ABSTRACTS

Aoki, Thomas T.; Müller, Walter A.; Brennan, Murray F.; and Cahill, George F., Jr. (Joslin Diabetes Foundation and Dept. of Med. and Surgery, Harvard Med. Sch. and Peter Bent Brigham Hosp., Boston, Mass.): EFFECT OF GLUCAGON ON AMINO ACID AND NITROGEN METABOLISM IN FASTING MAN. Metabolism *23*:805-14, 1974.

Intravenous infusion of small amounts of glucagon for four days in patients who were fasted for five to six weeks resulted in multiple metabolic changes. Circulating levels of alanine and glutamine decreased, which suggests that hepatic gluconeogenic activity diminished while renal ammoniagenesis and gluconeogenesis increased. Reduced hepatic gluconeogenesis was substantiated by a prolonged t½ for labeled alanine. Serum insulin levels decreased significantly during the glucagon infusion while plasma levels of branched-chain amino acids increased. These observations suggested that oxidation of branched-chain amino acids was inhibited, thus reducing the availability of $-NH_2$ groups for alanine formation and release by muscle. The infusion of glucagon may have depressed endogenous glucagon release which in turn depressed hepatic gluconeogenesis and increased renal ammoniagenesis and gluconeogenesis. Elevations of glycine and threonine were observed also which may reflect decreased utilizations of these amino acids by liver and kidney. C.R.S.

Bataille, D.; Freychet, P.; and Rosselin, G. (Inst. National de la Santé et de la Recherche Medicale, Hôpital Saint-Antoine, Paris, France): INTERACTIONS OF GLUCAGON, GUT GLUCAGON, VASOACTIVE INTESTINAL POLYPEPTIDE AND SECRETIN WITH LIVER AND FAT CELL PLASMA MEMBRANES: BINDING TO SPECIFIC SITES AND STIMULATION OF ADENYLATE CYCLASE. Endocrinology *96*:713-21, 1974.

Verbatim summary. To investigate the interactions of pancreatic glucagon, gut glucagon, vasoactive intestinal polypeptide (VIP) and secretin with liver and fat, the binding of the peptides to specific sites and the stimulation of adenylate cyclase were studied in the plasma membrane fraction. Binding studies indicated that the receptor sites for pancreatic glucagon are clearly distinct from the sites for VIP and secretin in both tissues: Unlabeled VIP and secretin did not affect the ^{125}I-glucagon binding, and unlabeled glucagon was without effect on the ^{125}I-VIP and ^{125}I-secretin binding. In contrast, secretin and VIP appear to share a common binding site in both tissues: Unlabeled secretins (natural and synthetic) were capable of displacing the ^{125}I-VIP and unlabeled VIP inhibited the binding of ^{125}I-secretin. Gut glucagon inhibited the binding of ^{125}I-glucagon as well as that of ^{125}I-VIP and ^{125}I-secretin in both tissues. In the ^{125}I-glucagon binding systems, the inhibitory effect of gut glucagon, which contrasts sharply with the lack of effect of VIP and secretin, indicates that pancreatic and gut glucagons share a common binding site. In liver membranes, pancreatic glucagon was the most effective in stimulating adenylate cyclase; gut glucagon produced about 70 per cent and VIP 15 to 20 per cent of the maximum stimulation elicited by pancreatic glucagon. In fat cell membranes, VIP was more potent than pancreatic glucagon and secretin. The presence of VIP or of a VIP-like component in the gut glucagon can partly explain the high degree of potency of gut glucagon in stimulating adenylate cyclase in fat cell membranes.

Berning, H.; Orellana, K.; and Selberg, W. (Medizinische Abteilung and Pathologische Abteilung des Allgemeinen Krankenhauses Hamburg-Barmbek): RENAL PAPILLARY NECROSIS. Deutsch. Med. Wochenschr. *99*:1749-54, 1974.

