta-hydroxybutyrate promoted further elevation of blood glucose. G.D.M.

Field, James B. (Dept. of Med. and Clin. Res. Unit, Univ. of Pittsburgh, Sch. of Med., Pittsburgh, Pa.): FACTORS CONCERNED WITH INSULIN SYNTHESIS AND RELEASE. Metabolism 13:407-21, May 1964.

A detailed review of the current knowledge of insulin production and secretion by the beta cells. The role of glucose, other hexoses, sulfonylureas, and leucine is described in the stimulation of the release of insulin. The concepts of Lacey depicting the ultrastructure of the beta cell and insulin formation are integrated with data concerning metabolic activity of these cells and the enzymatic pathways involved. The effects of various factors which may influence the synthesis and release of insulin are discussed. C.R.S.

Fishman, Robert A. (Dept. of Neurology, Coll. of Physicians and Surgeons, Columbia Univ., Neurol. Clin. Res. Center, Neurol. Inst., Presbyterian Hosp. and New York State Psychiatric Inst., New York, N.Y.): CARRIER TRANSPORT OF GLUCOSE BETWEEN BLOOD AND CEREBROSPINAL FLUID. Amer. J. Physiol. 206:836-44, April 1964.

The transfer of glucose, 2-deoxy-D-glucose, and fructose between blood and cerebrospinal fluid (CSF) of anesthetized dogs was studied, following either intravenous injection or intracisternal administration in artificial CSF. The findings support the hypothesis that there is a carrier transport system for glucose in the membranes which separate blood and cerebrospinal fluid. M.G.B.

Golding, Michael R.; Oberlander, Lawrence K.; and Enquist, Irving F. (Dept. of Surgery, State Univ. of New York, Downstate Medical Center, Brooklyn, N.Y.): CARTILAGE SPEEDS HEALING IN DIABETIC WOUNDS. Arch. Surg. 87:647-49, October 1963.

The authors report a stimulating effect of local cartilage powder on the gain in tensile strength of sutured, incised wounds in normal rats and in animals with poorly controlled alloxan diabetes, a state associated with deficient healing. L.S.S.

Goldman, Jack K.; and Cabill, George F., Jr. (Dept. of Med., Harvard Med. Sch., the Peter Bent Brigham Hosp., and the Baker Clinic Res. Lab., New England Deaconess Hosp., Boston, Mass.): INSULIN EFFECT ON GLUCOSE-C-14 INCORPORATION INTO RAT LIVER AND ADIPOSE TISSUE IN VIVO. Metabolism 13:572-78, June 1964.

The disposition of intravenously administered glucose C-14

was analyzed in rats in states of fasting and refeeding, with or without simultaneously injected insulin. In all animals, insulin decreased the specific activity of blood glucose. In the fed animals, insulin increased the specific incorporation of label into adipose glycogen, fatty acids and glyceride-glycerol and into liver fatty acids of both triglyceride and phospholipid fractions. There was a decrease in the specific activity of liver glycogen and liver triglyceride-glycerol. Fasting for forty-eight hours eliminated all insulin effects except those on blood glucose, liver glycogen and adipose glyceride-glycerol. Refeeding increased markedly the incorporation of label into liver fatty acids, glycogen and triglyceride-glycerol. C.R.S.

Hamilton, Henry E.; Stein, J. H.; and Sheets, Raymond F. (Univ. Hospitals, and State Univ. of Iowa, College of Med., Iowa City, Iowa): AGRANULOCYTOSIS CAUSED BY CHLORPROPAMIDE. *Arch. Intern. Med.* 113:186-90, February 1964.

A case of fatal chlorpropamide agranulocytosis. Leukoagglutinins were present and were accentuated by the addition of chlorpropamide "in vitro." Platelet agglutinins activated by chlorpropamide were also detected. The relationship of these agglutinins to the mechanisms resulting in agranulocytosis is discussed. C.A.R.

