BOOK REVIEWS

CURRENT TOPICS ON GLUCAGON, *edited by M. Austoni, C. Scandellari, G. Federspil, and A. Trisotto. 226 pages, Padova, Italy, Cedam, Publisher, 1971.*

This publication consists of papers and discussions presented at the Proceedings of the European Day on Glucagon, held in Padova in March, 1970. There are a total of fourteen papers, with nine papers in English and the remainder in several other languages. Summaries are in the same language as the papers and the discussions as well as introductory and concluding addresses are multilingual. Thirty-eight authors and participants, all from European countries, are represented. The papers deal with studies related to glucagon, including morphology, secretion, and actions. Some of the papers reviewed previously published data, others appeared to deal with new observations.

Several factors limit the value of this book largely to investigators actively working with glucagon. First, the conference was held in March of 1970 but the book was not published until over a year later. Second, the lack of a uniform language for summaries and discussions makes interpretation of the data difficult for the nonlinguist. Third, most of the papers deal with subjects which have no clinical significance at the present time.

This book may be of value to those involved in glucagon research, otherwise will likely see limited distribution and use.

ABSTRACTS

Anderson, James H., Jr.; Byrd, Gerald W.; and Blackard, William G. (Dept. of Med. Louisiana State Univ. Sch. of Med., New Orleans, La.): HYPERRESPONSIVENESS TO TOLBUTAMIDE OF DOGS PRETREATED WITH DIAZOXIDE. Metabolism 20: 1023-30, November 1971.

Both epinephrine and diazoxide inhibit insulin secretion but only diazoxide inhibition of plasma IRI is reversed by tolbutamide. Administration of tolbutamide to dogs given diazoxide and glucose resulted in a twofold rise in plasma IRI while those receiving glucose alone showed no further rise in plasma IRI following tolbutamide. Hyperresponsiveness to tolbutamide in diazoxide-treated animals was completely blocked by beta adrenergic blockade with propranolol. This effect of tolbutamide on diazoxide-treated dogs cannot be attributed to increased insulin accumulation during diazoxide treatment but may be related to an accentuation of enzyme activity or accumulation of a metabolite in the beta cell. Inhibition of the hyperresponsiveness to tolbutamide by beta adrenergic blockade is compatible with the hypothesis that cyclic AMP accumulation is responsible for the increased plasma insulin response. C.R.S.

Bhai, Idrees; Nath, N.; and Nath, M. C. (Univ. Dept. of Biochem., Nagpur, India): HEMATOLOGICAL CHANGES IN RATS INJECTED WITH ACETOACETATE. Proc. Soc. Exp. Biol. Med. *138*:597-99, November 1971.

Hypochromic microcytic anemia is produced in rats injected with acetoacetate for ninety days. Moderate fall in erythrocytes, packed cell volume, and hemoglobin followed injections of acetoacetate. Anemia was probably due to deficiency of iron and its malutilization for hemoglobin synthesis. Decrease in hemoglobin synthesis was attributed to deficiency of B vitamins especially pyridoxine. Defect in iron transport and utilization could be due to deficiency of ascorbic acid and glutathione.

J.D.G.

Caren, Raymond; and Corbo, Lucille (Cedars-Sinai Med. Res. Inst. and Div. of Med., Cedars-Sinai Med. Center, Los Angeles, Calif.; and Dept. of Med., Univ. of Calif. at Los Angeles, Los Angeles. Calif.): DEPRESSION OF PLASMA LIPID FRACTIONS AND INHIBITION OF PLATELET AGGREGATION BY ACTION OF GLUCAGON. Metabolism 20:1057-64, November 1971.

Intravenous glucagon caused significant depression of plasma

total lipids, triglyceride and cholesterol in twenty normal subjects. In ten subjects epinephrine caused both primary and secondary platelet aggregation. Glucagon administration resulted in significant inhibition of secondary platelet aggregation with the simultaneous depression of plasma lipids. It was concluded that the transfer of lipid to platelets by the action of glucagon may be associated with inhibition of epinephrine-induced platelet aggregation. C.R.S.

Chiumello, Giuseppe; Del Guercio, M. José; Carnelutti, Margherita; Devetta, Mario; Rossi, Livia; and Caccamo, Anna (Dept. of Pediat. and Child Health, Univ. of Milano, Milano, Italy): THE ROLE OF GROWTH HORMONE IN THE PATHOGENESIS OF DIABETES MELLITUS IN CHILDHOOD. J. Pediatr. 79:768-74, November 1971.

The authors have assessed plasma growth hormone response to insulin-induced hypoglycemia and arginine infusion in four groups of children, ages five to eleven. The groups studied were normal controls, obese children with chemical diabetes, normal weight children with chemical diabetes, and insulin-dependent diabetes. In a fifth group, with severe diabetic ketoacidosis, serial growth hormone levels were determined before and during therapy.

