ABSTRACTS

Alberti, K.G.M.M.; Christensen, N.J.; Christensen, S.E.; Hansen, Aa. P.; Iversen, J.; Lundbaek K.; Seyer-Hansen, K.; and *Orskov, H.* (Second Univ. Clin. of Intern. Med., Kommunehospitalet, Aarhus, Denmark): INHIBITION OF INSULIN SECRETION BY SOMATOSTATIN. Lancet *2*:1299-1301, 1973.

Somatostatin is a polypeptide which has been isolated from the hypothalamus and synthesized in a biologically active cyclic form. Its role is to inhibit the release of growth hormone by the pituitary. Because it may become useful in the treatment of acromegaly and in suppressing growth hormone in subjects with microvascular complications of diabetes, its effects on insulin secretion were studied. In five normal subjects plasma glucose and immunoreactive insulin were measured serially after intravenous administration of 25 gm. of glucose. The same study was done in the same subjects two minutes following the intravenous administration of 250 μg of somatostatin. The insulin response to glucose was markedly inhibited in all when somatostatin was given. In four of the five subjects the rate of glucose disappearance was reduced after administration of somatostatin. In another study glucose with and without somatostatin was perfused through the isolated dog pancreas. A reduction in insulin secretion was also observed. The authors point out that a bolus injection of somatostatin without sustained infusion influences insulin secretion over sixty minutes and that the mechanism may be inhibition of the initial insulin rise to glucose. They also state that concentrations of somatostatin similar to those under which the study was done are not likely to occur during normal physiological conditions. T.G.S.

Aliapoulios, M. A.; Morain, W. D.; and *Kacoyanis, G. P.* (Dept. of Surg., Harvard Med. Sch., Boston, Mass.): GLUCAGON AS A HYPOCALCEMIC AND HYPOPHOSPHATEMIC AGENT. Gastroenterology *65*:912-18, 1973.

Verbatim summary. Subcutaneously injected glucagon at the optimal dose of 800 μg per kg. produces hypocalcemia of 1.1 $\pm$ 0.21 mg. per 100 ml., one-half hour after administration in intact rats. As little as 40 kg. per 100 ml. also elicit hypocalcemia, but to a lesser degree. Thyrocalcitonin, also at optimal dosage, causes twice as great a decrease in serum calcium with maximum effect one hour after injection. Although glucagon produces hyperglycemia at one-half hour, thyrocalcitonin has no effect on serum glucose. When administered to the same animals, the two agents are additive in their effect on serum calcium and phosphate. The suggested mechanism of glucagon-induced hypocalcemia in the rat involves a site in the gastrointestinal tract other than the stomach, while the hypophasphatemic effects of glucagon are expressed primarily through the kidneys, and perhaps also through the stomach. Other mechanisms for the hypocalcemia and hypophosphatemia observed after glucagon are not ruled out.

Bortz, W. M. (Palo Alto Medical Clinic, Palo Alto, Calif.): THE PATHOGENESIS OF HYPERCHOLESTEROLEMIA. Ann. Int. Med. *80*:738-46, 1974.

Verbatim summary. Elevation of serum cholesterol level is caused by decreased output and increased input. Increased input, as manifested by increased synthesis, seems to be the more common mechanism. Many of the acknowledged risk factors in the development of coronary artery disease are characterized by increased cholesterol formation. It is proposed that the most frequent biologic risk factor that underlies a large number of the many other seemingly separate effectors is the excessive flux of fat to the liver.

Boyd, A. E., III; Giamber, S. R.; Mager, M.; and Lebovitz, H. E. (U.S. Army Res. Ins. of Environ. Med. Natick, Mass., and Div. of Endocrin., Dept. of Med. Duke Univ. Med. Ctr., Durham, N. C.): LACTATE IINHIBITION OF LIPOLYSIS IN EXERCISING MAN. Metabolism *23*:531-42, 1974.

Sodium lactate was infused into normal males during physical activity, which was capable of increasing arterial FFA and glycerol but not lactate. A marked rise in lactate and pyruvate associated with the infusion resulted in an inhibition of the increase in FFA and glycerol seen during control studies. The decreased release of FFA and glycerol could not be attributed to insulin release since the concentration of arterial insulin decreased during exercise. The results suggest that an increase in plasma lactate, pyruvate, or both, may cause a direct inhibition of exercise-mediated lipolysis in man. C.R.S.

Broun, J.; Molnar, I. G.; Clark, W.; and Mullen, Y, (Depts. of Med., Biol., Microbiol. and Immunol., Univ. of Calif., L.A., Calif.): CONTROL OF EXPERIMENTAL DIABETES MELLITUS IN RATS BY TRANSPLANTATION OF FETAL PANCREASES. Science *184*:1377-79, 1974.

Verbatim summary. Experimental diabetes mellitus in young Lewis rats was successfully treated by transplantation of fetal pancreases from syngeneic fetuses. Complete or partial control lasting up to 165 days was achieved in 64 per cent of recipients by using two to three pancreases of fetal age (fifteen to eighteen and one-half days) placed under each kidney capsule. Islets of Langerhans without exocrine elements were present in the transplants.