Haunz, E. A.; Cornatzer, W. E.; and Luper, M. (Univ. of North Dakota Sch. of Med. and Dept. of Med., Grand Forks Clinic, Grand Forks, N.D.): LIVER FUNCTION IN CHLORPROPAMIDE THERAPY. FIVE YEAR CLINICAL STUDY OF 181 PATIENTS. *JAMA* 188:237-40, April 20, 1964.

The patients were treated with chlorpropamide for an average of twenty months each (one week to fifty-seven months). The dosage employed was an average of 240 mg. per day (only one over 500 mg. per day). Liver function was measured serially by determination of serum glutamic oxaloacetic transaminase level, glutamic pyruvate transaminase, alkaline phosphatase, chemical gamma globulin, serum paper electrophoretic pattern and cephalin flocculation (Hanger). All tests were normal except the latter. There was an incidence of 54 per cent 2 plus and 3 plus test results among these chlorpropamide treated diabetics compared with an incidence of 52 per cent among forty-four diet-treated and 44 per cent among 126 insulin-treated patients. Initial control cephalin flocculation tests had not been performed and thirty-six weeks after initial detection of these abnormal tests in the twenty-four chlorpropamide treated patients thirteen had reverted to normal even with continued use of the same dose of the drug. The authors question the specificity of the cephalin flocculation test for liver function among diabetic patients.

Few significant side effects were noted clinically: the safety of dosage level of 250-375 mg. per day of chlorpropamide was underscored by this experience. The use of the maximum recommended dose of 500 mg. per day should be accompanied by proper supervision of patients. S.B.B.

Heiskala, Heikki; and Gylling, Martti (Dept. of Int. Med. and Surg., Maria Hospital, Helsinki, Finland): HYPOGLYCEMIA ASSOCIATED WITH SARCOMA. *Ann. Med. Intern. Fenn.* 52:147-54, 1963.

The first case of hypoglycemia associated with a large extrapancreatic tumor was described by Doege in 1930. Since that date, twenty-nine such cases have been reported, two from Scandinavia. Generally, the tumors are solitary, relatively large

and encapsulated. They are generally situated retroperitoneally or in the thorax. The histological picture is comparatively similar, although various diagnoses have been suggested: fibrosarcoma, fibroma, spindle cell sarcomaleiomyosarcoma, reticulum cell sarcoma, mesothelial sarcoma, fibrous mesothelioma and sarcomatous dysembryoplasia. The presenting symptoms are usually various neurological disturbances and disorientation, the severity of which varies from a feeling of slight weakness to convulsions and coma. Frequently there is restlessness, anxiety and temporary paralysis of varying degree. The blood sugar may fall as low as 9 mg. per 100 ml. The pathogenesis of hypoglycemia in these cases is still a matter of controversy. There are a number of possible explanations for the hypoglycemia observed in these cases:

1. The tumor secretes insulin or some similar substance that lowers the blood sugar level.
2. The tumor secretes a substance that causes hypoglycemia but that differs in composition and influence from insulin and similar substances.
3. The tumor consumes such excessive glucose that it brings about hypoglycemia.
4. Seckel has presented a theory according to which a sarcoma originating from the liver can give rise to hypoglycemia by pressing on the sympathetic nervous system — the splanchnic nerve and the coeliac ganglion.
5. Further, it has been suggested that the tumor secretes a substance that counteracts the effect of insulinase or that might stimulate the secretion of the pancreatic insulin. W.R.K.

Lerner, Phillip I.; and Weinstein, Louis (Dept. of Med., Tufts Univ. Sch. of Med. and Infectious Disease Serv. of the Pratt Clinic—New England Center Hosp., Boston, Mass.): ABNORMALITIES OF ABSORPTION OF BENZYL PENICILLIN G AND SULFISOXAZOLE IN PATIENTS WITH DIABETES MELLITUS. *Amer. J. Med. Sci.* 248:37-51, July 1964.