Renal papillary necrosis, focal or total necrosis of the papilla and adjacent regions of the renal medulla, is usually a complication of other renal diseases. Incidence, cause and clinical course have definitely altered during the last three decades. Out of 15,749 autopsies during the period 1961 to 1971, the frequency was 1.51 per cent (n=238). The relation of men to women was 1.1:1.218 patients; 91.5 per cent were over fifty years and 78.9 per cent were over sixty. The major proportion of the patients was found in medical departments (57.1 per cent), followed by urological and surgical departments (18.9 and 18.5 per cent, respectively). Etiologically the dominant factors were urinary obstruction (46.6 per cent), diabetes mellitus (21.4 per cent) and chronic interstitial nephritis (16.8 per cent). The proportions with acute or chronic pyelonephritis without diabetes or urinary obstruction were 6.7 and 6.3 per cent, respectively. In 13.4 per cent (n=32) there was a rarer cause. The pathogenesis also determined the clinical picture. Three types of clinical courses could be differentiated: (1) the acute renal disease with fever or rigors, oliguria, uremia, and high mortality, mainly with urinary obstruction and/or diabetes mellitus; (2) chronic, recurrent renal disease with episodes of renal colic and hematuria, urinary infection and occasionally ureteric obstruction due to a papillary sequester; and (3) progressive uremia and anemia without urologic symptoms, mainly in chronic interstitial nephritis after prolonged abuse of analgesics. J.P.A.

Cahill, George F., Jr.; and Soeldner, J. Stuart (Elliott P. Joslin Res. Lab. Boston, Mass.): "A NON-EDITORIAL ON NON-HYPOGLYCEMIA". N. Engl. J. Med. *291*:905-06, 1974.

This editorial is prompted by the article "Non-Hypoglycemia Is an Epidemic Condition" by Yager and Young (in the same issue) which points to the widespread misapplication of this diagnosis and the need for the physician to correct this error.

Cahill and Soeldner point out that, even in adults, it is difficult to correlate blood sugar levels with symptoms. Diabetic patients may have symptoms after a decrease in blood sugar levels, from hyperglycemia to normal, occurs. They point out that 23 per cent of the normal population have a blood sugar level below 50 mg. per 100 ml.; an occasional value may be below 35 without symptoms. Thus, "chemical hypoglycemia" may be present without clinically significant hypoglycemia. This, of course, compounds our understanding of this disorder and makes its diagnosis more difficult. H.G.M.

Chaudry, Irshad H.; Sayeed, Mohammed M.; and Baue, Arthur E. (Div. of Cell Physiol., Dept. of Surg., Washington Univ. Sch. of Med. and Jewish Hosp. of St. Louis, St. Louis, Mo.): INSULIN RESISTANCE IN EXPERIMENTAL SHOCK. Arch. Surg. *109*:412-15, 1974.

After induction of experimental shock by exsanguination, basal in vitro glucose uptake by pieces of soleus muscle taken from adrenalectomized rats was unaltered. These same tissues, however, did not respond to addition of insulin (0.001 to 0.2 U. per milliliter) with increased glucose uptake. The authors conclude that shock had induced tissue changes resulting in insulin resistance independent of adrenocorticosteroids and catecholamines. However, these conclusions must be accepted with reservation, since the necessity of employing unphysiologically large concentrations of insulin to demonstrate glucose uptake by control muscle suggests that the preparation used was itself insulin-resistant. Furthermore, the effect of catecholamines released from nerve endings was not taken into consideration. J.E.G.

Christensen, Niels Juel; and Videbaek, Jorgen (Second Clin. of Intern. Med. and Dept. of Cardiol., Kommunehospitalet, Aarhus, Denmark): PLASMA CATECHOLAMINES AND CARBOHYDRATE METABOLISM IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION. J. Clin. Invest. *54*:278-86, 1974.

Transient glucose intolerance is known to be associated with acute myocardial infarction; this metabolic alteration has been felt to be related to augmented adrenergic activity. The present study was designed to explore further the relationships of glucose, free fatty acids, insulin, and catecholamines. Plasma epinephrine and norepinephrine were found to be elevated significantly in patients with an acute myocardial infarction. Plasma norepinephrine was found to be correlated positively with the fasting glucose, negatively with the intravenous glucose tolerance expressed as the K value, and negatively with the "insulin index" expressed as the ratio of initial rise in insulin during the glucose tolerance to the fasting insulin; a negative correlation was also seen in the rate of fall of free fatty acids during intravenous glucose. Plasma epinephrine did not correlate with any of the measured parameters. While the authors caution against assuming a cause-and-effect relationship, they suggest that the levels of norepinephrine observed in these patients are known to be associated with a suppression of plasma insulin resulting in a reduction in glucose tolerance and a rise in free fatty acids. R.R.