Condon, R. E.; Poulin, T. L.; Wagner, W. G.; and Pissiotis, C. A. (Dept. of Surg., Med. Coll. of Wisconsin, Milwaukee; Surg. Serv, Vets. Admin. Ctr., Wood, Wisc.): EXPERIMENTAL PANCREATITIS TREATED WITH GLUCAGON OR LACTATED RINGER SOLUTION. Arch. Surg. *109*:154-58, 1974.

Glucagon is known to inhibit pancreatic exocrine secretion, and elevated levels of plasma glucagon are observed in acute pancreatitis. It has therefore been suggested that this hyperglucagonemia may serve as a natural defense mechanism and that administration of exogenous glucagon may be useful as adjunctive therapy for pancreatitis. In the present study, experimental pancreatitis was induced in dogs by the obstructed duodenum technic and by the injection of irritants into the pancreatic duct. Glucagon treatment (0.4 mg./hr., up to three times) alone or in combination with the

volume resuscitation was found to be no more effective than simple volume resuscitation in the treatment of pancreatitis. In mild to moderate pancreatitis, glucagon therapy was associated with pancreatic hemorrhage to a greater extent than in either fluid resuscitated or untreated control animals. This study suggests that administration of glucagon is not useful in the treatment of acute pancreatitis and may be detrimental. J.E.G.

Cuatrecasas, P. (Johns Hopkins Univ., Baltimore, Md.): PROBLEMS IN RECEPTOR IDENTIFICATION : CATECHOLAMINES. New Engl. J. Med. *291*:206, 1974.

This editorial points out the difficulties in equating studies of the binding of radioactive hormones to certain cells or subcellular fractions with the action of the hormones. This is best illustrated by the finding that the binding of catecholamines to certain cells is dependent on the catechol moiety of the hormones and does not distinguish between active and inactive catecholamines. Therefore, the binding studies are in no way related to the biologic action of the hormones with regard to the catecholamines at the present time. H.M.

Derr, R. F.; Zieve, L. (Minneapolis Vet. Adm. Hosp., Univ. of Minnesota, Minneapolis, Minn.): EFFECT OF CARBOHYDRATE LOAD BY INTRAVENOUS INFUSION IN FASTED RATS ON LIVER GLUCOSE-6-PHOSPHATE DEHYDROGENASE AND MALIC ENZYME. J. Nutr. *104*:65-68, 1974.

The authors demonstrated that both acute fasting and chronic starvation reduced the activity of glucose-6-phosphate dehydrogenase and malic enzyme to about the same extent in the liver. Infusion of chronically starved rats for twenty-two hours with a high carbohydrate solution caused an increase in these liver enzyme activities to levels that were two to three times above normal. Similar infusions, when carried out in normal rats, also revealed a two to threefold increase in these enzyme activities. These results together with data reported previously for normal and fasted rats fed high carbohydrate diets, indicated a "starve-refeed" response in which enzyme activities overshoot their normal levels in liver. This appears due to the administration of excess glucose relative to the rat's capacity to metabolize carbohydrate. T.J.M.

Dyck, W. P.; Bonnet, D.; Lasater, J; Stinson, C; and Hall, F. F. (Gastroint. Physiol. Res. Labs., and Sect. Biochem., Dept. Clin. Path., Scott and White Clinic, Temple, Texas): HORMONAL STIMULATION OF INTESTINAL DISACCHARIDASE RELEASE IN THE DOG. Gastroenterology 66:533-38, 1974.

Verbatim summary. Release of enteric enzymes, sucrase, maltase and lactase, into the perfused small intestinal lumen of the dog was augmented by the injection of secretin and cholecystokinin. A direct hormonal stimulation of the intestinal mucosa is considered responsible for the enzyme release, since bile and pamcreatic juice were excluded from the perfusion solution. Cholecystokinin exerted a much more pronounced effect on enzyme release than did secretin. Disaccharidase activities in mucosal tissue remained relatively constant after the injection of cholecystokinin.

Erwald, R.; Hed, R.; Nygren, A.; Rojdmark, S.; and Wiechel, K.-L. (Depts. of Med. II and Surg. II, Sodersjukhuset, Stockholm, Sweden): COMPARISON OF THE EFFECT OF INTRAPORTAL AND INTRAVENOUS INFUSION OF INSULIN ON BLOOD GLUCOSE AND FREE FATTY ACIDS IN PERIPHERAL VENOUS BLOOD OF MAN. Acta Med. Scand. *195*:351-57, 1974.

Insulin was infused over a thirty-minute period into either a peripheral vein or the portal vein at a dose of 0.05 units per kilogram of body weight or 0.02 units per kilogram in fourteen unanesthetized subjects. Interestingly enough the hypoglycemic response was the same, but the fall in free fatty acids was significantly greater when insulin was infused into the peripheral vein, presumably due to the fact that more insulin was actually reaching the peripheral tissue rather than being initially degraded in the liver. H.M.

Gharib H.; and Munoz J. M. (Mayo Clinic and Mayo Foundation, Rochester, Minn.): ENDOCRINE MANIFESTATIONS OF DIPHENYLHYDANTOIN THERAPY. Metabolism *23*:515-24, 1974.

