ABSTRACTS

Aleyassine, H.; and Lee, Sin Hang (Dept of Path., Path. Inst., McGill Univ., Montreal, Quebec, Canada): INHIBITION BY HYDRAZINE, PHENELZINE AND PARGYLINE OF INSULIN RELEASE FROM RAT PANCREAS. Endocrinology *89*:125-29, July 1971.

The intraperitoneal injection of hydrazine to fasted rats resulted in a significant fall in serum levels of glucose and insulin. In vitro, the stimulatory effect of high glucose concentration on insulin release from incubated pancreas was abolished by hydrazine. The same effect was obtained by the addition of phenelzine and pargyline to the incubation media. After a thirty-minute washout period, the responsiveness of hydrazine and pargyline-treated pancreas to glucose was restored while the inhibitory effect of phenelzine was irreversible. These data suggest that the concentration of certain biogenic amines in the beta cell may play an important role in the secretory process of insulin. C.R.S.

Baile, Clifton A.; McLaughlin, Carol L.; Zinn, William; and Mayer, Jean. (Dept. of Nutrition, Harvard School of Public Health, Boston, Mass.): EXERCISE, LACTATE, HORMONES, AND GOLD THIOGLUCOSE LESIONS OF THE HYPOTHALAMUS OF DIABETIC MICE. Am. J. Physiol., *221*:150-55, July 1971.

Function of the hypothalamus in transient hypophagia following severe exercise was studied utilizing the apparent relationship between glucose utilization rate and ventromedial hypothalamic (VMH) lesions following intraperitoneal injection of gold thioglucose (GTG) in mice. In contrast to control alloxan-diabetic (A-D) mice injected with GTG, A-D mice injected during running or after two, but not four, hours are sensitized to GTG and develop lesions in the VMH. Since transient elevated blood lactate levels can cause a sustained hypophagia, and increased lactate production is associated with exercise, lactate was injected intraperitoneally prior to GTG. Lactate sensitized for up to eight hours the VMH of A-D mice to GTG. Lesions of the A-D mice following exercise or lactate injection suggest that some insulin-like factor released from muscle may be involved in hypophagia following exercise. The VMH is sensitized to GTG by epinephrine, thyroxine, cholecystokinin-pancreozymin, and hydrocortisone, and less effectively by growth hormone, norepinephrine, secretin, and glucagon. Exercise or lactate could be acting via some means other than glucose utilization. J.D.G.

Beatty, Clarissa H.; and Boeck, Rose Mary (Depts. of Biochem., Oregon Regional Primate Res. Center, Beaverton, Ore. & Univ. of Oregon Med. Sch., Portland, Ore.): INTERRELATION OF CARBOHYDRATE AND PALMITATE METABOLISM IN SKELETAL MUSCLE. Amer. J. Physiol. *220*:1928-34, June, 1971.

Skeletal muscle fiber groups from sartorius muscle of rhesus monkey were incubated in media with and without 1.45 mM palmitate (ratio of free fatty acid to albumin = 3). Increase in oxygen consumption in presence of palmitate could be accounted for by observed increase in palmitate oxidation. Palmitate did not affect glucose uptake, production of lactate-C-14 from glucose-C-14, glycogen level, or incorporation of C-14 from glucose into glycogen; however it did cause a decrease in C-14-O_2 production. Results were similar when muscle was incubated in absence of exogenous insulin and in presence of 1 and 100 mU. of insulin per ml. of medium. When muscle fiber groups were incubated with palmitate-C-14 (1.45 mM), about 60 per cent of uptake appeared in the lipid fraction and about 10 per cent in CO_2; 16 per cent of total CO_2 was derived from palmitate. Effect of palmitate on skeletal muscle differs from that reported for perfused heart muscle in which fatty acids decreased glucose uptake and glycolysis. J.D.G.

Blickens, D. A.; and Riggi, S. J. (Dept. of Metabolic Chemotherapy, Lederle Labs., Pearl River, N.Y.): CARBOHYDRATE METABOLISM IN NORMAL AND HYPERGLYCEMIC ANIMALS TREATED WITH 1-METHYL-4-(3-METHYL-5-ISOXAZOLYL) PYRIDINIUM CHLORIDE AND PHENFORMIN. J. Pharmacol. Exp. Ther. *177*:536-45, June, 1971.