Geokas, Michael C.; Rinderknecht, Heinrich; Walberg, Clifford B. and Weissman, Robert (Depts. of Med., Sepulveda V.A. Hosp. and Univ. of Calif.-Los Angeles; and Main Lab., Los Angeles-Univ. of S. Calif. Med. Center, Los Angeles, Calif.): METHEMALBUMIN IN THE DIAGNOSIS OF ACUTE HEMORRHAGIC PANCREATITIS. Ann. Intern. Med. *81*:483-86, 1974.

Verbatim summary. The early differentiation between acute edematous and hemorrhagic pancreatitis is crucial for prognosis and treatment. By testing serum and ascites or pleural effusion for methemalbumin, the two types of pancreatitis can be distinguished early in the course of the disease. In a series of eighteen patients with acute hemorrhagic pancreatitis, we consistently found methemalbuminemia, whereas in twenty patients with severe edematous pancreatitis, five patients with gastrointestinal bleeding, and two patients with acute intraabdominal hemorrhage, methemalbumin in serum was not found. Detection of methemalbumin in serum and ascites or pleural effusion of patients with a history and performance of enzyme studies compatible with acute pancreatic inflammation should be considered virtually pathonomonic of the hemorrhagic form.

Goetz, Frederick C. (Univ. of Minnesota Med. Sch., Dept. of Med., Minneapolis, Minn.): CONFERENCE ON BETA CELL FUNCTION, TRANSPLANTATION, AND IMPLANTABLE GLUCOSE SENSORS: A SUMMARY. (Sponsored by the Kroc Foundation and held at headquarters in Santa Ynez Valley, Calif.) Metabolism *23*:875-84, 1974.

This concise and annotated review provides valuable information concerning the present status of experimental work on islet transplant procedures. Included are sections of transplantation of the intact pancreas with vascular anastomosis in human diabetic patients, islet transplants in animals, beta cell and islet cultures, and artificial substitutes for the beta cell. Among the conclusions reached, from the presentations at the conference, are the following: Islet transplantation does work either as whole-organ allografts in man or in rat isografts; islets are not immunogenically privileged (clear evidence of rejection is observed but is blunted in chronic uremic recipients); immunosuppressive treatment appears inescapable for human islet transplantation; there is no evidence of reduced rejection by keeping cells in tissue culture; isolated islets can implant themselves and function well in the host; impressive progress has been made in the development of a mechanical glucose sensor. While there are many problems to be overcome, significant progress is being made in these important investigations. C.R.S.

Hedstrand, Hans; and Aberg, Hans (Dept. of Intern. Med., University Hosp., Uppsala, Sweden): INSULIN RESPONSE TO INTRAVENOUS GLUCOSE DURING LONG-TERM TREATMENT WITH PROPRANOLOL. Acta Med. Scand. *196*:39-40, 1974.

Ten patients received an intravenous glucose tolerance test before and after an average of eleven months of taking an average dose of 510 mg. propranolol for hypertension. There was no difference in the four- and eight-minute insulin response or the sixty-minute insulin response to glucose. Glucose disappearance was not altered either. H.G.M.

Hill, Claire M.; Douglas, J.F.; Rajkumar, K.V.; Mc Evoy, J.; and McGeown, Mary G. (Renal Unit, Belfast City Hosp., Belfast, Northern Ireland): GLYCOSURIA AND HYPERGLYCEMIA AFTER KIDNEY TRANSPLANTATION. Lancet *2*:490-92, 1974.

