

# ABSTRACTS

*Adnitt, P. I.; and Taylor, Enid* (Diabetic Clin. and Dept. of Ophthal., St. Bartholomew's Hosp., London, England): PROGRESSION OF DIABETIC RETINOPATHY. RELATIONSHIP TO BLOOD SUGAR. *Lancet* 1:652-54, March 28, 1970.

The authors prospectively studied thirty-seven eyes of twenty-one patients for thirty to 103 months using serial retinal photographs and blood sugars done at least every six months to evaluate the relationship between diabetes control and retinopathy progression. The patients averaged fifty-six years of age and had a mean duration of diabetes of fourteen years and were observed an average of fifty months. Assessment of photographic fields for new disc vessels, fibrous change, as well as microaneurysms and exudates was made. No statistically significant relationship between retinopathy progression and mean blood sugar or duration of diabetes was found. T.G.S.

*Albutt, E. C.; and Chance, G. W.* (Univ. of Birmingham Inst. of Child Health, Francis Road, Birmingham 16, and Birmingham Children's Hosp., Birmingham, England): FASTING PLASMA CHOLESTERYL ESTERS IN DIABETIC CHILDREN CONSUMING CORN OIL. *Amer. J. Clin. Nutr.* 1552-54, December 1969.

A report is presented on the details of fatty acid composition of fasting plasma cholesteryl esters in a group of nineteen diabetic children on corn oil diet for four to seven years. Also studied were five children without a family history of diabetes mellitus, coronary artery disease or obesity and four children whose adipose tissue linoleic acid (18:2) concentration was less than 5 per cent.

No difference was found between the fatty acid composition of the fasting plasma cholesteryl ester fraction in normal children and in those diabetic children on a standard diet. The percentage of 18:2 in the fasting plasma cholesteryl ester fraction varied widely in all groups of the children studied. Both age and dietary 18:2 intake were considered responsible for the difference.

Where dietary adherence to corn oil was known to be optimal the plasma cholesteryl ester fraction reached a maximum value of 76 per cent when adipose tissue linoleic acid was 30 per cent. It was suggested that an obligatory proposition of cholesterol esterified with endogenously produced fatty acids was contained in the fasting plasma cholesteryl ester fraction. Furthermore linoleate increased at the expense of oleate which may account for a favorable effect on atherosclerosis since arteriosclerotic plaques have a high oleate content. B.R.B.

*Bailey, R. E.; Castro, A.; Kramer, R. M.; and Macfarlane, D.* (Div. of Diabetes and Metabolism, Dept. of Med., Univ. of Oregon, Med. Sch., Portland, Ore.): ENHANCEMENT OF INSU-

LIN RELEASE TO ACUTE GLYCAEMIC STIMULATION WITH DEPRESSION OF BASAL INSULIN PRODUCTION RATES IN INSULINOMA FOLLOWING DIAZOXIDE ADMINISTRATION. *Acta Endocr.* 63:392-404, March 1970.

*Verbatim summary.* Single and double load oral glucose tolerance tests were performed repetitively both before and during administration of diazoxide to a 15-year old girl who had an insulin secreting islet cell tumor. Plasma insulin concentrations increased above baseline values by a greater magnitude in response to a single acute oral glycemic stimulus following diazoxide treatment, compared to the increases resulting from comparable prediazoxide glucose tolerance tests, and plasma insulin either attained higher values or sustained elevations for a longer duration during the early part (first hour) of the single load tests. This provides evidence that diazoxide does not prevent the normal insulin release response to a glycemic stimulus, and that enhanced insulin secretion rates may occur with insulinomas under the study conditions employed.

Fasting plasma insulin concentrations were lower during the period of diazoxide administration which indicates that insulin biosynthesis was depressed under fasting steady-state conditions. Considering that the first part of the glucose tolerance curve reflects primarily insulin release, our data are consistent with the view that insulin storage within the insulinoma cells is preserved under the study conditions employed and may even be enhanced by diazoxide. Consequently, depression of insulin biosynthesis is considered to be a resultant effect and not a primary action of diazoxide. These results suggest a possible basis for distinguishing types of insulinomas should additional perspective reveal that glycemic-induced enhancement of insulin secretion rates cannot be made to occur uniformly in diazoxide treated patients having insulinomas.

*Beetham, W. P.; Aiello, L. M.; Balodimos, M. C.; and Koncz, L.* (Joslin Diabetes Foundation, Inc., New England Deaconess Hosp., and Depts. of Ophthal. and Med., Harvard Med. Sch., Boston, Mass.): RUBY LASER PHOTOCOAGULATION OF EARLY DIABETIC NEOVASCULAR RETINOPATHY. *Arch. Ophthal.* 83:261-72, March 1970.