Obese chemical diabetics showed a diminished response to stimuli of growth hormone release as compared with normals, while nonobese chemical diabetics responded normally. Obesity is thus associated with impaired growth hormone responsiveness, a finding frequently noted in previous studies. In insulin-dependent diabetic children basal growth hormone values are sometimes above normal, but the responses to hypoglycemia and arginine are normal. All ketoacidotic subjects exhibited increased growth hormone levels which returned toward normal with therapy. Growth hormone concentrations were not correlated with severity of ketoacidosis or hyperglycemia. These changes probably represent a nonspecific response to stress.

These studies do not provide support for the concept that growth hormone has a major role in the pathogenesis of diabetes. P.S.R.

Cornell, Robert P.; and Saba, Thomas M. (Dept. of Physiol., Univ. of Illinois Coll. of Med., Chicago, Ill.): VASCULAR CLEARANCE AND METABOLISM OF LIPID BY THE RETICULOENDOTHELIAL SYSTEM IN DOGS. Am. J. Physiol 221:1511-16, November 1971.

Phagocytic and metabolic activity of reticuloendothelial system (RES) in dogs were studied after intravenous administration of gelatinized triolein-I-131 RE-test-lipid emulsion at doses of 100, 300, and 5,500 mg./kg. Phagocytic clearance of lipid was initially exponential, and rate of clearance was inversely related to injected dose. Tissue-distribution analysis demonstrated that at fifteen minutes post-injection, 90 per cent of lipid was within liver and 93 per cent was within liver, spleen, and lungs collectively. Metabolic deiodination of ingested triglyceride-I-131 resulted in progressive accumulation of free I-131 within these three major RES organs and subsequent release into circulation. Radioassay of isolated hepatic Kupffer and parenchymal cells indicated active involvement of RES in deiodination process. Findings suggest that kinetics associated with clearance and deiodination of this emulsion may be used for evaluation of one aspect of RES phagocytic and metabolic activity. J.D.G.

Donabedian, Richard; and Nemerson, Yale (Sect. of Lab. Med. and Dept. of Intern. Med., Yale Univ. Sch. of Med., New Haven, Conn.): FATTY ACID OXIDATION BY HUMAN PLATELETS AND ITS STIMULATION BY THROMBIN. Am. J. Physiol. 221:1283-6, November 1971.

ATP generated from glucose metabolism by 10^9 platelets/hr. is approximately 950 mμmoles. When washed human platelets were incubated with albumin-bound palmitic acid, an average of 4.8 mμmoles of palmitate was oxidized by 10^9 platelets/hr. (theoretical yield of ATP approximately 600 mμmoles). Hence, fatty acid oxidation is a major potential source of energy for human platelets. Thrombin concentration of 0.25 NIH U./ml. increased fatty acid oxidation by 30 to 40 per cent. Diisopropyl fluorophosphate treatment of thrombin abolished stimulatory effect on fatty acid oxidation as well as glucose oxidation. Thrombin had no effect on glucose oxidation by erythrocytes, nor did it stimulate fatty acid oxidation by human leukocytes. One thrombin preparation which aggregated platelets and clotted fibrinogen had no effect on oxidation of glucose and fatty acids. J.D.G.

Efendic, Suad; Cerasi, Erol; and Luft, Rolf (Dept. of Endocr. and Metabolism, Karolinska Hosp., S-104 01, Stockholm, Sweden): ARGININE-INDUCED INSULIN RELEASE IN RELATION TO THE CYCLIC AMP SYSTEM IN MAN. J. Clin. Endocr. 34:67-72, January 1972.

The insulin-releasing action of the amino acid arginine in man is inhibited by hypoglycemia. Furthermore, arginine potentiates glucose-induced insulin release, probably by amplifying the insulinogenic signal evoked by glucose in the beta cell. The beta-adrenergic blocking agent propranolol, in doses known to suppress glucose-induced insulin release, did not alter insulin response to arginine infusion. Arginine markedly augments insulin release secondary to glucose, whereas, under the same experimental conditions, it has no effect on insulin release secondary to glucagon. Finally, pretreatment with aminophylline potentiated the insulinogenic potency of the amino acid.

The authors have previously postulated that glucose elicits insulin release by acting directly on a specific cell membrane receptor. The signal thus evoked is probably mediated through the adenyl cyclase-cyclic AMP system. In light of this hypothesis and the above results, the authors suggest that arginine acts on the beta cell by amplifying the transmission of the glucose-induced signal at a locus between the glucose receptor and cyclic AMP. T.J.M.