In 1964, Starzl reported that glucose intolerance was found in all his patients who were treated with prednisolone after renal transplantation. He stated that thirteen of his first forty-two patients had severe glucose intolerance. Since then, few comments concerning diabetes in transplant patients have been made. The authors observed the onset of clinical diabetes in three of their thirty-one transplant patients and initiated a survey to assess the prevalence and severity of post-transplantation glucose intolerance. They found glycosuria in seventeen of thirty-one patients and did oral glucose tolerance tests in all but one who initially had hyperosmolar ketotic coma. When they compared the glucose and insulin levels of post-transplant patients with those of control subjects, they discovered that more than half had glucose intolerance which was characterized by subnormal insulin secretion. Interestingly, their post-transplant patients without glucose intoler-

ance also had reduced insulin secretion. Although adrenal corticosteroid therapy may be suspected as a factor in the genesis of glucose intolerance and diabetes, in other steroid-treated patients who develop diabetes, the serum insulin response is usually greater than normal. This fact suggests that azothioprine, the cytotoxic agent used together with steroids, may also be a factor. These investigators found that glycosuria and/or diabetes (1) became manifest usually within three months after transplant, (2) was more common if there was a family history of diabetes, and (3) appeared to be related to an increase in an antirejection therapy. They recommend that post-transplant patients be followed to detect glycosuria so that overt diabetes, with its increased susceptibility to infections, can be prevented. T.G.S.

Imawari, Michio; Akatsuka, Nobuharu; Ishibashi, Miyuki; Beppu, Hirokuni; Suzuki, Hidero, and Yoshitoshi, Yawara (1st Dept. of Intern. Med. and Dept. of Neurol., Fac. of Med., Univ. of Tokyo, Tokyo, Japan): SYNDROME OF PLASMA CELL DYSCRASIA, POLYNEUROPATHY, AND ENDOCRINE DISTURBANCES. Ann. Intern. Med. *81*:490-93, 1974.

Verbatim summary. A case of a small amount of IgGλM component, chronic progressive polyneuropathy, primary hypothyroidism, diabetes mellitus, elevated serum estrogen level, gynecomastia, impotence, generalized lymphadenopathy, peripheral edema, hirsutism, pigmentation and thickening of the skin, slight fever, and excessive perspiration is reported. Five similar cases, all in Japan, are known, and a new syndrome of plasma cell dyscrasia, polyneuropathy, and endocrine disturbances has been suggested recently by other researchers. We think that our case is the sixth case of this syndrome. The pathogenesis of this syndrome is unknown, but some genetic or racial factor may contribute to it.

Kaneto, Akio; and Kosaka, Kinori (3rd Dept. of Intern. Med., Fac. of Med., Univ. of Tokyo, Tokyo, Japan): STIMULATION OF GLUCAGON AND INSULIN SECRETION BY ACETYLCHOLINE INFUSED INTRAPANCREATICALLY. Endocrinology *96*:676-81, 1974.

Verbatim summary. Acetylcholine, infused at a dose of 1 μg./kg. min. for ten minutes into the cranial pancreaticoduodenal artery of anesthetized dogs, caused a prompt elevation of plasma levels of both immunoreactive glucagon (IRG) and insulin (IRI) in the cranial pancreaticoduodenal vein. Mean pancreatic venous plasma concentration of IRG showed a uniphasic increase during the infusion, and IRI, a biphasic augmentation. A delayed rise in plasma IRG and IRI was observed in the femoral artery, and a significant increase in the blood glucose level followed the administration. The elevation of plasma IRG and IRI during infusion of acetylcholine was inhibited by the prior local infusion of atropine at a dose of 3 μg./kg. min. for nine minutes. Simultaneous measurement of pancreatic vein blood flow and hormone concentrations revealed a rapid increase of the flow along with the concentrations of both hormones during infusion of acetylcholine, indicating a great augmentation in their output. These results suggest a role of the parasympathetic nerves in regulation of both glucagon and insulin secretion in the dog.

Kavanagh, Terry; Shephard, Roy H.; and Pandit, Veena (Toronto Rehabilitation Centre and Dept. of Environmental Health, Sch. of Hygiene, Univ. of Toronto, Toronto, Canada): MARATHON RUNNING AFTER MYOCARDIAL INFARCTION. JAMA *229*:1602-05, 1974.