Verbatim summary. 1-Methyl-4-(3-methyl-5-isoxazolyl)-pyridinium chloride (I) has been reported to be an orally active hypoglycemic agent in guinea pigs, mice, cockerels and alloxan-treated rats and mice. Hypoglycemia in normal mice was associated with metabolic alterations similar to those occurring after phenformin treatment. The present studies were conducted to evaluate the metabolic effects of I in several experimental hyperglycemic models in an attempt to further elucidate the mechanism of action of I. Blood glucose was decreased after I administration to partially eviscerated guinea pigs, obese diabetic mice (C57BL/Ks-db) and alloxan- or streptozotocin-treated rats suggesting that hypoglycemia is independent of pancreatic insulin release. Increased blood lactate in normal and alloxan-treated rats after I or phenformin treatment suggested an enhanced anaerobic glycolysis. Decreased glycosuria in alloxan-treated rats after I or phenformin and in streptozotocin-treated rats after I treatment essentially eliminated urinary glucose as contributory to hypoglycemia. After a single dose of I or phenformin in hyperglycemic rats, liver glycogen decreased and skeletal muscle glycogen increased. These data suggest that liver glycogenolysis was unimpaired and that increased skeletal muscle uptake may play a major role in development of hypoglycemia. These and previous studies indicated that I and phenformin exert similar effects on carbohydrate metabolism in normal and hyperglycemic states.

Brown, Henry; and Myers, Virginia (Harvard Surg. Unit, Boston City Hosp., Boston, Mass.): INSULIN SECRETION AND

METABOLISM AFTER PORTACAVAL SHUNTING. Fed. Proc. 30 (362):257, March-April, 1971.

This study was done to determine whether rate of insulin breakdown was influenced by the portacaval shunt operation. Observations in five shunted patients, confirmed by laboratory experiments with two dogs, indicated either high normal or abnormally elevated plasma insulin levels during oral glucose tolerance tests. Rate of metabolism of intravenously administered I-131-labeled beef insulin was measured in five dogs before and after portacaval shunting in nineteen tests. Rate of insulin breakdown was measured by decline in radioactivity in trichloroacetic acid precipitated plasma protein, the fraction containing insulin. Data indicated that rate of plasma insulin metabolism was not altered by portacaval shunting. Of possible reasons for elevated plasma insulin levels, one may be that larger than usual amounts of insulin are secreted because of a disturbed relationship between pancreas and liver. J.D.G.

Cain, Roy E.; Skriver, Christian P.; and Carlson, Richard H. (Dept. of Pyschology, Texas Tech. Univ., Lubbock, Tex.): HABITUATION OF ELECTRICALLY INDUCED READINESS TO GNAW. Science *173*:262-64, July 16, 1971.

Electrical stimulation of hypothalamus in prairie dogs produced a readiness to gnaw which decreased over time, exhibited spontaneous recovery, and could be dishabituated by foot shock. Response decrement was in part habituatory and could modify interaction between stimulation-induced readiness to gnaw and physiologically-induced hunger. Functional plasticity of stimulation-induced behavior might be accounted for, in part, by habituation. J.D.G.

Cherrington, Alan; and Vranic, Mladen (Dept. of Physiol., Univ. of Toronto, Toronto, Canada): ROLE OF GLUCAGON AND INSULIN IN CONTROL OF GLUCOSE TURNOVER. Metabolism 20:625-28, June, 1971.

Glucagon and insulin were administered intraportally to pancreatectomized dogs in the postabsorptive state to determine the interplay of these hormones on glucose turnover. An infusion of glucagon administered with a twelvefold increase in the rate of insulin supply above the basal insulin infusion doubled the turnover of glucose with little change in its concentration. These results were similar to those obtained with glucagon infusions in normal dogs. With four- to eightfold increases in insulin supply given concurrently with glucagon, a significant hyperglycemia developed with the rate of glucose production exceeding its rate of utilization. These data are consistent with the hypothesis that simultaneous supply of glucagon and insulin can regulate glucose turnover. C.R.S.