A comparison was made of the absorption rates, blood levels and excretion rates and times of single doses of benzyl penicillin G and sulfisoxazole in nineteen diabetic patients over fifty years of age and sixteen normal subjects, the dosages given first intramuscularly and then intravenously. The doses used were 10,000 units of benzylpenicillin G and 40 mg. of sulfisoxazole per kg. body weight. The diabetic subjects manifested delayed and lower peaks of blood levels of each drug by the intramuscular route as compared with normals, while no variations in disposal of the drugs was noted by the intravenous route. The significance of this finding in therapy is discussed. S.B.B.

Liguori, G.; Guiso, G. F.; and Campanacci, L. (Inst. of Physiol. and Inst. of Med. Path. of the Univ. of Cagliari, Cagliari, Italy): THE EFFECTS OF METOPIRONE OF GLUCOSE METABOLISM. *Metabolism* 13:499-506, June 1964.

Metopirone was found to have the following effects on the isolated hearts of *Bufo vulgaris* or on homogenates of this organ: (1) an increase or inhibition of the contraction force depending on concentration of the agent; (2) potentiation of the temporary repolarization phenomena of cardiac muscle; (3) increase in phosphorylase activity; (4) increase in the penetration of 2-desoxyglucose into myocardial cells. C.R.S.

Mabler, R. J.; Grann, V.; and Purdy, R. (Dept. of Med., New York Med. College, Flower and Fifth Ave. Hospitals, New York, N.Y., Met. Center and Presbyterian-St. Luke's Hosp.,

Chicago, Ill.): FUNCTIONING ISLET CELL ADENOMA. *JAMA* 188:791-93, June 1, 1964.

The case of an eighty-two-year-old female with a functioning, nonmalignant insulinoma of the pancreas is described in detail. The symptoms resembled those of cerebrovascular insufficiency. Studies included blood sugar levels during a fifteen-hour fast, a standard oral glucose, and intravenous tolbutamide (1.5 gm.) and an oral l-leucine stimulating tests. Blood insulin values rose decisively after oral glucose and intravenous tolbutamide but not after oral l-leucine stimulation. The authors underscore the need for considering this lesion in the differential diagnosis of symptoms of cerebrovascular insufficiency of the aged. S.B.B.

Makman, Maynard H.; and Sutherland, Earl W., Jr. (Dept. of Pharmacol., Sch. of Med., Western Reserve Univ., Cleveland, Ohio): USE OF LIVER ADENYL CYCLASE FOR ASSAY OF GLUCAGON IN HUMAN GASTRO-INTESTINAL TRACT AND PANCREAS. *Endocrinology* 75:127-34, July 1964.

The procedure for assay of glucagon with cat liver adenyl cyclase was found to be sensitive to .005 mg. of glucagon per ml. This system was almost completely dependent upon glucagon for the formation of cyclic 3'-5'-AMP and was employed for the detection and characterization of the hormone in human and dog gastrointestinal tissues. Epinephrine did not inhibit or compete with the glucagon effect in this system. The assay procedure revealed glucagon-like activity in the mucosal and muscular layers throughout the gastro-intestinal tract of man except for the esophagus. The concentration of glucagon activity in these tissues was about 2 mg. per gm. or about one eighteenth that in human pancreas. C.R.S.

Martin, Donald B.; and Castleman, Benjamin (Dept. of Med., Harvard Med. Sch., and Mass. Gen. Hosp., Boston, Mass.): PAIN IN LEFT UPPER QUADRANT OF ABDOMEN IN DIABETIC PATIENT. *New England J. Med.* 270:848-52, April 16, 1964.

An eighty-year-old white male entered the hospital complaining of pain in the left upper quadrant just the left of the epigastrium, of three years' duration. He had fever, leukocytosis, negative barium enema and a negative gall bladder X ray. He was found to have diabetes mellitus which was unresponsive to tolbutamide. He had a positive family history of diabetes. The patient died and at postmortem was found to have carcinoma of the body and tail of the pancreas. A lucid discussion brought up the following points: (1) Carcinoma of the pancreas is more common in men by ratio of 2 or 3 to 1; (2) the body and tail are involved in roughly a third to a fourth of the cases; (3) average age of onset is fifty to sixty years of age; (4) weight loss occurs in 85 per cent of the patients; (5) abdominal pain in 95 per cent; (6) constipation in 70 per cent; (7) anorexia in 70 per cent; and (8) emotional lability and symptoms of depression in 10-30 per cent. Half of the patients with carcinoma of the pancreas of the body and tail have a palpable liver and one third ascites. Half of the patients with carcinoma of the pancreas have anemia. G.I. series is normal in half the patients and barium enema in one third. B.R.B.