Verbatim summary. Eight patients, who had an aerobic power (maximum oxygen consumption) initially predicted as 72 per cent of normal, were trained to the point of participation in the Boston Marathon one to four years after a demonstrated myocardial infarction. Seven of the eight completed the race at an average speed of 5.4 mph, corresponding to 81 per cent of their maximum oxygen consumption. Symptoms and signs, both immediately after the race and later, were remarkably few. However, a substantial (4 kg.) weight loss was incurred, with attendant dangers of heat stress. There was evidence of increased membrane permeability and protein catabolism (elevated levels of blood urea, creatinine, and creatinine phosphokinase) to a total of some 50 gm. Resting serum uric acid levels were normal. Marathon running should not be undertaken as a routine endeavor in post-myocardial infarction rehabilitation.

Lindsey, C. Alfred; Faloona, Gerald R.; and Unger, Roger H. (Veterans Administration Hosp. and Depts. of Intern. Med. and Biochem., Univ. of Texas Southwestern Med. Sch., Dallas, Texas): PLASMA GLUCAGON IN NONKETOTIC HYPEROSMOLAR COMA. JAMA *229*:1771-73, 1974.

Verbatim summary. To determine if hyperglucagonemia is present in the nonketotic hyperglycemic hyperosmolar syndrome as it is in diabetic ketoacidosis, we measured plasma glucagon in seven patients hospitalized with the former diagnosis. Despite blood glucose levels ranging from 812 to 1,224 mg. per 100 ml., plasma glucagon averaged 689 pg. per milliliter (S.E.M. ±215), and ranged from 130 to 1,825 pg. per milliliter. Hyperglucagonemia is a common finding in this form of poorly controlled diabetes.

Mortimer, C.H.; Tunbridge, W.M.G.; Carr, D.; Yeomans, Lynne; Lind, T.; Coy, D.H.; Bloom, S.R.; Kastin, A.; Mallinson, C.N.; Besser, G.M.; Schally, A.V.; and Hall, R. (Medical Professional Unit, St. Bartholomew's Hosp., London, England): EFFECTS OF GROWTH HORMONE RELEASE-INHIBITING HORMONE ON CIRCULATING GLUCAGON, INSULIN, AND GROWTH HORMONE IN NORMAL, DIABETIC, ACROMEGALIC, AND HYPOPITUITARY PATIENTS. Lancet *1*:697-701, 1974.

Growth hormone release-inhibiting hormone (GH-RIH) is a synthetic cyclic tetradecapeptide which suppresses growth hormone rises in healthy people after insulin-induced hypoglycemia, exercise, levodopa and arginine and lowers growth hormone in acromegalic subjects. Two normal subjects were infused with either saline or GH-RIH in a dose of 480 μg. for about three hours. GH-RIH caused basal insulin levels to fall to zero, suppressed basal glucagon and had little effect on basal glucose or nonesterified fatty acids (NEFA). When 50 gm. of glucose was given orally after two hours of GH-RIH infusion, glucose tolerance deteriorated to diabetic levels as insulin release was suppressed. During OGTT, when GH-RIH was stopped, peak insulin secretion promptly rose threefold over saline control and glucose fell below 50 mg. per cent. When the effects of arginine infusion were compared in normal subjects during saline and GH-RIH infusions, plasma insulin, arginine and glucagon responses were blunted. Identical studies in two diabetic subjects were similar to the normals. When two acromegalic subjects were infused with 1,000 μg. of GH-RIH over 150 minutes, orally administered

glucose rose slowly and glucose tolerance was less impaired as basal insulin was higher and GH-RIH infusion both lowered growth hormone and impeded insulin response to glucose. Glucagon levels were also lower. When GH-RIH was infused in a hypopituitary patient, arginine infusion was associated with higher glucose and lower insulin and glucagon levels. The infusion of GH-RIH in a patient with a glucagonoma was associated with a fall of pancreatic glucagon from 948 to 340 pg. per milliliter in forty minutes and glucose fell from 82 to 28 mg. per cent after ninety minutes. There were no important effects of GH-RIH on plasma corticosteroids, pulse, blood pressure, electrolytes or liver function tests. Thus GH-RIH, in doses which must exceed physiologic levels, inhibits not only growth hormone secretion but also insulin and glucagon. Since growth hormone and glucagon are elevated in the insulin-dependent diabetic, a long-acting form of GH-RIH might be of value for a trial designed to test its influence on microangiopathy. T.G.S.