Fahlén, M.; Odén, A.; Björntorp, P.; and Tibblin, G. (First Med. Service, Sahlgren's Hosp., and Dept. of Mathematics, Univ. of Gothenburg, Gothenburg, Sweden): SEASONAL INFLUENCE ON INSULIN SECRETION IN MAN. Clin. Sci. 41: 453-58, November 1971.

Oral glucose tolerance tests were performed and levels of blood glucose, plasma insulin and triglycerides were measured in 100 men three months after myocardial infarction. The patients were under the age fifty-five years and had normal carbohydrate tolerance. They were grouped in equal numbers, into the four calendar periods during which the studies had been performed. Fasting blood glucose and the sum of plasma insulin measured after glucose ingestion were significantly lower during the two warm and light periods of the year than those during the two cold and dark periods. Fasting plasma insulin and triglycerides, as well as age and body weight were similar

in all groups. These findings suggest that seasonal variations in glucose tolerance and insulin secretion may exist in man and are analogous to previous observations made in laboratory animals. S.P.

Farmer, R. W.; Pellizzari, E. D.; Fabre, L. F., Jr.; Nonaka, K.; Sugase, T.; and Foà, P. P. (Texas Res. Inst. of Mental Sciences, Houston, Tex.; and Div. of Res., Sinai Hosp. of Detroit, Detroit, Mich.): FAILURE OF GROWTH HORMONE TO STIMULATE GLUCAGON SECRETION. Proc. Soc. Exp. Biol. Med. *138*: 491-93, November 1971.

In partially eviscerated dogs, growth hormone failed to stimulate glucagon secretion. Results suggest that rise in plasma glucagon observed in a variety of experimental conditions may have been caused by surgical trauma. J.D.G.

Gaut, Z. N.; Pocelinko, R.; Solomon, H. M.; and Thomas, G. B. (Special Treatment Unit, Martland Hosp., Newark, N.J. and Res. Statistics Dept., Hoffman-LaRoche, Nutley, N.J.): ORAL GLUCOSE TOLERANCE, PLASMA INSULIN, AND URIC ACID EXCRETION IN MAN DURING CHRONIC ADMINISTRATION OF NICOTINIC ACID. Metabolism *20*:1031-35, November 1971.

Antilipemic doses of nicotinic acid administered to five subjects resulted in sustained increases of plasma uric acid and of plasma glucose after glucose tolerance tests. Glycosuria and ketonuria were observed. Plasma insulin levels increased along with the increased glycemia indicating that inhibition of insulin release is not the mechanism by which glucose intolerance is produced or aggravated. Renal excretion and clearance of uric acid decreased significantly which may account for the rise in plasma uric acid concentrations. The diminished clearance of uric acid may result from altered tubular handling of urate by ketoacids or nicotinic acid and its metabolites. C.R.S.

Goberna, Raimundo; Voight, Karl H.; Fussgänger, Rolf D.; Laube, Heinrich; and Pfeiffer, Ernst F. (Dept. of Endocr. and Metabolism, Center of Intern. Med. and Pediat., Univ. of Ulm, Germany): EFFECT OF THE SYNTHETIC PROGESTIN CHLORMADINONE ACETATE ON THE INSULIN RESPONSE TO GLUCOSE IN NORMAL AND SUBTOTALLY PANCREATECTOMIZED RATS. Endocrinology *89*:974-80, October 1971.

Following daily administration of a progestational agent, chlormadinone acetate, to normal and partially pancreatectomized rats for one to three months, intravenous glucose loads were given to evaluate the effect of this agent upon insulin release. Treated animals were found to have improved insulin releases following glucose loads compared to untreated animals which became diabetic following subtotal pancreatectomy. In normal rats, the treated group displayed a higher insulin level five minutes following glucose than did untreated control animals. These studies demonstrate that the progestin, chlormadinone acetate, improved carbohydrate tolerance in partially depancreatectomized female rats. C.R.S.

Gorden, Phillip; Sherman, Barry; and Roth, Jesse (Diabetes Sect., Clin. Endocr. Branch, National Inst. of Arthritis and Metabolic Diseases, NIH, Bethesda, Md.): PROINSULIN-LIKE COMPONENT OF CIRCULATING INSULIN IN THE BASAL STATE AND IN PATIENTS AND HAMSTERS WITH ISLET CELL TUMORS. J. Clin. Invest. 50:2113-22, October 1971.