McIntyre, Neil; Holdsworth, C. D.; and Turner, D. S. (Medical Unit Royal Free Hospital, London, England): NEW INTERPRETATION OF ORAL GLUCOSE TOLERANCE. *Lancet* 2:20-21, July 4, 1964.

Several studies suggest that the level of blood glucose may not

be the sole factor which regulates the secretion of insulin. Since the uptake of glucose as reflected by the shape of the glucose tolerance curve is greater after intestinal absorption than after intravenous infusion, an intestinal factor stimulating insulin secretion might exist. Proof for such a factor is suggested by the finding of higher blood insulin levels and lower blood sugar levels when the same dose of glucose is infused into the jejunum rather than into a peripheral vein. Two normal studies were done and further investigations are in progress. T.G.S.

Monasterio, G.; Oliver, J.; Muesan, G.; Pardelli, G.; Marinuzzi, V.; and MacDowell, M. (Clin. Med. and Inst. of Path., Univ. of Pisa, Italy; Inst. de Recherch. Scientif. sur le Cancer, Villejuif (Seine); and Renal Res. Unit, Summit, N.J.): RENAL DIABETES AS A CONGENITAL TUBULAR DYSPLASIA. *Amer. J. Med.* 37:44-61, July 1964.

A study of two patients with renal glycosuria of different degrees of severity. Large renal specimens removed surgically were studied, after microdissection, by light and electron microscopy. Mitochondria were stained with Heidenhain's iron hematoxylin stain.

Pathologic lesions were confined to the proximal tubules of the glomeruli and consisted of ectasia of the lumen, flattened and irregular-sized epithelial cells with degeneration or disappearance of the "brush border" of the luminal surface, thickening of the basement membrane and definite abnormalities of the mitochondria. However, there was no abnormality of the histochemical reaction for alkaline phosphatase.

The authors favor a single pathologic and clinical classification of the disease as a congenital tubular dysplasia with some dynamic features and discuss previous studies of such cases. S.B.B.

Montgomery, D. A. D.; Rastogi, G. K.; and Weaver, J. A. (Sir George E. Clark Metabolic Clinic, Royal Victoria Hosp., Belfast, Northern Ireland): ACETOHEXAMIDE IN TREATMENT OF DIABETES MELLITUS. *Brit. M. J.* 1:868-71, April 4, 1964.

Forty women and ten men were treated with acetohexamide. The age range was 44 to 77 yrs., and the duration of diabetes 1 to 24 yrs. with an average of 3 to 3/4 yrs. According to the authors' criteria of effectiveness (good—blood glucose less than 150 mg. per 100 ml., and fair—blood glucose 150-200 mg. per 100 ml. at three hours postprandially) 70 per cent of the patients showed a good response and 12 per cent fair.

No severe toxic effects due to acetohexamide were noted. The drug was discontinued in only two patients, one with vomiting and abdominal cramps after a single dose of 1,000 mg., and another with edema of the feet, painful breasts, and malaise after taking the drug for four months. A statistically significant rise in the level of serum alkaline phosphatase was found at three and six month intervals in twenty-four patients, persistent in fifteen individuals.

Acetohexamide appeared to be effective in a single daily dose of 1,000 mg. At the end of six months, the average daily dose was 500 mg. In patients not responding to acetohexamide alone, the addition of metformin, 500 mg. two or three times a day, improved the control of the diabetes. Acetohexamide did appear to improve the diabetic control in patients previously not adequately responding to tolbutamide, but did not show any improvement in patients previously treated with chlorpropamide.

The authors state that more extensive clinical trial is desired.

able before acetohexamide can be recommended without reservation in the treatment of diabetic patients. R.F.B.