In this review, the influence of diphenylhydantoin (DPH) on a variety of metabolic and endocrinologic processes is summarized with sections devoted to hypothalamico-hypophyseal neurosecretion, the adrenal cortex, thyroid, calcium metabolism and blood glucose. In the latter, it is recalled that hyperglycemia, glycosuria and hyperosmolar coma have been observed in DPH-treated patients. The drug inhibits glucose-induced insulin release from isolated rat pancreas, an effect mediated by alterations in enzyme-dependent cation fluxes. Defective hydroxylation of the drug may occur as a genetic characteristic leading to a high concentration of DPH in the blood resulting in toxic manifestations from a usual dose. DPH may intensify the diabetic process and, in insulinoma, may depress the secretion of insulin. C.R.S.

Giorgio, M. A.; Johnson, C. B.; and Blecher, M. (Dept. of Biochem., Schs. of Med. and Dentistry and Grad. Sch., Georgetown Univ., Washington, D.C.): HORMONE RECEPTORS III. PROPERTIES OF GLUCAGON-BINDING PROTEINS ISOLATED FROM LIVER PLASMA MEMBRANES. J. Biol. Chem. *249*:428-37, 1974.

Purified rat liver plasma membranes, rich in glucagon-stimulatable adenylate cyclase activity, were extracted by the non-ionic detergent, Lubrol-PK. Glucagon binding proteins could be identified in crude and purified membrane extracts by gel filtration following saturation of binding sites with I^{125} glucagon before or after extraction. The quantitative micro-binding assay required as little as 0.25 micrograms of partially purified glucagon binding proteins. The partially purified protein had a molecular weight calculated on a calibrated agarose column of about 190,000. This protein also bound I^{125} insulin, although to a lesser extent than I^{125} glucagon. It did not bind I^{125} adrenal corticotropic hormone. A detailed description of the method of isolating this protein was given in the article. T.J.M.

Haour, F.; and Bertrand, J. (Unite de Recherches Endocr. et Metabolique Chez l Enfant INSERM-U. 34, Hosp. Debrousse, 69005 Lyon, France): INSULIN RECEPTORS IN THE PLASMA MEMBRANES OF HUMAN PLACENTA. J. Clin. Endocrinol. Metab. *38*:334-37, 1974.

Verbatim summary. The binding of insulin, glucagon, and chorionic somatomammotropin (HCS or HPL) to the plasma membranes of human placenta was examined, Insulin showed specific binding to the plasma membranes, whereas glucagon and HCS did not. The findings suggest that insulin receptors with high affinity and high capacity are present in human placental membranes.

Haymond, M. W.; Karl, I. E.; and Pagliara, A. S. (Depts. of Pediat. and Med., Divs. of Endocrinol. and Metab., Washington Univ. Sch. of Med., St. Louis, Mo.): INCREASED GLUCONEOGENIC SUBSTRATES IN THE SMALL-FOR-GESTATIONAL-AGE INFANT. N. Engl. J. Med. *291*:322-28, 1974.

This study shows that small-for-gestational-age infants have increased levels of lactate and alanine in their blood in association with lowered blood glucose values during the first twenty-four hours of life. Their plasma cortisol and growth hormone levels are also higher than in normal size infants while their insulin values are in the normal range. The authors conclude from their data the relative activity of phosphoenolpyruvate carboxykinase, one of the rate limiting enzymes in gluconeogenesis, is less in these infants accounting for the lower than normal blood sugar values in the face of increased blood levels of gluconeogenic substrates. H.M.

Hermreck, A. S.; Thomas, C. Y. IV; and Friesen, S. R. (Dept. of Surgery, Univ. of Kansas Med. Ctr., Kansas City, Kan.): IMPORTANCE OF PATHOLOGIC STAGING IN THE SURGICAL MANAGEMENT OF ADENOCARCINOMA OF THE EXOCRINE PANCREAS. Am. J. Surg. *127*:653-57, 1974.

This is a short, interesting article describing the staging of pancreatic carcinoma with emphasis on the surgical management and prognosis of the various stages. As the title implies the article is aimed mainly at the exocrine portion of the pancreas with no mention of endocrine abnormalities. F.G.B.

Hirata, Y.; Tominaga, M.; Ito, J. I.; and Noguchi, A. (First Dept. of Intern. Med., Tottori Univ. Sch. of Med., Yonago; and Beppu-Noguchi Hosp., Beppu, Japan): SPONTANEOUS HYPOGLYCEMIA WITH INSULIN AUTOIMMUNITY IN GRAVES' DISEASE. Ann. Intern. Med. *81*:214-18, 1974.

Verbatim summary. A patient with Graves' Disease developed spontaneous hypoglycemia after treatment for three weeks with methimazole. The hypoglycemic attacks lasted for four days and disappeared spontaneously. Although the patient had never received exogenous insulin, significant insulin-binding antibodies were found in the serum, and a huge amount of immunoreactive insulin (23,100 to 35,280 μU/ml.) was extracted from the serum obtained during the hypoglycemic attacks. One year after the episode of hypoglycemia, insulin-binding antibodies and elevated serum immunoreactive insulin were still present in the patient. The autoimmune concept might provide the most plausible explanation for the combination of Graves' Disease and spontaneous hypoglycemia in this case.