Nervi, F.O.; Gonzalez, A.; and Valdivieso, V.D. (Sch. of Med. and Inst. of Biol. Sci., Catholic Univ. of Chile, Santiago, Chile): STUDIES ON CHOLESTEROL METABOLISM IN THE DIABETIC RAT. Metabolism *23*:495-503, 1974.

Alloxan diabetic rats were found to have significant hypercholesterolemia and elevated hepatic content of cholesterol suggesting an expansion of the cholesterol pool. In elucidation of the mechanisms involved in this phenomenon, it was demonstrated that (1) biliary excretion of cholesterol and bile salts was increased, a change which could be reversed by insulin, (2) an increased synthesis and pool size of trihydroxycholanic acid, and (3) a significant augmentation of cholesterol absorptive rates. The results demonstrate an increased rate of conversion of cholesterol into bile salts in the alloxanized rats and suggest that the expanded cholesterol pool may be related to an increased rate of cholesterol absorption. C.R.S.

Olefsky, J.M.; Batchelder, T.; Colome, S.; and Reaven, G.M. (Dept. of Med., Stanford Univ. Sch. of Med. and Vet. Adm. Hosp., Palo Alto, Calif.): EFFECT OF INTRAVENOUS GLUCOSE INFUSION ON PLASMA INSULIN REMOVAL RATE. Metabolism *23*:543-48, 1974.

The effects of different intravenous glucose loads on plasma insulin removal rates were studied in dogs receiving infusions of porcine insulin in various concentrations. Endogenous insulin secretion was suppressed by constant administration of propranolol and epinephrine so that plasma insulin concentrations were a function solely of entry and removal of the infused porcine insulin. The findings showed that steady state insulin concentrations were unchanged during the different glucose infusion loads and during the various insulin infusion rates. These data demonstrate that the rate of glucose administration and the subsequent blood glucose concentrations have no effect on plasma insulin removal. C.R.S.

Palmer, Warren K.; and Tipton, Charles M. (Exercise Physiol. Lab., Univ. of Iowa, Iowa City, Iowa): EFFECT OF TRAINING ON ADIPOCYTE GLUCOSE METABOLISM AND INSULIN RESPONSIVENESS. Fed. Proc. *33*:1964-68, 1974.

Verbatim summary. Fifty-seven male Sprague-Dawley rats were used to determine the effect of chronic exercise on glucose metabolism and insulin sensitivity of adipocytes isolated from epididymal fat pads. Animals were assigned to one of three weight-matched groups: exercise trained (ET), pair-weight control (PWC), and free-eat control (FEC). Each group had nineteen animals. ET rats ran five days per week on a motor-driven treadmill at progressive speeds, grades, and durations. Pair-weighting technics were used to keep the body weight of the ET and PWC groups approximately equal. Body weights of FEC animals were not controlled. At sacrifice, epididymal fat pads were removed and adipocytes were isolated by the collagenase technic. (U-^{14}C) Glucose metabolism was measured at thirty- and sixty-minute incubation times, with and without insulin, in all three groups. Metabolic activity was evaluated as a function of tissue weight, cellularity, and cell size. Training had no effect on adipocyte glucose oxidation but did stimulate glucose lipogenesis above FEC levels in sixty-minute samples in both the basal and insulin-stimulated conditions. Basal activity for ET cells was 303 nmoles glucose converted to lipid/$10^{11}\mu^2$ compared to a FEC activity of 194. In the presence of insulin, mean ET cell activity was 358 nmoles/$10^{11}\mu^2$ while that of FEC cells was 202. Glucose oxidation and lipogenesis were only minimally stimulated by insulin in this investigation.

Potter, D.E.; Wilson, L.M.; and Ellis, S. (Dept. of Pharmacol. and Toxicol., Univ. of Texas Med. Branch, Galveston, Tex.): SUPPRESSION OF ISOPROTERENOL-INDUCED HYPERGLYCEMIA BY ETHANOL. Proc. Soc. Exp. Biol. Med. *146*:972-74, 1974.