Chick, William L., and Like, Arthur A. (Elliott P. Joslin Res. Lab., Harvard Med. Sch., Boston, Mass.): EFFECTS OF DIET ON PANCREATIC BETA CELL REPLICATION IN MICE WITH HEREDITARY DIABETES. Am. J. Physiol., *221*:202-08, July 1971.

Effects of caloric intake and dietary composition on beta cell replication were studied in diabetic mutant mice. Mitotic activity was evaluated following thymidine-^{3}H administration both by autoradiography and by determining islet DNA specific activity. Food restriction early in the diabetic syndrome reduced hyperglycemia and hyperinsulinemia and resulted in low incorporation of label. Animals refed ad libitum with either commercial laboratory chow or with synthetic diet containing a combination of carbohydrate, protein, and fat showed greatest increases in labeling, with rises in both blood glucose and serum insulin levels. Mice refed with only protein had a lower daily caloric intake and remained normoglycemic, yet serum insulin levels and incorporation of label were both significantly increased. Mice refed with carbohydrate alone remained normoglycemic and showed only a small rise in serum insulin, with no increased labeling, even though daily caloric intake was similar to protein diet. Increased beta cell mitotic activity occurred in the absence of hyperglycemia, but not in the absence of hyperinsulinemia. J.D.G.

Cotmore, John M.; Nichols, George, Jr.; and Wuthier, Roy E. (Harvard Sch. of Dental Med. and Cancer Res. Inst., New England Deaconess Hosp., Boston, Mass.; and Univ. of Vermont Coll. of Med., Burlington, Vt.): PHOSPHOLIPID-CALCIUM PHOSPHATE COMPLEX: ENHANCED CALCIUM MIGRATION IN THE PRESENCE OF PHOSPHATE. Science *172*:1339-41, June 25, 1971.

In the presence of acidic phospholipids, inorganic phosphate greatly enhances the net migration of calcium ions from the aqueous phase to the organic phase, an effect that does not occur at less than the physiological pH. The calcium complex in the organic phase is shown by electron microscopy to consist of spherules, composed of stoichiometric amounts of calcium, inorganic phosphate, and phospholipid. The demonstration of complex formation between calcium phosphate and acidic phospholipids adds support to the concept that phospholipids are involved in biological mineralization. J.D.G.

Dethier, V. G.; and Goldrich, Nancy (Dept. of Biol., Princeton Univ., Princeton, N.J.): BLOWFLIES: ALTERATION OF ADULT TASTE RESPONSES BY CHEMICALS PRESENT DURING DEVELOPMENT. Science *173*:242-44, July 16, 1971.

Addition of certain sugars to food consumed during larval development increases the taste sensitivity of adult blowflies to some sugars, decreases it to others, and is without effect on the sensitivity to still others. No correlation with metabolic phenomena is apparent. The hypothesis that repression of inductible enzyme synthesis by glucose is a relevant mode is not supported. J.D.G.

Dokas, Linda A.; and Kleinsmith, Lewis J. (Dept. of Zoology, Univ. of Michigan, Ann Arbor, Mich.): ADENOSINE 3′,5′-MONOPHOSPHATE INCREASES CAPACITY FOR RNA SYNTHESIS IN RAT LIVER NUCLEI. Science *172*:1237-38, June 18, 1971.

Liver nuclei isolated from rats injected with adenosine 3′,5′-monophosphate exhibit an increased capacity for RNA synthesis compared with nuclei from control animals. This effect, which is highly specific for the cyclic nucleotide, can be observed within one hour after injection in both unoperated and adrenalectomized rats. These findings suggest that induction of enzyme synthesis mediated by way of adenosine 3′,5′-monophosphate may be controlled, at least in part, at the level of gene transcription. J.D.G.

Drash, Allan (Dept. of Pediat., Univ. of Pittsburgh Sch. of Med. & the Pediat. Diabetes Clin., Children's Hosp. of Pittsburgh, Pa.): DIABETES MELLITUS IN CHILDHOOD: A REVIEW. J. Pediat. 78:919-41, June, 1971.