Isaacson, R.; Weiland, L. H.; and McIlrath, D. C. (Mayo Clinic and Mayo Foundation, Rochester, Minn.): BIOPSY OF THE PANCREAS. Arch. Surg. *109*:227-30, 1974.

Laparotomy and biopsy of the pancreas were performed on 527 patients during a ten-year period. All but one case was diagnosed by examination of fresh frozen sections and with review of permanent slides. Complications occurred in seventeen cases. These included pancreatitis (7), sepsis (2), peritonitis (2), abscess (4), gastrointestinal bleeding (1), and bleeding from the drain site (1). Nine deaths occurred following the procedure. The over-all incidence of complications considered to be secondary to the procedure was 4.1 per cent and the mortality was 1.5 per cent. The authors suggest that biopsy of the pancreas either by wedge or needle technic and examination of fresh frozen sections provide a reasonably safe and reliable way to establish the diagnosis of pancreatic disease. J.E.G.

Kamm. D. E.; and Strope, G. L. (Dept. of Med., Rochester General Hosp., Univ. of Rochester Sch. of Med., Rochester, N.Y.): EFFECT OF ACID-BASE STATUS ON TISSUE GLYCOGEN IN NORMAL AND DIABETIC RATS. Am. J. Physiol. *226*:371-76, 1974.

Acid base status has been demonstrated to influence multiple aspects of carbohydrate metabolism, including glycolysis, gluconeogenesis, hexomonophosphate shunt activity, and glucose tolerance. The authors investigate the possibility that acidosis may be the factor responsible for the decrease in tissue glycogen content during diabetes. This has been suggested by some workers, but contradicted by others.

Glycogen content of liver, muscle and renal cortex was examined in normal and diabetic rats given ammonium chloride, ammonium bicarbonate ($NaHCO_3$) and and sodium chloride. In normal animals acidosis increased glycogen content in liver and muscle, but did not affect renal cortical glycogen content or plasma insulin. In diabetic animals, although glycogen content was decreased in muscle and liver and increased in renal cortex, it was not altered by changes in acid base status. Muscle from normal and diabetic rats incubated at pH 7.1 had increased final glycogen content, and conversion of glucose to glycogen, and decreased lactate CO_2 production when compared with incubations conducted at pH 7.7.

The results, according to the authors, indicate that the decrease in liver glycogen during uncontrolled diabetes is secondary to impaired carbohydrate metabolism and not to the associated acidosis. T.J.M.

Kelly, P. A.; Posner, B. I.; Tsushima, T.; and Friesen, H. G. (Dept. of Exp. Med. and McGill Univ. Clin., Royal Victoria Hosp., Montreal 112, Quebec, Canada): STUDIES OF INSULIN, GROWTH HORMONE AND PROLACTIN BINDING: ONTOGENESIS, EFFECTS OF SEX AND PREGNANCY. Endocrinology *25*:532-39, 1974.

Verbatim summary. The ontogenesis of specific binding of ^{125}I-labeled insulin, hGH and oPRL was measured in tissues from rat, rabbit and guinea pig. Binding of ^{125}I-oPRL and ^{125}I-hGH was very low in liver membranes from fetal and immature rats. A ninefold (oPRL) and 3.5-fold (hGH) increase in binding occurred between twenty and forty days of age with a greater increase in binding in mid and late pregnancy. Binding to male liver membranes was significantly lower at all stages of development. There were no significant changes in the binding of ^{125}I-hGH from fetal through thirty-day rabbit liver membranes. Between thirty and sixty days of age, a sixfold increase in binding occurred, with a further increase in binding during pregnancy. A similar overall pattern was observed with ^{125}I-bGH. The increase in specific binding of ^{125}I-oPRL was more gradual and occurred earlier than for ^{125}I-GH. In the guinea pig, three patterns of ^{125}I-insulin binding with respect to development were observed. Fetal placenta and kidney showed marked increase in specific binding between earlier (50g) and later (50g) fetal stages. Binding to liver membranes at both early and late fetal stages remained constant. In contrast, heart membranes from both fetal stages bound ^{125}I-insulin at twice adult levels. Scatchard analysis of displacement curves of rat liver membranes incubated with ^{125}I-oPRL revealed similar affinity constants ranging form 0.7 to $0.9 \times 10^9 M^{-1}$. However, pregnancy increased binding capacity 3.5-fold. In rabbit liver membranes exhibited similar affinity constants ranging from 0.8 to 1.5 = $10^9 M^{-1}$.

King, A. J.; Cooke, N. J.; McCuish, A.; Clarke, B. F.; and Kirby, B. J. (Dept. of Med., Univ. of Edinburgh, and Diabetic and Dietetic Dept., Royal Infirmary, Edinburgh, Scotland): ACID-BASE CHANGES DURING TREATMENT OF DIABETIC KETOACIDOSIS. Lancet *1*:478-81, March 23, 1974.