Rutstein, David D.; Castelli, William P.; Sullivan, Julia C.; Newell, John M.; and Nickerson, Rita J. (Dept. of Preventive Med., Harvard Med. Sch., Boston, Mass.): EFFECTS OF FAT AND CARBOHYDRATE INGESTION IN HUMAN BEINGS ON SERUM LIPIDS AND INTRACELLULAR LIPID DEPOSITION IN TISSUE CULTURE. *New Eng. J. Med.* 271:1-11, July 2, 1964.

The authors evaluated the effect of diets varying in fatty acid content and concentration on the intracellular lipid deposition in human aortic cells in tissue culture. Serum samples were drawn in the fasting state and three, six, nine and twenty-four hours after the ingestion of seven different test meals. Six of the seven meals contained fats. The other was a 2,000-calorie fat-free meal consisting almost entirely of carbohydrate. Polyunsaturated, natural saturated and saturated fats were utilized. Deposition of fat in human aortic cells, incubated in serum taken in the fasting state correlated with the level of total lipids, triglycerides and total cholesterol but not to that of the phospholipids. After the ingestion of each of the fat meals, lipid deposition was increased over the initial fasting deposition level. The polyunsaturated fat meal was followed by the greatest increase in lipid deposition over the fasting level. The carbohydrate meal caused suppression of fat deposition during the first six hours which was followed by a return almost to baseline in nine hours. The implications of this study are obvious. The importance of the acute changes in the level and composition of plasma fat on atherosclerosis compared to the chronic levels, however, remain to be delineated. B.R.B.

Schipper, Hirsch L. (Dept. of Surgery, Westminster Hosp., and Dept. of Veterans Affairs, London, Ont., Canada): EFFECT OF TOLBUTAMIDE ON WEIGHT GAIN, BLOOD SUGAR AND SERUM PROTEINS IN GERIATRIC PATIENTS. *Canad. Med. Ass. J.* 89:717-19, Oct. 5, 1963.

A double-blind study was carried out on eighteen domiciliary geriatric apparently healthy patients forty-three to eighty-five years of age. The tolbutamide dosage was 1,000 mg. before breakfast and lunch. From the statistical analysis of the results there was no effect on body weight, fasting blood sugar, total serum proteins, serum ratios, or serum protein fractions separated electrophoretically. B.F.K.

Schultz, Stanley G.; and Zalusky, Ralph (Bionucleonics Dept., U. S. Air Force Sch. of Aerospace Med., Brooks Air Force Base, Tex.): ION TRANSPORT IN ISOLATED RABBIT ILEUM. II. THE INTERACTION BETWEEN ACTIVE SODIUM AND ACTIVE SUGAR TRANSPORT. *J. Gen. Physiol.* 47:1043-59, July 1964.

The active transport of sodium ions from the mucosal to serosal surface of isolated segments of distal rabbit ileum was studied by measuring the potential difference across the gut wall, the short-circuit current, and the flux of Na. The addition of glucose or 3-o-methylglucose to the solution bathing the mucosal surface resulted in an increase in the rate of active sodium transport. Both of these sugars are actively transported, but 3-o-methylglucose is not metabolized. Fructose did not augment sodium transport. Fructose can be taken up and metabolized by intestinal cells, but is not actively transported. The transport of glucose follows saturation type kinetics, and the effect of glucose on sodium trans-

port also becomes relatively less and less as the glucose concentration is increased. When phlorizin, an inhibitor of sugar transport, is added to the mucosal solution, it inhibits the effect of 3-o-methylglucose on sodium transport. Phlorizin does not affect sodium transport when added to the serosal surface, or when applied in the absence of an actively transported sugar. The active transport of sodium is blocked by the addition of ouabain to the serosal surface of the intestinal preparation. The observations support the concept that there is a coupled uptake of sodium and actively transported sugars by intestinal epithelial cells. H.T.N.