Dr. Drash briefly reviews carbohydrate metabolism and then proceeds to discuss many aspects of diabetes mellitus in the child. These include considerations of the genetics and pathophysiology of the disease, management and prognosis. Special problems that are reviewed include ketoacidosis, obesity, growth and maturation as well as chronic complications in diabetic children. There are 119 bibliographical references. R.K.K.

Grad, Bernard; Rosenberg, Gilbert M.; Liberman, Henry; Trachtenberg, John; and Kral, Vojtech A. (Gerontologic Unit, Allan Memorial Inst. of Psychiatry, McGill Univ., Montreal, Quebec, Canada): DIURNAL VARIATION OF THE SERUM CORTISOL LEVEL OF GERIATRIC SUBJECTS. J. Geront. *26*: 351-57, July, 1971.

The authors measured the diurnal variation in the serum cortisol level of elderly people with and without diabetes, chronic brain syndrome and heart disease. The competitive protein-binding technic of Murphy was used. The diabetic group had higher levels than the control and chronic brain syndrome groups and this was statistically significant. The chronic brain syndrome and control subjects with heart disease had higher serum cortisol values than the corresponding group without heart disease (due primarily to elevation of the evening values) but there was no statistically significant difference between the diabetics with and without heart disease. B.R.B.

Gutman, Raul A.; Lazarus, Norman R.; Penhos, Juan C.; Fajans, Stefan; and Recant, Lillian (Diabetes Res. Lab., V. A. Hosp., Wash., D. C., and Georgetown Univ. and Univ. of Michigan Schs. of Med., Washington, D.C. and Ann Arbor, Mich.): CIRCULATING PROINSULIN-LIKE MATERIAL IN PATIENTS WITH FUNCTIONING INSULINOMAS. New Eng. J. Med. *284*:1003-08, May 6, 1971.

The secretion of proinsulin in eleven patients with functioning beta-cell tumors of the pancreas was investigated. Proinsulin and insulin were separated by gel filtration and polyacrylamide gel electrophoresis and quantitated by the radioimmunoassay. Nine of the eleven patients had elevated plasma proinsulin values which represented from 28 to 89 per cent of the total IRI. However, there was no correlation between the total IRI value in the insulinoma patients and the amount of proinsulin present. One patient was re-examined ten months after a partial pancreatectomy for removal of the insulinoma and found to have no circulating proinsulin as opposed to her elevated preoperative values.

One obese control subject had an elevated fasting proinsulin value in the range of the insulinoma patients but this made up only 20 per cent of the total IRI (a relatively normal amount). The authors suggest that the normal percentage of proinsulin in obese subjects might help differentiate these subjects with high IRI values from patients with insulinomas. They also suggest that the normal levels of proinsulin following therapy might be useful in assessing the effectiveness of therapy. B.R.B.

Hahn, Theodore J.; Downing, Sylvia J.; and Phang, James M. (Metabolism Branch, National Cancer Inst., N.I.H., Bethesda, Md.): INSULIN EFFECT ON AMINO ACID TRANSPORT IN BONE: DEPENDENCE ON PROTEIN SYNTHESIS AND NA^+. Amer. J. Physiol. *220*:1717-23, June, 1971.

Insulin stimulates membrane transport of *a*-aminoisobutyric acid (AIB) and L-proline in fetal rat calvaria in vitro. Simultaneously, proline incorporation into protein and hydroxyproline formation were increased. Induction of the stimulatory effect on amino acid transport was time dependent and blocked by inhibitors of protein synthesis. Insulin increased glucose oxidation without increasing cellular uptake of 3-o-methylglucose. It is concluded that insulin stimulates cellular uptake of amino acids but not glucose analogue in bone. Amino acid transport appears to be mediated through increased synthesis of a membrane carrier protein. J.D.G.

Henneman, Dorothy H. (Ortho Res. Foundation, Raritan, N.J.): GROWTH HORMONE INHIBITION OF PROLINE HYDROXYLATION IN VITRO. Amer. J. Physiol. *220*:1808-13, June, 1971.