Proinsulin-like component in human plasma and in incubation media of islet cell tumors from Syrian hamsters was estimated by radioimmunoassay for insulin, after the samples were subjected to Sephadex column filtration. In three healthy subjects basal plasma proinsulin corresponded to approximately 20 per cent of total insulin immunoreactivity. In patients with obesity, hyperadrenocorticism, acromegaly and myotonic dystrophy, basal plasma proinsulin was similar to that in healthy subjects. Among four patients with hypokalemia, one had markedly elevated levels of basal plasma proinsulin. In five patients with an insulin-producing islet cell adenoma or carcinoma, basal plasma insulin comprised 26 to 79 per cent of total insulin. In healthy subjects and in patients without islet tumors, ingestion of glucose led to early increases in insulin but not in proinsulin component. Two hours after glucose, insulin component decreased, while proinsulin increased, so that the contribution of proinsulin to the total immunoreactivity was restored to that seen in the basal state. In patients with islet tumors, the administration of glucose, tolbutamide or leucine also resulted in early increases in the insulin component alone. The increases in total insulin immunoreactivity which occurred after the addition of tolbutamide or glucagon to the hamster tumor media was due principally to increases in the insulin component. These studies suggest that (a) the mechanisms regulating the release of the proinsulin-like and the insulin-like components are different, and (b) in response to stimuli, islet tumors behave qualitatively similar to nontumorous islets. S.P.

Gürson, C. T.; and Saner, G. (Univ. of Istanbul, Istanbul Faculty of Med., Cerrahpasa, Istanbul, Turkey): EFFECT OF CHROMIUM ON GLUCOSE UTILIZATION IN MARASMIC PROTEIN-CALORIE MALNUTRITION. Am. J. Clin. Nutr. *24*:1313-19, November 1971.

Fourteen cases of marasmus in infants from Istanbul, Turkey were carefully studied by intravenous glucose tolerance tests (IVGTT). Nine responded to a single oral chromium dose of 250 μg. with a significant improvement of glucose removal rate. Five untreated marasmic controls showed no significant differences between two IVGTT's performed under otherwise identical conditions. Five nonresponders to chromium did normalize their IVGTT's after a variable period of caloric and vitamin replacement. This study confirms others that chromium deficiency may contribute to glucose intolerance. P.H.S.

Hertelendy, F. (Dept. of Life Sciences, New Enterprise Div., Monsanto Company, St. Louis, Mo.): STUDIES ON GROWTH HORMONE SECRETION. II. STIMULATION BY PROSTAGLANDINS IN VITRO. Acta Endocrinol. (Kbh.) *68*:355-62, October 1971.

Immunoreactive growth hormone release from hemisected rat anterior pituitary glands was studied in vitro. Prostaglandin E_1 (PGE_1) and E_2 stimulated growth hormone release. On a molar basis prostaglandins were at least 1,000 times more potent stimulants of growth hormone secretion than theophylline or dibutyryl cyclic AMP. In presence of ethyleneglycol tetraacetic acid in a calcium-free medium, growth hormone release in response to PGE_1 was reduced drastically. Removal of potassium from the medium did not influence basal or PGE_1-stimulated hormone release. High concentrations of potassium induced marked increases in growth hormone, PGE_1 had an additive effect. Dinitrophenol abolished PGE_1-stimulated hormone release, indicating that the latter is an energy-dependent phenomenon. S.P.

Hirschel, Bernhard J.; Gabbiani, Giulio; Ryan, Graeme B.; and Majno, Guido (Dept. of Pathol., Univ. of Geneva, Geneva, Switzerland): FIBROBLASTS OF GRANULATION TISSUE: IMMUNOFLUORESCENT STAINING WITH ANTISMOOTH MUSCLE SERUM. Proc. Soc. Exp. Biol. Med. *138*:466-69, November 1971.

Human antibody against smooth muscle (found in patients with autoimmune hepatitis) binds to rat fibroblasts in contracting granulation tissue but not to normal rat fibroblasts. This suggests a link between granulation tissue fibroblasts and smooth muscle cells. J.D.G.

Huttunen, Jussi K. (Third Dept. of Medicine, Univ. of Helsinki, Helsinki, Finland): FRUCTOSE IN MEDICINE. A REVIEW WITH PARTICULAR REFERENCE TO DIABETES MELLITUS. Postgrad. Med. J. *47*:654-59, October 1971.

This is a review of the metabolism of fructose. Emphasis is upon absorption and assimilation of fructose through pathways not identical to those of glucose. Metabolism of fructose is largely insulin-independent, although ultimate fate of fructose carbons is determined by presence or absence of insulin. J.D.G.

Iversen, Johan (Second Univ. Clin. of Intern. Med., Kommunehospitalet, Århus, Denmark): SECRETION OF GLUCAGON FROM THE ISOLATED, PERFUSED CANINE PANCREAS. J. Clin. Invest. *50*:2123-36, October 1971.