There is dispute regarding the use of bicarbonate for the treatment of diabetic ketoacidosis. The authors attribute this uncertainty to a lack of data describing recovery from acidosis in patients treated with insulin and nonbicarbonate replacement fluids. In this study serial arterial pH, PCO_2, PO_2 and lactate values were measured in ten patients. Their mean admission findings were: age forty-five years, blood glucose 753 mg. per cent, urea 103 mg. per cent, Na 133 mEq/L, bicarbonate (below) 8 mEq/L, arterial pH 7.09 and calculated osmolality, 323. During an average period of thirty-eight hours post admission, they were treated intravenously with average amounts of: water 9.2 L; Na 516 mEq and insulin 1480 U. Blood-gas analyses showed no overall change in arterial pH or bicarbonate during the first hour of therapy. Thereafter, blood gasses returned to normal but even at twenty-four hours there was a compensated metabolic acidosis. Lactate levels were 2.17 ± S.D. 0.90 mmole/L and were elevated in four to seven patients studied. Initial and twenty-four hour C.S.F. pH did not vary significantly in the three subjects in whom it was measured. One patient died at twenty-two hours and autopsy revealed severe renal papillary necrosis. Another died of cardiac arrest and autopsy showed severe chronic renal disease and atherosclerosis. The authors conclude that intravenous bicarbonate is probably only required when serial measurements of arterial pH and carbon dioxide show no improvement with conventional treatment by insulin and intravenous fluids. T.G.S.

Kumar, D.; Mehtalia, S. D.; and Miller, L. V. (Diabetes Section, Dept. of Med. School of Medicine, Univ. of So. Calif. L. A., Calif.): DIAGNOSTIC USE OF GLUCAGON-INDUCED INSULIN RESPONSE. Ann. Int. Med. *80*:697-701, 1974.

Verbatim summary. The intravenous glucagon stimulation test was assessed as a diagnostic tool in the differential diagnosis of hypoglycemia. Six of seven patients with insulinoma had peak insulin values over 130 μU/ml. None of the controls with normal weight or patients with hypoglycemia as a result of other causes had a peak insulin value over 98 μU/ml. In this study and in glucagon tests done by other investigators, the peak insulin responses occurred from three to thirty minutes after injection of glucagon. Since this peak is highly transient, it may be missed unless sampling is done every five minutes for at least thirty minutes. When done properly, this test was positive in over 80 per cent of insulinoma patients. False-negative results occur in patients treated with diazoxide, hydrochlorthiazide, or diphenylhydantoin. False-positive tests may be seen in individuals who are obese or treated with tolbutamide.

Lampe, E. W. II; Ruiz, J. O.; Simmons, R. L.; and Najarian, J. S. (Dept. of Surg., Univ. of Minnesota Health Sciences Center, Minneapolis, Minn.): HYPERGLYCEMIC NONKETOTIC COMA AFTER RENAL TRANSPLANTATION. Am. J. Surg. *127*:342-44, 1974.

Verbatim summary. A case of nonketotic hyperglycemic coma with neurologic sequelae in a patient with a renal transplant is presented. A review of 253 patients in whom 284 kidney transplantations were performed at the University of Minnesota showed the incidence of this syndrome to be 0.4 per cent. Although the administration of steroids is the predisposing factor, this patient did not manifest nonketotic hyperglycemic coma until subjected to a situation of physical and mental stress. Neurologic sequelae required six months of rehabilitaiton. The initial renal dysfunction was resolved after treatment of hyperglycemia and dehydration. Impaired renal function during hyperglycemia does not necessarily indicate a rejection episode and should not be treated with increased doses of steroids until hyperglycemia is controlled and renal dysfunction has been verified.

Lassman, M. N.; Genel, M.; Wise, J. K.; Hendler, R.; and Felig, P. (Depts. of Internal Med. and Pediatrics, Yale Univ. School of Med., New Haven, Conn.): CARBOHYDRATE HOMEOSTASIS AND PANCREATIC IISLET CELL FUNCTION IN THALASSEMIA. Ann. Int. Med. *80*:65-69, 1974.

Verbatim summary. Glucose tolerance and pancreatic alpha- and beta-cell functions were evaluated in eight thalassemic patients, from five to thirty-one years of age, receiving chronic transfusion therapy. Two patients had insulin-dependent diabetes, and two had a diabetic glucose tolerance test; one patient had a blood glucose response compatible with reactive hypoglycemia. All but two patients had a delayed or diminished insulin response, or both, to glucose infusion. In seven of eight patients the glucagon response to infusion of alanine was significantly reduced. Abnormalities of carbohydrate homeostasis are frequently seen in regularly transfused thalassemic patients. In such patients iron overload often results in diminished alpha- and beta-cell function.

Lin, T.; and Tucci, J. R. (Dept. of Med., Roger Williams General Hosp. and Div. of Biol. and Med. Sciences, Brown Univ., Providence, R. I.): PROVOCATIVE TESTS OF GROWTH-HORMONE RELEASE. Ann. Int. Med., *80*:464-69 1974.