*Verbatim summary.* Between February 1967 and April 1969, 329 patients with various degrees of diabetic proliferating retinopathy have been treated by a circumferential ruby laser photocoagulation technic. Of these, 178 patients represent controls in which both eyes have equal degree of neovascular retinal disease in each eye on the basis of funduscopy, photography, and fluorescein angiography. One eye is treated, the opposite serving as a control. Seventy-two of these control patients had early neovascular retinopathy, have one or more years of follow-up, and are presented herein as a preliminary

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report of a detailed ongoing control study. Eighty per cent of treated eyes have shown a definite improvement to a lesser stage of neovascular retinopathy. Fifty-four per cent have had complete disappearance of neovascularization. All untreated controls have remained unchanged or have worsened.

*Beisswenger, P. J.; and Spiro, R. G.* (Depts. of Biological Chem. and Med., Harvard Med. Sch., and E. P. Joslin Res. Lab., Boston, Mass.): HUMAN GLOMERULAR BASEMENT MEMBRANE: CHEMICAL ALTERATION IN DIABETES MELLITUS. *Science* 168:596-98, May 1, 1970.

*Verbatim summary.* The human glomerular basement membrane belongs to the collagen family of proteins. It contains about 7 per cent carbohydrate, half of which occurs as glucosylgalactose disaccharide units linked to hydroxylysine. Glomeruli from diabetics contain increased amounts of basement membrane material. In addition, these membranes show a distinct chemical alteration characterized by a significant decrease in lysine, accompanied by an equivalent increase in hydroxylysine and hydroxylysine-linked disaccharide units.

*Blotner, Harry* (Dept. of Med., Beth Israel Hosp., Boston, Mass.): THE USE OF CHLORPROPAMIDE IN THE TREATMENT OF DIABETES INSIPIDUS. *J. Maine Med. Ass.* 61:59-61, March 1970.

*Verbatim summary.* This paper presents a study of the use of chlorpropamide in the treatment of eight patients with diabetes insipidus, six of idiopathic origin and two following brain surgery. Complete relief from the polyuria and polydipsia was obtained in three cases of idiopathic diabetes insipidus and one due to hypophysectomy. Considerable relief from the polyuria and polydipsia or prolonged effect of the Pitressin tannate in oil occurred in two cases of idiopathic diabetes insipidus and one following a craniopharyngioma operation. There was no effect in one case of idiopathic diabetes insipidus. The effect of the chlorpropamide on the fluid intake and output may take place within thirty-six hours. The simultaneous administration of chlorpropamide with the intramuscular injection of Pitressin tannate in oil may prolong the effect of the Pitressin tannate in oil considerably after a period of three to four weeks.

The mode of action of the drug appears in part at least, similar to that of the antidiuretic hormone. Chlorpropamide increases the salivary output and abolishes thirst. Rarely, hypoglycemia may occur in patients with diabetes insipidus taking chlorpropamide when not eating sufficiently. Patients should be advised of this possibility and told how to prevent it. Chlorpropamide appears to be a useful drug in the treatment of diabetes insipidus.

*Bretz, Gedeon W.; Baghdassarian, Alice; Graber, John D.; Zacherle, Barry J.; Norum, Robert A.; Blizzard, Robert M.* (Children's Med. and Surg. Center, The Johns Hopkins Univ. Sch. of Med., The Johns Hopkins Hosp., Baltimore, Md.): COEXISTENCE OF DIABETES MELLITUS AND INSIPIDUS AND OPTIC ATROPHY IN TWO MALE SIBLINGS. *Amer. J. Med.* 48:398-403, March 1970.

*Verbatim summary.* Two male siblings with diabetes mellitus, diabetes insipidus and optic atrophy are described. Chlorpropamide was of value in treating the diabetes insipidus in the one patient tested but refractoriness apparently developed. Lysin-8-vasopressin was effective as treatment over a several month period. A review of the literature suggests

that diabetes insipidus and mellitus may occur either as coincident diseases without a common genetic pathway or possibly as a genetically transmitted disease. In the latter instance primary optic atrophy also occurs in some instances.

*Brunfeldt, K.; Hansen, B. A.; and Nielsen, J. H.* (Steno Memorial Hosp. Res. Lab., Gentofte, Denmark): BINDING OF ZINC TO INSULIN AND SOME INSULIN DERIVATIVES STUDIED BY PAPER ELECTROPHORESIS. *Acta Endocr.* 61:561-76, July 1969.

*Verbatim summary.* Paper electrophoretic fractionation in barbiturate (barbital) buffer, pH 9, of iodine-substituted insulin 0-10.8 I/mole showed that substitution with 4-6 I/mole influences the binding of zinc to a demonstrable extent. The effect appears to be due to substitution in the imidazole groups of the histidine residues. Substitution with iodine in the tyrosine residues seems to be without significance, at least at the lower degrees of iodination. The importance of the histidine residues for the binding of zinc is shown by selective destruction of the imidazole groups by photo-oxidation, sensitized by methylene blue. Carbamylation of the N-terminal  $\alpha$ -amino groups in the A- and B-chains with KOCN only slightly influences the ability to bind zinc while carbamylation with fluorescein isothiocyanate in the N-terminal of the B-chain brings about a more pronounced reduction in the zinc binding capacity.