An isolated canine pancreas preparation was perfused with various secretagogues of islet hormones. The secretion of glucagon was stimulated by gastrin, pancreozymin and arginine, but not by secretin. The magnitude of the increases was greater when the perfusate contained glucose at low concentrations. Insulin was released in response to glucose, gastrin, pancreozymin, arginine and secretin; high perfusate concentrations of glucose augmented these responses. Secretion of both pancreatic hormones always followed a biphasic response pattern. In response to stimuli common to both, the increases in levels of glucagon and insulin occurred simultaneously within a ten-second period. These results confirm the concept that glucagon is a hormone of "glucose need" and suggest that it may be important in a moment-to-moment control of glucose homeostasis. S.P.

Jung, Y.; Hohmann, T. C.; Gerneth, J. A.; Novak, J.; Wasserman, R. C., D'Andrea, R. J.; Newton, R. H.; and Danowski, T. S. (Univ. of Pittsburgh, and Magee-Womens and St. Francis Hosps., Pittsburgh, Pa.): DIABETIC HAND SYNDROME. Metabolism *20*:1008-15, November 1971.

Two findings in diabetic neuropathy of the upper extremity were investigated in fifty-one adults: (1) flexion contractures of the fingers, and (2) delays in transmission of median and ulnar nerve motor impulses from wrist to hand. Flexion contractures of the fingers were found to correlate positively with the duration of diabetes and were associated with a delay in motor nerve transmission in the forearm as well as from wrist to fingers and reduced vibratory sensation. Delays in median nerve transmission in the hands of diabetic patients were accompanied frequently with similar delays in ulnar nerve transmission. These findings suggest that decreased rates of transmission may be related to diabetic neuropathy rather than entrapment of the median nerve. C.R.S.

Kato, Mikio (Dept. of Physiol., Osaka Med. Coll., Takatsuki, Osaka, Japan): SENSITIVITY OF CHOLESTEROL TURNOVER IN RAT LIVER TO COLD ENVIRONMENTAL STRESS. Am. J. Physiol. *221*:1255-59, November 1971.

Experiments were designed to compare cholesterol turnover of diabetic rat liver with that of controls and to compare effects of temperature on cholesterol turnover of alloxan diabetic and normal liver. Long, continuous cold environment on normal and diabetic rats decreased cholesterol turnover rates in liver. Results indicated that the diabetic rat had decreased rates of cholesterol turnover as compared to controls, perhaps due to a defective mechanism of cholesterol degradation. J.D.G.

Kaufman, C. F.; and Bergman, E. N. (Dept. of Physiol., Biochem. and Pharmacol., New York State Vet. Coll., Cornell Univ., Ithaca, N.Y.): RENAL GLUCOSE, FREE FATTY ACID, AND KETONE BODY METABOLISM IN THE UNANESTHETIZED SHEEP. Am. J. Physiol. *221*:967-72, October 1971.

Net renal production or utilization rates of glucose, free fatty acids, and ketone bodies were measured in three groups of sheep: fed, fasted, and three- to six-day acidotic. Kidneys produced a significant amount of glucose, but no significant difference existed between groups. Net renal production or release of free fatty acids was not significantly different between groups. Ketone bodies were utilized by the kidneys of all groups, but utilization by the fasted group was significantly greater than either the fed or acidotic group ($P < 0.01$). Ketone bodies are a significant source of energy for the sheep kidney. J.D.G.

Levine, Rachmiel (City of Hope Med. Center, Duarte, Calif.): NEW HORIZONS IN OUR KNOWLEDGE OF DIABETES MELLITUS. J. Am. Geriatr. Soc. *19*:897-908, November 1971.

The author reviews what he feels are the latest advances in our understanding of diabetes mellitus. He points out that proinsulin is not properly cleaved to insulin in certain islet cell tumors and that a failure to convert proinsulin to insulin may be involved in some types of diabetes mellitus. He discusses insulin secretion and the delay in the first phase of insulin secretion which some investigators have found in mild diabetes and genetic prediabetes. He points out that obesity resulting from increased carbohydrate intake is associated with hyperinsulinemia, hyperplasia of the beta cells and insulin resistance. Damaging the beta cells decreases the insulin levels and the insulin resistance. He postulates that the beta cells produce an insulin antagonist which accounts for the resistance associated with islet cell hyperplasia.

In discussing the effect of insulin at the cellular level, he postulates that insulin interacts with the cell membrane to release a chemical signal that carries out the action of insulin on glycogen, fat and protein. Turning to the vascular complications of diabetes mellitus he points out that about 20 per cent of all diabetics escape significant vascular complications. The degree of vascular disease best correlates with the duration of diabetes rather than its severity. He suggests that diabetic mice which develop vascular complications and the recent finding of an abnormal amount of hydroxylysine and hydroxyproline in the basement membrane of diabetics may offer some clues about this poorly understood but very important area of diabetes. H.G.M.