Verbatim summary. Seven tests of growth-hormone release were evaluated in thirty-one hospitalized nonobese persons without evidence of endocrine disease. Plasma growth-hormone levels were measured before and after administration of insulin, 0.1 unit/kg. body weight intravenously; glucagon, 1 mg. intramuscularly; levodopa, 500 mg. by mouth; metyrapone, 750 mg. by mouth; alpha 1-24-ACTH (cosyntropin), 0.25 mg. intravenously; and one to two hours after the onset of nocturnal sleep, and after fifteen minutes of vigorous stair climbing. Insulin uniformly stimulated growth-hormone release in all nineteen persons tested, whereas twenty-one of twenty-four (87 per cent) responded to levodopa and seventeen of twenty-one (81 per cent) to glucagon. ACTH stimulated growth-hormone release in only seven of twelve persons, whereas metyrapone had no effect. A growth-hormone response to sleep was found in only two of eleven, whereas exercise stimulated growth-hormone release in four out of ten. Although the highest growth-hormone levels were associated with insulin hypoglycemia, these were not significantly different from levels after administration of levodopa or glucagon (P greater than 0.05). These data suggest that levodopa is a reasonably effective alternative to insulin hypoglycemia as a test of growth-hormone release. Its advantages are that it is given orally, and there are minor side effects. The efficacy of glucagon approaches that of levodopa.

Malagelada, J. R.; Go, V. L. W.; and Summerskill, W. H. J. (Gastroenterology Unit, Mayo Clinic and Mayo Foundation, Rochester, Minn.): ALTERED PANCREATIC AND BILIARY FUNCTION

AFTER VAGOTOMY AND PYLOROPLASTY. Gastroenterology 66:22-27, 1974.

Verbatim summary. Changes in pancreatic enzyme secretion and gall bladder contraction occurring after vagotomy and pyloroplasty were investigated and compared with findings from healthy volunteers and patients with duodenal ulcer. Total lipase and bile acid outputs were quantified, using duodenal perfusion, under basal conditions and in response to both endogenous cholecystokinin-pancreozymin (CCK-PZ) (released by intraduodenal perfusion of essential amino acids) and to exogenous (porcine) CCK-PZ given by vein. After vagotomy and pyloroplasty, basal pancreatic enzyme outputs were reduced, as were responses to both intraduodenal essential amino acid perfusion and lower doses of intravenous CCK-PZ than in healthy subjects or in patients with duodenal ulcer, although the response to intraduodenal essential amino acids was normal. Our results suggest that (a) vagal impulses contribute to pancreatic enzyme secretion in the interdigestive periods; and (b) after vagotomy and pyloroplasty sensitivity of the pancreas to CCK-PZ decreases and that of the gall bladder increases.

Manchester, K. L. (Dept. of Biochem., Univ. of the West Indies, Kingston, Jamaica, W.I.): EFFECT OF INSULIN AND DENERVATION ON THE ACTIVITY OF RIBOSOMES OF RAT DIAPHRAGM MUSCLE. Biochemistry *13*:3062,68, 1974.

Vertabim summary. A procedure is described for the isolation of ribosomes from 0.5 to 1.0-g quantities of diaphragm muscle. The ribosomes have an A_{260}/A_{280} ratio greater than 1.8 and an A_{260}/A_{235} ratio greater than 1.5. Probably 60 to 70 per cent of the ribosomes available are collected. Ribosomes prepared from muscle first incubated in vitro show a diminished capacity for incorporatin of leucine and phenylalanine into protein by comparison with ribosomes from fresh tissue. When insulin is present during incubation, incorporating capacity of the ribosomes declines less rapidly. The long established effect of insulin to promote incorporation of amino acids into protein of muscle in vitro can thus be seen to be associated with an influence of the hormone on the ribosomes of the tissue. Insulin maintains the activity of the ribosomes during incubation because it reduces the extent of polysome disaggregation during incubation. By use of (^{3}H) puromycin it can be seen that in the presence of insulin a larger proportion of the ribosomes carry nascent peptide chains. Ribosomes from incubated tissue remain active in translation of poly(U)—a greater response to poly(U) being seen at 5 mM Mg the greater the extent of polysomal disaggregation. The presence of a mixture of amino acids during incubation reproduces the effects of insulin. During denervation hypertrophy of diaphragm muscle, although there is a large increase in the number of ribosomes, their specific activity in incorporation is little changed nor is there obvious difference in polysome profile or proportion of ribosomes bearing nascent chains. The denervated tissue is known to respond poorly to insulin and this is reflected in the finding that polysome disaggregation during incubation is less and the incorporating capacity of the ribosomes of the denervated tissue declines less than does that of normal tissue even when the latter is incubated in the presence of insulin.

Mandell, F.; and Fellers, F. X. (Children's Hospital Medical Center, Boston, Mass.): HYPERGLYCEMIA IN HYPERNATREMIC DEHYDRATION. Clin. Pediatr. *13*:367-69, 1974.