Addition of bovine growth hormone (BGH) to medium containing L-proline-C-14 during incubation of guinea pig granuloma and rat skin and bone produced a decrease in rate of incorporation of label as hydroxyproline (OH-P-C-14) into several collagen fractions of these tissues. Specific activity of OH-P was reduced in neutral salt-soluble and total collagen of granuloma, in neutral salt and acid-soluble and insoluble collagen of weanling rat skin, and in neutral salt-soluble fractions of weanling rat metaphyseal bone. BGH administered to weanling rats in vivo increased incorporation of label into bone collagen both as proline (P) and as OH-P. P specific activity in skin was also increased. Increased hydroxylation of proline in bone with in vivo BGH but not with in vitro BGH suggests that factors other than BGH are responsible for hydroxylation in vivo. Growth hormone may stimulate formation of proline-rich collagen under in vivo conditions of increased collagen turnover, degradation, or resorption, depending upon relative availability of these factors. J.D.G.

Kalkhoff, Ronald; and Ferrou, Carlos (Dept. of Med., Med. Coll. of Wisconsin, the Clin. Res. Center, Milwaukee County Gen. Hosp., and Deaconess Hosp., Milwaukee, Wis.): METABOLIC DIFFERENCES BETWEEN OBESE OVERWEIGHT AND MUSCULAR OVERWEIGHT MEN. New Eng. J. Med. *284*:1236-39, June 3, 1971.

Ten obese overweight men, ten muscular overweight men, and ten ideal body weight men were compared with respect to their plasma insulin response to the standard 100 gm. oral glucose tolerance test and the 1 gm. intravenous tolbutamide tolerance test and their plasma growth hormone response to insulin-induced hypoglycemia. The muscular group was 39 per cent above ideal body weight and the obese group 42 per cent. The skinfold thickness of the obese group was eight times that of the muscular group and four times that of the ideal body weight group.

The plasma insulin responses to glucose and tolbutamide were significantly greater in the obese group and the plasma growth hormone response significantly less as compared to the ideal and muscular overweight group indicating that the increase in adiposity rather than the increase in body weight accounts for these metabolic differences in obesity. B.R.B.

Kohner, E. M.; Dollery, C. T.; Lowy, C.; and Schumer, B. (M. R. C. Clin. Pharmacol. Res. Group and Depts. of Clin. Pharmacol., Med. and Chem. Path., Royal Postgrad. Med. Sch., Hammersmith Hosp., London, England.): EFFECT OF DIURETIC THERAPY ON GLUCOSE TOLERANCE IN HYPERTENSIVE PATIENTS. Lancet *1*:986-90, May 15, 1971.

Many reports have previously stated that both thiazide diuretics and nonthiazide diuretics may cause or exacerbate diabetes mellitus. This study was made in nondiabetic subjects attending a hypertension clinic to determine the magnitude of the risk of diuretic-induced diabetes. At the time, 137 patients having an average blood pressure 187/112, a mean age of 49.1 yr. and mean weight of 158 lb. were treated with frusemide, 40 mg. twice weekly, clorexolone, 25 mg. daily, ethacrynic acid, 50 mg. twice daily or hydrochlorothiazide, 50 mg. daily for one year. Prior to treatment an oral GTT was done. The glucose dose was 50 gm./M^2 and blood glucose was measured at 0, 30, 60, 120, and 150 min. In selected individuals serum insulin and FFA levels were measured. The

mean glucose values for all 137 subjects were below 90 mg./100 ml. fasting and peaked below 150 mg./100 ml. at 30 or 60 min. and fell to below 110 mg./100 ml. at 120 min. prior to treatment. After twelve to sixteen months of therapy all mean values at the various times were somewhat lower. Of twenty-four patients who initially had borderline GTT, fourteen improved to "normal" during the year, two developed symptomatic diabetes and eight remained the same. Six patients who had initially normal GTT had borderline tests after a year. In forty-four persons who had insulin measured with GTT before and during diuretic therapy the only change was a statistically significant lowering of the sixty-minute insulin value. No differences in glucose/insulin ratios were found. There was no difference between GTT results except in the frusemide treated group in whom glucose tolerance improved. The results indicate that the diuretics investigated have little if any diabetogenic effect when given to hypertensive patients and suggest that withholding them would probably not diminish the risk of developing diabetes. T.G.S.