Mahler, Richard J.; and Szabo, Olga (Dept. of Med., Sect. of Endocr., New York Med. Coll., New York, N.Y.): AMELIORATION OF INSULIN RESISTANCE IN OBESE MICE. Am. J. Physiol. *221*:980-83, October 1971.

Verbatim summary. Littermate lean and obese mice were studied for insulin sensitivity. Obese intact mice were insulin

insensitive. Alloxan administration caused reduction of pancreatic beta cell hyperplasia and decrease in plasma immunoreactive insulin without change in body weight. Following alloxan administration to obese animals, insulin sensitivity was restored to normal both in vivo and in vitro.

Malone, John I.; Wells, Henry J.; and Segal, Stanton (Div. of Biochem. Development and Molecular Diseases, Children's Hosp. of Philadelphia, and Dept. of Pediat., Univ. of Pennsylvania Sch. of Med., Philadelphia, Pa.): GALACTOSE TOXICITY IN THE CHICK: HYPEROSMOLALITY. Science *174*:952-54, November 26, 1971.

Galactose-fed chicks develop severe hyperosmolar dehydration. Though biochemical abnormalities occur in brain of galactose-toxic chick, observed physiologic alteration of serum osmolality could be the major factor responsible for galactose toxicity syndrome. J.D.G.

Martin, R. J.; and Baldwin, R. L. (Dept. of Animal Science, Univ. of Calif., Davis, Calif.): EFFECTS OF INSULIN ON ISOLATED RAT MAMMARY CELL METABOLISM: GLUCOSE UTILIZATION AND METABOLITE PATTERNS. Endocrinology *89*: 1263-69, November 1971.

Production of CO_2, lactose and lipid from glucose in isolated mammary cells was stimulated two- to threefold by insulin while casein synthesis was only slightly stimulated. Increasing glucose concentrations in the medium did not reduce insulin stimulation of CO_2 and fatty acid productions but abolished insulin stimulation of glyceride glycerol synthesis. Insulin enhances the activity of the pentose phosphate pathway in glucose oxidation. The values of free nicotinamide adenine nucleotides in isolated cells shifted toward a more reduced state when insulin was not added to the medium. These observations indicated that the action of insulin in regulating mammary gland metabolism may be mediated through effects on the redox state of the cell. C.R.S.

Nitzan, M.; and Groffman, H. (Dept. of Pediat., Univ. of Illinois Med. Center, Chicago, Ill.): METABOLIC CHANGES INDUCED BY TISSUE INJURY: IN VITRO STUDIES WITH RAT LIVER SLICES. Quart. J. Exp. Physiol. *56*:108-12, April 1971.

To study the metabolic response to tissue injury, in vitro studies with rat liver slices have been conducted. Liver slices, from fasted rats which had undergone standard midline laparotomy twenty-four hours before, showed a fourteenfold increase in the incorporation of acetate-2-C-14 into cholesterol, with no change in the conversion of the acetate to other lipid fractions or C-14-O_2.

The fate of L-alanine-C-14 has also been determined. The same physical injury brought about a sevenfold increase in the production of cholesterol-C-14, a 66 per cent increase in the incorporation of the alanine into liver proteins, and a 35 per cent increase in the evolution of lactic acid-C-14. The radioactivity of other lipid classes, C-14-O_2, glucose or glycogen was not significantly different from the corresponding control values.

These data are compatible with a striking and specific stimulating action of surgical injury upon cholesterogenesis. In addition, though the known effect of physical injury in the peripheral tissues is excessive breakdown of proteins, the results suggest enhanced hepatic protein synthesis after injury. P.F.

Oldendorf, William H. (Res. Serv., Wadsworth Hosp., Veterans Administration, Los Angeles, Calif.; and Dept. of Neurol., UCLA Sch. of Med., Los Angeles, California): BRAIN UPTAKE OF RADIOLABELED AMINO ACIDS, AMINES, AND HEXOSES AFTER ARTERIAL INJECTION. Am. J. Physiol. *221*: 1629-39, December 1971.

Loss of C-14-labeled test substances to brain during capillary passage following injection into rat was measured relative to simultaneously injected ^{3}HOH. Essential nutritional amino acid uptake was greater than nonessential. Two blood-brain barrier (BBB) carrrier systems for amino acids were identified. Putative transmitter substances were less taken up than precursors. Saturability of D-glucose uptake was demonstrated, and evidence presented that five hexoses shared a common carrier. Cycloleucine and 3-o-methylglucose showed saturable uptakes. Amino acid uptake was incompletely stereospecific whereas glucose uptake was stereospecific. Phlorizin inhibits brain uptake of D-glucose. Relative BBB permeabilities to many substances resemble red-cell permeabilities. Carrier systems for amino acids are independent of glucose carrier. J.D.G.