Twenty-two of twenty-five children with hypernatremic dehydration secondary to gastroenteritis had serum glucose concentrations that were greater than 120 mg. per 100 ml. prior to intravenous therapy. The serum glucose values were as high as 685 mg. per 100 ml. (mean serum glucose 234 mg. per 100 ml.). For comparison the serum glucose concentration of thirty children of comparable age who had gastroenteritis and isotonic dehydration (serum sodium 130 to 147 mEq/L) were investigated. None of these children had elevated serum glucose levels. The present clinical observations correlate well with previous studies with rats that demonstrate that neither water deprivation or corticosteroid treatment alone raises serum glucose. When water deprivation is combined with steroid therapy the rats develop hyperglycemia. The serum glucose of the patients in the present study declined with fluid replacement alone and insulin therapy was not required. J.M.F.

Marquardt, J. L.; and Loriaux, L. (Clinical Branch, Nat'l Eye Instit. and Reprod. Res. Branch, NICHD, N. I. H., E. W., Bethesda, Md.): DIABETES MELLITUS AND OPTIC ATROPHY. Arch. Intern. Med. *134*:32-37, 1974.

Verbatim summary. Two siblings had diabetes mellitus, diabetes insipidus, and optic atrophy. Abnormal findings include color blindness, neurosensory hearing loss, hyposmia, thermoregulatory failure in both hot and cold environments, electroencephalographic epileptiform activity, partial diabetes insipidus, blunted plasma cortisol response to pyrogen infusion and aminoaciduria, predominantly of alanine. We propose a clinical entity consisting of bilateral optic atrophy, diabetes mellitus, diabetes insipidus, neurosensory hearing deficit and hypothalamic dysfunction of variable degree.

Massaro, R. P. (Dept. of Med. State Univ. of N.Y. at Buffalo, The Buffalo General Hosp., Buffalo, N.Y.): HORMONAL RESPONSES TO INTRAVENOUS AND ORAL GLUCOSE TOLERANCE TESTING IN A PATIENT WITH A GASTRINOMA AND A GASTROJEJUNOSTOMY. Gastroenterology *66*:1058-62, 1974.

Verbatim summary. A case is reported of a patient with recurrent ulcer disease and a previous gastrojejunostomy in whom a gastrinoma was diagnosed and subsequently confirmed at surgery. Prior to surgery, hormonal responses to intravenous and oral glucose tolerance testing were recorded and are reported because of three main unexpected and unusual abnormalities: (1) a sudden increase in serum gastrin level after oral glucose ingestion but not after intravenous infusion; (2) failure of suppression of pancreatic glucagon during ingestion-induced hyperglycemia; and (3) the failure of insulin release in response to infusion-induced hyperglycemia with preservation of insulin release after oral glucose ingestion. The possibility is raised that chronic hypergastrinemia may inhibit or suppress certain insulin pools, unlike acute or bolus type gastrin "pulses" which have been associated with transient elevations of plasma insulin levels.

Narins, R. G.; Weisberg, J. S.; and Myers A. R. (Renal-Electrolyte and Rheumatology Sections, Dept. of Med., Hosp. of the Univ. of Pennsylvania, Phila., Pa.): EFFECTS OF CARBOHYDRATES ON URIC ACID METABOLISM. Metabolism *23*:455-65, 1974.

The rapid intravenous infusion of fructose produced in normal males a 30 per cent rise in serum uric acid concentration. This effect was not observed with similar infusions of glucose and galactose although all three hexoses increased the renal excretion of uric acid, phosphate, bicarbonate and glucose, probably by inhibition of renal proximal tubular function. The mechanism involved in fructose-induced hyperuricemia may be that of stimulating the conversion of adenine nucleotides to uric acid. The chronic ingestion of a fructose-rich diet did not alter serum or uric acid. C.S.

Printen, K. J.; Paulk, S. C.; Liebschutz, D.; and Mason, E. E. (Dept. of Surg., Univ. of Iowa Coll. of Med., Iowa City, Iowa): DIFFERENTIAL FREE FATTY ACID RESPONSE TO HEPARIN IN DIABETICS. Br. J. Surg. *61*:183-84, 1974.

In this study, two groups of ten diabetics, one insulin dependent and the other receiving a variety of oral hypoglycemic drugs, were evaluated. Free fatty acid response to 5,000 units of intravenous heparin were determined basally and the four time intervals up to ninety minutes. No significant differences were noted between the two groups.

The authors conclude, on the basis of these data, that both varieties of diabetics respond similarly to heparin in terms of free fatty acid release in spite of the observation that was pointed out in the article that tremendous differences occurred within each group. T.C.H.

Shatney, C. H.; and Grage, T. B. (Dept. of Surg., Univ of Minnesota Hosp., Minneapolis, Minn.): DIAGNOSTIC AND SURGICAL ASPECTS OF INSULINOMA. Am. J. Surg. *127*:174-84, 1974.

Verbatim summary. The clinical features of twenty-seven patients with insulinoma are discussed. The best diagnostic test is a seventy-two-hour fast with multiple determinations of blood glucose and insulin. Preoperative arteriography and intraoperative blood glucose monitoring are recommended in all patients. In the present series there are no operative mortality, and all patients were rendered asymptomatic.

Starr, J. I.; and Rubenstein, A. H. (Dept. of Med., Univ. of Chicago, Pritzker Sch. of Med., Chicago, Ill.): METABOLISM OF ENDOGENOUS PROINSULIN AND INSULIN IN MAN. J. Clin. Endocrinol. Metab. *38*:305-08 1974.