Shaw, Walter N.; and Shuey, Eldon W. (Lilly Res. Labs., Eli Lilly and Co., Indianapolis, Ind.): THE PRESENCE OF TWO FORMS OF INSULIN IN NORMAL HUMAN SERUM. *Biochemistry* 2:286-89, March-April 1963.

The insulin activity of human serum was assayed by measuring the effect on glucose uptake of rat hemidiaphragm. In accordance with the findings of Antoniades and Gundersen, incubation of serum with a saline extract of rat adipose tissue caused an increase in the insulin activity found by bioassay. The additional activity was assumed to represent insulin that had been released from a less active "bound" form. Analysis of ten serum samples revealed a mean free insulin activity of 49 microunits per ml. and a "bound" insulin activity of 567 microunits per ml. The serum was treated with Dowex 50 in order to remove free insulin. The resultant eluate, when lyophilized and reconstituted to the volume of the original serum, contained 47 microunits of free and 586 microunits of "bound" insulin per ml. The presence of free insulin in the eluate was attributed to dissociation of some of the "bound" form. The ability of human serum to stimulate the synthesis of glycogen from glucose in rat hemidiaphragms was augmented after treatment of the serum with adipose tissue extract. The increase in insulin activity that resulted from the treatment of serum or resin eluate with adipose tissue extract was counteracted by antiserum to crystalline beef insulin. H.T.N.

Singer, Adolf (Brooklyn, N.Y.): SEGMENTAL DISTRIBUTION OF PERIPHERAL ATHEROSCLEROSIS. *Arch. Surg.* 87:384-90, September 1963.

Based upon direct measurement with calipers of the caliber of the lumen in lower limb arteriograms of 205 patients with clinically evident ischemia, the author has confirmed the concept that atheromatous lesions are segmentally deposited. He has demonstrated definite recurring patterns of atherosclerosis in the arteries to the lower limbs and has furnished support for the belief that proximal arterial stenosis and thrombosis exerts protective effect against more distal lesions. L.S.S.

Sneyd, J. G. T. (Dept. Biochem., Med. Sch., Univ. of Otago, New Zealand): PANCREATIC AND SERUM INSULIN IN THE NEW ZEALAND STRAIN OF OBESE MICE. *J. Endocr.* 28:163-72, January 1964.

A strain of New Zealand obese mice has been studied that exhibits a syndrome of hereditary obesity and hyperglycemia similar to but less pronounced than that found in mice from the Jackson Memorial Laboratory. The insulin content of the pancreas and the insulin-like activity of serum from the New Zealand obese strain of mice were considerably higher than in material from control nonobese mice. Adipose tissue and hemidiaphragms obtained from obese mice showed a response to insulin in vitro, as revealed by meas-

urements of glucose uptake, that was similar in magnitude to the response of tissue from nonobese control animals. It has been reported that New Zealand mice with hereditary obesity and hyperglycemia exhibit elevated levels of serum corticosterone, and it is suggested that the hyperglycemia and resistance to injected exogenous insulin might be attributable to an insulin antagonist. H.T.N.

Spritz, Norton (Second Med. Div., Bellevue Hosp., and Dept. of Med., Cornell Univ. Med. Coll., New York, N. Y.): CARBOHYDRATE-INDUCED LIPEMIA: REPORT OF A FAMILIAL OCCURRENCE. *New Eng. J. Med.* 271:291-93, Aug. 6, 1964.

Most familial cases of lipemia have been shown to have a deficiency of the enzyme, lipoprotein lipase. This report describes a father and son with hyperlipemia in which both the effect of dietary fat on the blood glyceride concentration and the nature of the particulate fat were characteristic of "carbohydrate-induced" rather than "fat-induced" lipemia. Abnormal carbohydrate metabolism, similar to that of prediabetes, has been described in most of the subjects with carbohydrate-induced lipemia. The father in this presentation had overt diabetes mellitus whereas carbohydrate metabolism was normal in the son. B.R.B.