Macaulay, Michael B. (Med. Div., Sefton Gen. Hosp., Liverpool, England): HYPEROSMOLAR NONKETOTIC DIABETES. Postgrad. Med. J. *47*:191-96, April, 1971.

Hyperosmolar nonketotic crises occur chiefly in mild, maturity-onset diabetics, yet present a medical emergency carrying a high mortality. This may in part be due to a lack of awareness of the clinical presentation, and of the principles of treatment. Five cases are described, in all of which excessive consumption of a proprietary "glucose" drink played an important part in the development of their hyperosmolar state. The characteristic clinical picture is one of thirst, increasing confusion and severe dehydration in a middle-aged or elderly patient not known to be diabetic. Greater awareness of this presentation, together with greater understanding of the principles of treatment should lead to reduced mortality. J.D.G.

Misbin, Robert I.; Edgar, Paul J.; and Lockwood, Dean H. (Clayton Labs., Dept. of Med., Johns Hopkins Univ. Sch. of Med.; and The Greater Baltimore Med. Center, Baltimore, Md.): INFLUENCE OF ADRENERGIC RECEPTOR STIMULATION ON GLUCOSE METABOLISM DURING STARVATION IN MAN: EFFECTS ON CIRCULATING LEVELS OF INSULIN, GROWTH HORMONE AND FREE FATTY ACIDS. Metabolism *20*:544-54, June, 1971.

Glucose intolerance, ketonuria and diminished insulin response to intravenous glucose occurred after three days of starvation in twenty-three healthy subjects. Serum concentrations of GH, FFA and the urinary excretion of free catecholamines were elevated while free plasma cortisol was unchanged. Adrenergic blockade with phentolamine or phentolamine-propranolol had no effect on the glucose intolerance after starvation. Control subjects exhibited a decrease in glucose-stimulated insulin secretion while those receiving phentolamine exhibited a marked rise in insulin secretion; those receiving both blocking agents showed a modest decline in insulin release. Alpha adrenergic blockade restored GH to prefasting levels in three subjects and total adrenergic blockade partially returned the FFA concentrations to prefasting levels. The results indicate that sympathetic tone reflected in rising catecholamine excretion is increased during starvation and may play a role in the regulation of insulin, GH, and FFA release; that acute reversal of insulin deficiency during fasting does not restore normal glucose tolerance; and that peripheral insulin antagonism due to GH and FFA does not appear to be a major cause of glucose intolerance during starvation. C.R.S.

Prockop, Leon D. (Dept. of Neurol., Univ. of Pennsylvania and Penn. Neurol. Serv., Philadelphia Gen. Hosp., Philadelphia, Pa.): HYPERGLYCEMIA, POLYOL ACCUMULATION, AND INCREASED INTRACRANIAL PRESSURE. Arch. Neurol. *25*:126-40, August 1971.

Verbatim summary. Increased intracranial pressure reproducibly occurs in hyperglycemic dogs when the blood glucose level is permitted to fall precipitously and they are rehydrated with isotonic saline solutions. Water intoxication, carbon dioxide accumulation, and osmotic and electrolyte differences between the cerebrospinal fluid (CSF) and plasma did not play major roles in the production of the observed increases in CSF pressure. There was a significant rise in CSF and brain concentrations of fructose and sorbitol in response to hyperglycemia, suggesting that the level of blood glucose regulates the rate of sorbitol and fructose synthesis within the central nervous system, and that there was an increased activity of the polyol (glucose/sorbitol/fructose) pathway. This potential for the production of increased intracranial pressure may be responsible for the fatal acute cerebral edema observed during the treatment of diabetic acidosis.