Verbatim summary. The disappearance of endogenous serum proinsulin and insulin was measured in three patients following removal of beta-cell adenomas of the pancreas. The mean half-disappearance time for proinsulin (17.2 min.) was much longer than for insulin (4.8 min.). This difference in the metabolic rate of the two hormones together with previously described differences in their hepatic extraction are sufficient to explain the higher proinsulin:insulin ratio in serum compared to the pancreas.

Thomas, D.; Bourdillon, C.; Broun, G.; and Kernevez, J. P. (Universite de Technologie de Compiegne, Compiegne, France): KINETIC BEHAVIOR OF ENZYMES IN ARTIFICIAL MEMBRANES. INHIBITION AND REVERSIBILITY EFFECTS. Biochemistry *13*:2995-3000, 1974.

Verbatim summary. The artificial binding of enzymes into artificial membranes makes possible a study of the interaction between membrane structure and enzyme kinetics within a well defined context. Artificial proteic membranes bearing immobilized enzymes are produced by using a co-cross-linking method. The influence of competitive and noncompetitive inhibitors on the kinetic behavior of enzymes in a membrane is described. The effect of the diffusion limitations on a reversible enzyme system is observed. The studies are performed from both the experimental and theoretical point of view. Some of the results obtained with artificial enzyme membranes may be used in the elucidation of the action of enzymes contained in biological membranes.

Way, L. W.; Gadacz, T.; and Goldman, L. (Dept. of Surg. Univ. of California Sch. of Med., San Francisco): SURGICAL TREATMENT OF CHRONIC PANCREATITIS. Am. J. Surg. *127*:202-09, 1974.

Verbatim summary. The results of surgery for chronic pancreatitis in fifty-seven patients treated between 1958 and 1972 were reviewed. The findings have been used to outline a surgical strategy for the management of this disease.

Operations on the biliary tract gave disappointing results. Biliary disease must be treated when present, but this will not always lessen chronic pancreatic pain.

The surgical treatment of pseudocysts by internal drainage was uncomplicated in the short run, but almost half the patients continued to have pain months or years later.

Direct operations on the pancreas are most successful in chronic pancreatitis. Sphincterotomy, splanchnicectomy, gastric operations, and caudal pancreaticojejunostomy are no longer recommended. When the pancreatic duct is dilated, longitudinal pancreaticojejunostomy (Puestow operation) will effect improvement in 80 to 90 per cent of patients. Pancreatitis localized to the tail of the gland is optimally treated by hemipancreatectomy. Subtotal (95 per cent) pancreatectomy is reserved for diffuse pancreatitis when the pancreatic duct is small or when previous longitudinal pancreaticojejunostomy is unsuccessful.

Weinsier, R.L.; Seeman, A.; Herrera, M.G.; Assal, J.-P.; Soeldner, J.S.; and Gleason, R.E. (Dept. of Nutrition, Harvard Sch. of Public Health; Dept. of Med., Peter Bent Brigham Hosp; and Elliott P. Joslin Res. Lab.: Boston, Mass.): HIGH- AND LOW-CARBOHYDRATE DIETS IN DIABETES MELLITUS. Ann. Intern. Med. *80*:332-41, 1974.

Verbatim summary. Eighteen diabetic patients, not dependent on insulin, given diets high in carbohydrate (60 per cent, 25 per cent fat) or relatively low in carbohydrate (40 per cent, 45 per cent fat), were followed for forty weeks as outpatients in a group-oriented educational program. Diabetic control was measured by the fasting and postprandial blood sugar levels and quantitative and qualitative urine-sugar tests. Glucose-insulin relationships were evaluated by measuring fasting immunoreactive insulin levels and by intravenous and oral glucose tolerance tests and a modified insulin infusion test after each twenty-week diet period. Despite the increased carbohydrate load, control of diabetes and insulin secretory capacity were maintained. Serum cholesterol values were not altered by the change in dietary fat, and the high carbohydrate intake did not increase mean levels of serum triglycerides. The data suggest a seasonal trend for both serum cholesterol and triglycerides.

Wolstenholme, J. T. (Surgical Service, V.A. Center, White River Junction, Vt., and Dartmouth Med. Sch., Hanover, N.H.): MAJOR GASTROINTESTINAL HEMORRHAGE ASSOCIATED WITH PANCREATIC PSUEDOCYST. Am. J. Surg. *127*:377-81, 1974.

Verbatim summary. Although the pancreas is not a frequent source of major gastrointestinal hemorrhage, bleeding in patients with pancreatitis is not an uncommon complication. In patients with bleeding who are known to have pancreatitis or a pseudocyst, this organ must be considered a possible site of hemorrhage.

It is recommended that celiac axis and superior mesenteric artery angiography be performed prior to barium contrast studies.

If bleeding is originating from a pancreatic pseudocyst, aggressive surgical intervention should be undertaken. Three cases are described in which prompt operation was successful.

Intracystic suture-ligation of the bleeding vessel together with cystogastrostomy was performed in two cases. One case of bleeding from a pseudocyst in the head of the pancreas and involving the gastroduodenal artery was treated by excision of the cyst and head of the pancreas.