Verbatim summary. Ethanol inhibited markedly the hyperglycemic response to isoproterenol in the fasted rat, whereas the hyperglycemic response to epinephrine was not changed significantly. Since ethanol is a potent inhibitor of gluconeogenesis, these data give support to the suggestion that isoproterenol produces its hyperglycemic effect in the fasted rat by mechanisms involving gluconeogenesis. Furthermore, this work suggests that isoproterenol-induced hyperglycemia in the fasted rat may provide an animal model for testing other inhibitors of gluconeogenesis.

Reid, D.D.; Brett, G.Z.; Hamilton, P.J.S.; Jarrett, R.J.; Keen, Harry; and Rose, Geoffrey (Dept. of Med. Stat. and Epidemiol., London Sch. of Hygiene and Tropical Med.; Mass Radiography Service, North-West Metropolitan Regional Hospital Board; and Dept. of Med., Guy's Hosp., London, England): CARDIORESPIRATORY DISEASE AND DIABETES AMONG MIDDLE-AGED MALE CIVIL SERVANTS. Lancet *1*:469-73, 1974.

The authors conducted a survey to detect the prevalence of disorders which are leading causes of premature death in men. Males (18,403) aged 40 to 64 representing 77 per cent of all nonindustrial government workers living within two miles of Whitehall, London, were screened. Glucose tolerance was evaluated by measuring capillary blood glucose two hours after 50 gm. of oral glucose. The presence of known diabetes reported by questionnaire ranged from 0.6 per cent in those under age 50 to 1.6 per cent in those over age 60. After excluding known diabetics, the percentages by age of "new diabetics" as designed by a two hour capillary glucose over 200 mg. per 100 ml. were: ages 40 to 49, 0.1 per cent; ages 50 to 59, 0.4 per cent; ages 60 to 64, 0.9 per cent. Almost 25 per cent of all the men were 21 lb. or more over desirable weight and 3.2 per cent had blood pressures exceeding 200/115 mm. Hg. In addition, 11 per cent had symptoms suggesting coronary or peripheral vascular disease and 6.3 per cent had electrocardiographic evidence consistent with ASHD. The study will be continued to evaluate the effect of treatment. T.G.S.

Riedler, G.F.; Keusch, G.; and Schmid, M. (Medizinische Klinik, Stadtspitals Waid, Zurich, Switzerland): KNOCHENMARKTOXIZITAT, LAKTATAZIDOSE UND DISSEMINIERTE INTRAVASALE GERINNUNG NACH PHENFORMINMEDIKATION. Schweiz. Med. Wochenschr. *104*:1160-66, 1974.

A diabetic woman treated with phenformin was admitted to the hospital with severe lactic acidosis. In spite of the correction of the metabolic disorder, a hematoma of the abdominal wall developed. Obvious signs of bone marrow toxicity were shown.

The authors believe that phenformin was involved in the above toxic effect. No similar data are available in the literature. N.K.

Robertson, R. Paul; Gavareski, David J.; Porte, Daniel, Jr.; and Bierman, Edwin L. (Univ. of Washington Sch. of Med. and V.A. Hosp., Seattle, Wash.): INHIBITION OF IN VIVO INSULIN SECRETION BY PROSTAGLANDIN E_1. J. Clin. Invest. *54*:310-15, 1974.

The effect of prostaglandin E_1 (PGE_1) on insulin secretion was studied in anesthetized dogs by the infusion of PGE_1 into the femoral vein or into the thoracic aorta to preclude degradation in the pulmonary circulation; in both experiments basal insulin levels and glucose-stimulated insulin levels were significantly decreased over controls. Alpha adrenergic blockade with phentolamine caused the expected increase in basal insulin levels but did not block PGE_1 inhibition of basal or glucose-stimulated insulin levels. The authors suggest that PGE_1 either directly or indirectly inhibits endogenous insulin secretion in anesthetized dogs, and this effect does not appear to be related to alpha adrenergic activity. R.R.

Schneider, Louis E.; Hargis, Gary K.; Schedl, Harold P.; and Williams, Gerald A. (Div. of Gastroenterol., Dept. of Med., Univ. of Iowa Coll. of Med., Iowa City, Iowa): PARATHYROID FUNCTION IN THE ALLOXAN DIABETIC RAT. Endocrinology *96*:749-52, 1974.