Rappaport, A. M.; Kawamura, T.; Davidson, J. K.; Lin, B. J.; Ohira, S.; Zeigler, M.; Coddling, J. A.; Henderson, J.; and Haist, R. E. (Dept. of Physiol. and Inst. of Bio-Med. Electronics, Univ. of Toronto, Toronto, Canada): EFFECTS OF HORMONES AND OF BLOOD FLOW ON INSULIN OUTPUT OF ISOLATED PANCREAS IN SITU. Amer. J. Physiol. *221*:343-48, July, 1971.

In twenty-eight partially depancreatized dogs, the isolated pancreatic uncinate process supplied by one artery and one vein was exteriorized. Rates of pancreatic blood flow were measured and outflowing venous blood was collected for determination of insulin output. Effects of hormones infused directly into inferior pancreatic artery and of decreased and increased blood flow on insulin output were tested. Norepinephrine infusion decreased blood flow and insulin output to one-seventh of the initial value for over one hour. Epinephrine infusion significantly decreased blood flow insulin output; recovery occurred 1 to 1.5 hr. after the infusion. With growth hormone (1, 10, and 100 mg./min.), insulin output and pancreatic blood flow decreased only during the infusion of the highest dose. Mechanical constriction of inferior pancreatic artery diminished blood flow but did not give proportionate decrease in insulin output; plasma insulin concentration rose in the majority of cases. Infusion of Na-dehydrocholate caused a 50 per cent increase in blood flow and insulin output. J.D.G.

Robinson, M. J.; Clarke, A. Murray; Gold, Hugo; and Connelly, J. F. (Royal Children's Hosp., Parkville, Melbourne, Australia): ISLET CELL ADENOMA IN THE NEWBORN: REPORT OF TWO PATIENTS. Pediatrics *48*:232-36, August 1971.

Two infants of normal birth weight are reported who presented with manifestations of hypoglycemia one to two days afetr birth. In the first case, plasma growth hormone and cortisol were normal, and plasma insulin was 13 μU/ml., a value considered to be inappropriately high in relation to the simultaneous blood glucose of 17 mg./100 ml. Laparotomy was performed, no tumor was visualized, and a 75 per cent pancreatectomy carried out. A small islet-cell adenoma was found in the excised pancreas, and the patient recovered completely.

The second patient died of uncontrollable hypoglycemia on the fourth day of life. An islet-cell adenoma was found at autopsy.

The authors recommend early laparotomy in obscure cases of uncontrollable hypoglycemia in infancy. If no islet-cell tumor is found, they suggest a 75 per cent pancreatic resection. P.S.R.

Rosenbloom, Arlan L.; Savory, John; and Londono, Javier H. (Div. of Endocrin. and Metab., Depts. of Pediat., Path. and Med., Univ. of Florida Coll. of Med., Gainesville, Fla.): THE HALF-HOUR SYNTHETIC 1-24 CORTICOTROPIN TEST OF ADRENOCORTICAL RESERVE IN CHILDREN. J. Pediat. 79:489-93, September 1971.

A rapid and convenient test for adrenocortical insufficiency is described. Following collection of a baseline blood sample, 0.25 mg. of synthetic 1-24 corticotropin is injected intravenously and an additional blood sample obtained after thirty minutes. Samples are assayed for cortisol. Nine normal children responded with a mean increase in plasma cortisol of 11.8 μg per 100 ml., with a range of 6.1 to 19.7 μg per 100 ml. Seventeen patients suspected of adrenocorticol insufficiency had normal responses with the exception of one with previously demonstrated ACTH unresponsiveness, and another with meningitis and a markedly elevated baseline plasma cortisol of 109.0 μg per 100 ml.

In addition to ease and rapidity, this test has the advantage that 1-24 corticotropin is far less antigenic than the natural hormone. Allergic reactions, common with the natural hormone, should be rare with this substance. None were observed in the present study. P.S.R.

Sirtori, Cesare; Hurwitz, Aryeh; and Azarnoff, Daniel L. (Depts. of Med. and Pharmacol., Clin. Pharmacol.-Toxicology Center, Univ. of Kansas Med. Center, Kansas City, Kans.): HYPERINSULINEMIA SECONDARY TO CHRONIC ADMINISTRATION OF MAZINDOL AND D-AMPHETAMINE. Am. J. Med. Sci. 261:341-49, June 1971.