Streeten, David H. P.; Gerstein, Mordecai M.; Woolfolk, Donald; and Doisy, Richard J. (Dept. of Med. and Biochem., State Univ. of New York Upstate Med. Center, Syracuse, N. Y.): MEASUREMENT OF GLUCOSE DISPOSAL RATES IN NORMAL AND DIABETIC HUMAN SUBJECTS AFTER REPEATED INTRAVENOUS INJECTIONS OF GLUCOSE. *J. Clin. Endocr.* 24:761-74, August 1964.

Thirty-eight normal subjects and fifteen diabetic patients were given 25 gm. of glucose intravenously three times at intervals of forty minutes. Blood sugars were followed and from the difference obtained ten minutes and thirty-five minutes after a single injection the "Glucose Disposal Rate" (GDR) of the load was calculated taking into account glucose space and also correcting for glycosuria. GDR was calculated for each of the three glucose loads and the mean values for young normal individuals were 17.4 gm./35 min., 21.66 gm./35 min., and 23.43 gm./35 min. The values were lower in normal elderly subjects (>70 years) and still lower in tolbutamide-treated diabetics. The lowest values were obtained in insulin-dependent diabetic patients. Simultaneous injections of 10 units of insulin with the first, 15 units with the second, and 20 units with the third glucose load brought GDR close to normal. The value of this method for assessing pancreatic insulin reserve is discussed. O.V.S.

Sullivan, M. Bruce, Jr.; and Patton, Thomas B. (Veterans Administration Hosp., and Med. Coll. of Alabama, Birmingham, Ala.): INSULIN, TOLBUTAMIDE, SEROTONIN AND THE DUMPING REACTION. *Ann. Surg.* 159:742-47, May 1964.

Verbatim conclusion: Tolbutamide sodium and cyproheptadine hydrochloride are effective therapeutic agents in the dumping reaction. The incidence of an abnormal or delayed insulin release in two thirds of the patients studied suggests the importance of carbohydrate metabolism. The variation of the serotonin response and its failure to correlate with the clinical response suggests that serotonin per se is not the critical determinant in the dumping reaction. E.A.W.

Taylor, K. W.; and Sheldon, Joanna (Diabetic Dept., King's College Hosp. Med. Sch., London, England): THE NATURE OF INSULIN DERIVED FROM AN ISLET CELL ADENOMA OF THE PANCREAS. *J. Endocr.* 29:99-100, April 1964.

An islet cell tumor of the pancreas was obtained from a patient who had been suffering from hypoglycemic episodes. A crude extract of insulin was prepared from the tumor with acid alcohol. Bioassay, using the rat hemidiaphragm glucose uptake method, revealed an insulin content of eight units per gram of tumor tissue. The effect of the tumor extract in stimulating glucose uptake by diaphragm was completely neutralized by antiserum against ox insulin. The insulin in the extract was further purified by paper chromatography and electrophoresis. The electrophoretic mobility of the insulin and of the A-chain obtained by performic acid oxidation was the same as that for crystalline ox insulin (or human pancreatic insulin). Although it has been reported that fluorescent antibody against insulin does not react well with the insulin in islet cell tumors in tissue sections, the present studies revealed no chemical or immunologic abnormality in purified islet cell insulin that could account for the observation. H.T.N.

Tidball, M. E. (Dept. of Pharmacology, The George Washington Univ. Sch. of Med., Washington, D.C.): INSULIN AND EPINEPHRINE EFFECTS ON PLATELET HISTAMINE RELEASE IN A PLASMA-FREE SYSTEM. *Amer. J. Physiol.* 207:177-80, July 1964.

When rabbit platelets were isolated from plasma and resuspended in a simple saline medium, minimal histamine release occurred. Resuspension of platelets in Krebs-Henseleit bicarbonate buffer was associated with spontaneous and complete histamine release. The presence of glucose in the Krebs buffer reduced release to about half, thereby enabling the study of both stimulation and inhibition of platelet histamine release in the same test system. In the presence of glucose, insulin decreased histamine release whereas epinephrine increased it. The results suggest that glucose metabolism is implicated in the release of histamine from rabbit platelets, and that histamine release is a phenomenon related to other homeostatic mechanisms which regulate cell processes under physiological conditions. M.G.B.