Oschman, James L.; and Berridge, Michael J. (Inst. of Biol. Chem., Univ. of Copenhagen, Copenhagen, Denmark; and Dept. of Zoology, Univ. of Cambridge, Cambridge, England): THE STRUCTURAL BASIS OF FLUID SECRETION. Fed. Proc. *30*:49-56, January-February 1971.

Observations that led to standing-gradient hypothesis of fluid absorption were confirmed for secretory epithelia, Malpighian tubules and salivary glands of an insect. Rate of fluid secretion is proportional to rate of solute transport. Transported fluid is isosmotic to bathing medium over wide range of concentrations and transport rates. Adding impermeant solutes to bathing medium causes proportional increase in concentration of transported fluid. Secretory epithelia lack extensive intercellular spaces characteristic of absorptive epithelia. Instead, they have elaborate plications of cell surface including microvilli, basal infolds, and canaliculi. Authors suggest that channels at cell surface may be analogues of intercellular spaces of absorptive epithelia, i.e. sites of standing osmotic gradients. Since secretory epithelia draw solutes from blood, consideration must be given to "sweeping-in" effect that carries nontransported solutes into basal channels. Selectivity of transport may be partly due to channel geometry and properties of basement membrane. Experiments using colloidal gold as tracer support view that basement membrane is a barrier to larger solute molecules. J.D.G.

Pitkin, R. M.; Plank, C. J.; and Filer, L. J., Jr. (Depts. of Obstet. and Gynecol. and Pediat., Univ. of Iowa Hosps., Iowa City, Ia.): FETAL AND PLACENTAL COMPOSITION IN EXPERIMENTAL MATERNAL DIABETES. Proc. Soc. Exp. Biol. Med. *138*:163-66, October 1971.

Verbatim summary. A mild diabetic-like state was induced with streptozotocin in rats prior to breeding, and fetal and placental composition was examined on Day 21 of pregnancy. Fetuses of untreated diabetic rats were larger than those of controls and had significantly more fat, less water, and more DNA. These alterations in fetal size and composition were prevented by maternal insulin treatment during pregnancy.

Quickel, Kenneth E., Jr.; Feldman, Jerome M.; and Lebovitz, Harold E. (Div. of Endocr., Dept. of Med., Duke Univ., Durham, N.C.): ENHANCEMENT OF INSULIN SECRETION IN ADULT-ONSET DIABETICS BY METHYSERGIDE MALEATE: EVIDENCE FOR AN ENDOGENOUS BIOGENIC MONOAMINE MECH-

ANISM AS A FACTOR IN THE IMPAIRED INSULIN SECRETION IN DIABETES MELLITUS. J. Clin. Endocr. *33*:877-81, December 1971.

To investigate the possible role of endogenous catecholamines and serotonin in the impaired insulin release of adult-onset diabetes mellitus, intravenous glucose-stimulated insulin secretion was measured in adult-onset diabetic patients and in normal volunteers before and during administration of the serotonin blocker, methysergide maleate (2 mg. every six hours for two days) or placebo. The increase in insulin secretion as measured by per cent change in area under the insulin curve compared to the control study was significantly greater ($p < 0.05$) during methysergide treatment (48.8 per cent) than during placebo administration (5.1 per cent) in the diabetic patients. The normal volunteers showed no significant difference in insulin secretion between the methysergide (5.2 per cent) and the placebo (10.2 per cent). Glucose disappearance constants were unchanged during methysergide administration in most diabetic patients and in the group of normal volunteers. These studies suggest the existence of an endogenous pancreatic biogenic monoamine mechanism which inhibits insulin release in adult-onset diabetic patients and could play a role in the pathogenesis of diabetes mellitus. T.J.M.

Reitano, G.; Grasso, S.; Distefano, G.; and Messina, A. (Depts. of Pediat., Morbid Anatomy, and General Path., Univ. of Catania, Catania, Italy): THE SERUM INSULIN AND GROWTH HORMONE RESPONSE TO ARGININE AND TO ARGININE WITH GLUCOSE IN THE PREMATURE INFANT. J. Clin. Endocr. *33*: 924-28, December 1971.

Serum insulin and human growth hormone (HGH) levels were measured in thirty-three premature infants during the first twenty-four hours of life, following the infusion of arginine, glucose, and glucose plus arginine. Infusion of arginine (2.5 gm.) was followed by a moderate early rise in serum insulin and a marked and delayed rise in serum HGH. Glucose (1.25 gm.) infusion resulted in a small insulin response and a rise of serum HGH. However, the simultaneous administration of arginine and glucose, each in amounts of 1.25 gm., was associated with a prompt marked rise of serum insulin and a delayed rise of serum HGH. T.J.M.