Verbatim summary. A new appetite suppressant, mazindol, and d-amphetamine were given to obese and lean volunteers for a period of six weeks, doubling the dose of both medications after the third week. Assay of various metabolic parameters showed a progressive rise in insulinemia, accompanied by decreased fasting blood glucose and triglyceride levels. No significant change in plasma levels of free fatty acids or acetoacetate was noticed. The possibility that the hyperinsulinemia retards the rate of weight loss due to d-amphetamine is considered.

Strauss, Franklin G.; and Sullivan, Mary Ann (Dept. of Med., Baltimore City Hosp., Baltimore, Md.): PHENFORMIN INTOXICATION RESULTING IN LACTIC ACIDOSIS. Johns Hopkins Med. J. 128:273-81, May 1971.

Verbatim summary. Lactic acidosis is known to be associated with phenformin therapy in diabetic individuals. This report is of interest in that phenformin intoxication in an otherwise healthy diabetic patient resulted in documented lactic acidosis which was successfully treated. A stuporous thirty-three-year-old diabetic man was admitted twelve hours after ingestion of 2.5 gm. of phenformin with suicidal intent. Clinical data indicated severe metabolic acidosis, with undetermined anions of 31 mEq./L., serum lactate 11.1 mEq./L., serum glucose 26 mg./100 ml., and normal serum urea nitrogen. He was treated with 1,000 mEq. of sodium bicarbonate, glucose, insulin, and recovered uneventfully, without evidence of cardiovascular impairment or an infectious process.

The demonstration that massive phenformin intoxication is associated with lactic acidosis supports an etiologic role for phenformin. The patient's successful recovery suggests that the prognosis of lactic acidosis may not be grave if the basic source of lactic acid overproduction can be identified and reversed.

Watkins, Dudley; Cooperstein, S. J.; and Lazarow, A., with technical assistance of James A. Jackson (Dept. of Anat., Univ. of Connecticut Sch. of Med., and Dental Med., Farmington, Conn.; Dept. of Anat., Univ. of Minnesota Sch. of Med., Minneapolis, Minn.; and Marine Biological Lab., Woods Hole, Mass.): STIMULATION OF INSULIN SECRETION BY PYRIDINE NUCELOTIDES. Endocrinology 88:1380-84, June 1971.

The release of insulin from toad fish islets as affected by pyridine nucleotides was examined using rat epididymal fat pad to measure insulin-like activity (ILA). Islets incubated with NADPH released three to four times as much ILA into the medium as did the control islets. NADH produced less stimulation and only at much higher concentrations. In these experiments tritiated NADPH and NADH did not enter the islet cells since the uptake of the coenzymes paralleled that of mannitol which is known to be restricted to the extracellular compartments. These findings suggest that the pyridine nucleotides stimulated insulin release by acting at the cell membrane. C.R.S.

Wiley, Joyce H.; and Leveille, Gilbert A. (Lab. of Nutritional Biochem., Dept. of Animal Sci., Univ. of Illinois at Urbana-Champaign, Urbana, Ill.): ADAPTIVE NATURE OF GLYCOGEN SYNTHETASE ACTIVITY IN RAT ADIPOSE TISSUE. REQUIREMENT FOR INSULIN AND ENERGY. Proc. Soc. Exp. Biol. Med. 137:798-802, July 1971.

Total glycogen synthetase activity in adipose tissue from fasted meal-fed or nibbling rats increased when tissue was incubated for 2.5 hours in buffer containing glucose and insulin. Inclusion of puromycin in the incubation medium depressed increase in glycogen synthetase activity by less than 25 per cent, indicating that protein synthesis was responsible for only a small part of increase in enzyme activity. Glycogen synthetase activity also increased when adipose tissuse was incubated with glucose, fructose, or pyruvate without insulin. Greatest increase in enzyme activity occurred in tissue incubated in presence of both glucose and insulin. Results are consistent with hypothesis that increase in glycogen synthetase activity results from conversion of a form of the enzyme which is inactive under usual assay conditions to an assayable form. J.D.G.