Verbatim summary. Serum immunoreactive parathyroid hormone (IPTH) was measured in control and in alloxan-induced diabetic rats ingesting a normal calcium diet and in control rats ingesting a low calcium diet. Serum IPTH levels in controls ingesting the low calcium diet were three times those of controls on the normal calcium diet. Serum IPTH in diabetic rats was double that in controls. Therefore the diabetic rat manifests an appropriate parathyroid response to diminished calcium abosrption. The deficiency of duodenal calcium binding protein and the duodenal calcium malabsorption previously observed in diabetic rats are not the result of a defect in PTH regulation of vitamin D metabolism.

Stout, Robert W.; Brunzell, John D.; Porte, Daniel, Jr.; and Bierman, Edwin L. (Dept. of Med., Univ. of Washington Sch. of Med., and V. A. Hosp., Seattle, Wash.): EFFECT OF PHENFORMIN ON LIPID TRANSPORT IN HYPERTRIGLYCERIDEMIA. Metabolism *23*:815-28, 1974.

Phenformin was given to hypertriglyceridemic patients consuming isocaloric liquid formula diets. On a fat-free, 85 per cent carbohydrate diet, plasma TG, cholesterol and FFA levels decreased significantly. The predominant effect of the drug was on VLDL levels with no change in low density lipoprotein. Plasma TG and cholesterol levels were reduced also in the majority of subjects on a diet containing 40 per cent of calories as fat and 45 per cent as carbohydrate, but there was no effect of the drug on carbohydrate induction of TG elevation. Basal insulin levels were reduced in all subjects, and fasting glucose levels were lowered in the majority. The plasma lipolytic rate measured on endogenous substrate was reduced, although the postheparin lipolytic activity on an artificial substrate was unchanged. FFA turnover fell in parallel with the fatty acid levels. It was proposed that phenformin reduced plasma TG by decreasing the rate of endogenous TG production; this effect may be related to the influence of the drug on glucose, insulin and FFA homeostasis. In some patients, phenformin may impair TG clearance from plasma, which may account for the variable therapeutic response, since in three subjects, phenformin did not decrease TG levels on both diets. C.R.S.

Tattersall, R.B. (Diabetic Dept., King's Coll. Hosp., London, England): MILD FAMILIAL DIABETES WITH DOMINANT INHERITANCE. Q. J. Med. (New Series) *43*:339-57, 1974.

The author describes in detail three families in which a dominantly inherited form of diabetes occurs. The remarkable feature of this syndrome is that, despite onset of diabetes before the age of twenty, the disease assumes a pattern usually observed for maturity-onset diabetes. Ketoacidosis is not observed, and insulin therapy usually is not required. Complications are uncommon and mild. Seven out of twelve diabetics diagnosed under the age of thirty and having a mean duration of diabetes for thirty-seven years did not have retinopathy. None of the diabetics had renal disease or proteinuria. Once established, the severity of diabetes did not progress. In four cases, insulin secretion studies demonstrated a delayed and subnormal response during oral glucose tolerance tests. This syndrome is clearly distinct from the usual insulin-dependent diabetes mellitus occurring before the age of twenty and provides evidence that diabetes is genetically heterogenous. J.E.G.

Vandeweghe, Mark; Vermeulen, Alex (Dept. of Intern. Med., Div. of Endocr. and Metabol., Academic Hosp., Ghent, Belgium): GROWTH HORMONE AND CORTISOL SECRETION AFTER PROPRANOLOL-GLUCAGON TESTING IN THE ADULT. Metabolism *23*:853-62, 1974.

Pituitary HGH response to propranolol-glucagon stimulation was tested in patients with obesity, hypothyroidism and hypopituitarism as well as normal subjects. In the normal and obese subjects, the positive HGH response was significantly lower than that obtained with the insulin tolerance test. A blunted HGH was observed in primary myxedema and hypopituitarism. An increase in plasma cortisol was comparable to that obtained with insulin in a group of normal subjects. It was concluded that the propranolol-glucagon test is a safe and reliable procedure, although normal nonresponders do exist and that it is a weaker stimulus for HGH release than insulin-induced hypoglycemia. The test may also be useful for the evaluation of the pituitary-adrenal axis. C.R.S.