Rössner, S.; Larsson-Cohn, V.; Carlson, L. A.; and Boberg, J. (Depts. of Obstet. and Gynec. and Geriatrics, Univ. of Uppsala, Dept. of Intern. Med., Karolinska Hosp., and King Gustav V Res. Inst., Stockholm, Sweden): EFFECTS OF AN ORAL CONTRACEPTIVE AGENT ON PLASMA LIPIDS, PLASMA LIPOPROTEINS, THE INTRAVENOUS FAT TOLERANCE AND THE POSTHEPARIN LIPOPROTEIN LIPASE ACTIVITY. Acta Med. Scand. *190*:301-05, October 1971.

The response of the plasma lipids to an oral contraceptive containing a progestational agent (chlormadinone acetate, 3 mg.) and an estrogenic agent (mestranol, 0.1 mg.) and to the progestational component alone was studied in twelve healthy women. The plasma triglyceride level was elevated in all lipoprotein groups (VLDL, LDL and HDL) on the combination therapy, but returned to near the basal values on the progestational drug alone. The cholesterol level increased slightly but the intravenous fat tolerance was unaffected by the contraceptive agent. The postheparin lipolytic activity was decreased. The authors restate the idea that increased synthesis of triglycerides by the liver under the influence of the estrogenic component may be the reason for the increase in plasma lipids during therapy with oral contraceptives. H.G.M.

Stern, Judith; Johnson, P. R.; Greenwood, M. R. C.; Zucker, L. M.; and Hirsch, Jules (The Rockefeller Univ., New York, N.Y.; and Harriet G. Bird Memorial Lab., Stowe, Mass.): INSULIN RESISTANCE AND PANCREATIC INSULIN RELEASE IN THE GENETICALLY OBESE ZUCKER RAT. Proc. Soc. Exp. Biol. Med. *139*:66-69, January 1972.

Zucker obese rats are normoglycemic, hyperinsulinemic, and release more insulin from isolated pancreatic islets than do nonobese controls. Basal glucose conversion to glycogen by muscle and to CO_2 by isolated adipocytes is similar in obese and nonobese; insulin resistance is present in both tissues in the obese. There is significant correlation between adipocyte response to insulin and pancreatic insulin release in obese and nonobese rats. Authors suggest a role for adipocytes in determining pancreatic function. J.D.G.

Sybulski, S.; and Maughan, G. B. (Hellenic Res. Lab., Dept. of Obstet. and Gynec., Royal Victoria Hosp., Montreal, Quebec, Canada): USE OF STREPTOZOTOCIN AS DIABETIC AGENT IN PREGNANT RATS. Endocrinology *89*:1537-40, December 1971.

Rats injected with streptozotocin during early pregnancy, unlike those treated with alloxan, remained alive until termination of pregnancy without requiring insulin therapy although overt diabetes developed in the animals. Both streptozotocin and alloxan-treated animals had abnormally small fetuses for gestational age. The former rats had larger than normal placentas with markedly increased glycogen content; their fetuses were hyperglycemic at term and had increased liver glycogen levels. C.R.S.

Tanaka, Kay; Isselbacher, Kurt J.; and Shih, Vivian (Dept. of Med., Massachusetts Gen. Hosp. (Gastrointestinal Unit), and Harvard Med. Sch.; Dept. of Neurol., Harvard Med. Sch., and Joseph P. Kennedy Labs., Massachusetts Gen. Hosp., Boston, Mass.): ISOVALERIC AND a-METHYLBUTYRIC ACIDEMIAS INDUCED BY HYPOGLYCIN A: MECHANISM OF JAMAICAN VOMITING SICKNESS. Science *175*:69-71, January 7, 1972.

Hypoglycin A, causative agent of Jamaican vomiting sickness, markedly increased isovaleric acid in plasma of rats. a-Methylbutyric acid, a position isomer, also accumulated. Hypoglycin A reproduced some features of human isovaleric acidemia. Accumulation of branched pentanoic acids may contribute to pathogenesis of Jamaican vomiting sickness. J.D.G.

Wannemacher, R. W., Jr.; Pekarek, R. S.; and Beisel, W. R. (U. S. Army Med. Res. Inst. of Infectious Diseases, Frederick, Md.): MEDIATOR OF HEPATIC AMINO ACID FLUX IN INFECTED RATS. Proc. Soc. Exp. Biol. Med. *139*:128-32, January 1972.

Live D. pneumoniae (but not endotoxin or double-stranded polynucleotides) stimulate flux of cycloleucine into liver. Sterile two-hour serum from D. pneumoniae-infected rats and secretions obtained from rat peritoneal leukocytes can also mediate flux of cycloleucine into liver of normal rats. Data suggest that one or more proteins synthesized and excreted by leukocytes can act as humoral intermediates in stimulation of amino acid flux into liver tissue. J.D.G.