*Buse, Maria G.; Johnson, Allen H.; Kuperminc, Denis; and Buse, John* (Dept. of Med., Div. of Endocr. & Metabolism, Med. Univ. of South Carolina, Charleston, S.C.): EFFECT OF  $\alpha$ -ADRENERGIC BLOCKADE ON INSULIN SECRETION IN MAN. *Metabolism* 19:219-25, March 1970.

Intravenous glucose tolerance tests performed under basal conditions and following alpha adrenergic blockade with IV phentolamine revealed that the insulin secretory response to glucose was increased by alpha blockade. Fasting levels of IRI and glucose were unaffected by phentolamine. Five minutes after the injection of glucose the mean plasma IRI levels were 38 per cent higher with phentolamine than during control tests. The distribution space or rate of disappearance of injected glucose were not influenced by alpha blockade and no changes were observed in plasma growth hormone levels. The evidence supports the view that endogenous catecholamines or the "sympathetic tone" modulate the insulin secretory response to a glucose load in man. C.R.S.

*Castleman, Benjamin and McNeely, Betty U.* (Massachusetts Gen. Hosp., Boston, Mass.): CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL—CASE 53-1969. *New Eng. J. Med.* 281:1473-81, Dec. 25, 1969.

The following case history was presented. A sixty-one year old woman was admitted to the hospital initially for recurrent hematemesis. During this visit, an end to side portacaval shunt was performed with a biopsy of the liver showing post-necrotic cirrhosis. On the second admission three years later for subsequent follow-up treatment, the patient had an abnormal glucose tolerance test. Glucose levels were 82 mg. fasting, 163 mg. at thirty minutes, 178 mg. at one hour, 155 mg. at two hours and 43 mg. at three hours. The patient was discharged on an 1800 calorie diet. Three months later the patient was admitted in a weakened state from her chronic liver condition and died.

Anatomical diagnoses confirmed the clinical diagnoses of

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postnecrotic cirrhosis of the liver, hemosiderosis (after porta-caval shunt) of liver, pancreas, stomach, adrenal cortex and heart, and hepatic encephalopathy, with proliferation of astrocytes. Acute purulent pericarditis (*Staphylococcus aureus*) was found at posting.

The derangement of carbohydrate metabolism was discussed. It was suggested that presence of iron in the pancreas may have caused impairment of carbohydrate metabolism. Also faulty carbohydrate metabolism may have resulted from liver disease. Other suggested mechanisms of abnormal carbohydrate tolerance in liver disease patients were increased peripheral resistance to insulin or increased concentration of growth hormone in the plasma. B.R.B.

*Chazan, Bernard I.; and Balodimos, Marios C.* (Elliott P. Joslin Res. Lab., Dept. of Med., Harvard Med. Sch., Boston, Mass.): CONJUNCTIVAL VASCULAR LESIONS. CLASSIFICATION AND CLINICAL SIGNIFICANCE WITH SPECIAL REFERENCE TO DIABETES. *Acta Diabet. Lat.* 6:355-70, April-June 1969.

*Verbatim summary.* A simple method for screening and photographing the conjunctival vasculature is described. A practical grading system is presented for the commoner variations such as venular congestion, tortuosity, irregular dilations and microaneurysms, capillary ischemia and ectasias and arteriolar constriction and red-cell aggregation. The significance of the various vascular anomalies is discussed as they are present in the collecting venules, postcapillary venules, capillaries, and in the terminal and branching arterioles. Special emphasis is laid on conjunctival vascular changes in diabetes.

*Chisholm, D. J.; Young, J. D.; and Lazarus, L.* (The Garvan Inst. of Med. Res., St. Vincent's Hosp., Sydney, N.S.W., Australia): THE GASTROINTESTINAL STIMULUS TO INSULIN RELEASE. *J. Clin. Invest.* 48:1453-60, August 1969.

*Verbatim summary.* The gastrointestinal stimulus to the release of insulin has been investigated in man by the use of a radioimmunoassay for secretin. Serum secretin levels rose rapidly after the oral ingestion of glucose or protein and preceded the elevation of serum insulin. An intravenous infusion of highly purified secretin caused a release of insulin when the serum secretin levels were within the physiological range.

Infusion of hydrochloric acid into the duodenum caused an elevation of serum secretin and serum insulin levels in normal subjects. A similar response of secretin and insulin was seen after intravenous infusion of pentagastrin even when the acid stimulus to the duodenum was prevented. The latter observation suggests that pentagastrin (and probably gastrin) releases secretin by a direct humoral effect which is later fortified by the arrival of gastric acid in the duodenum.

These studies suggest that secretin participates in the augmentation of insulin release after oral stimuli, and that a rapid sequence of humoral events takes place, gastrin releasing secretin and secretin releasing insulin. Subsequently secretin release would be augmented by a local stimulus in the duodenum and insulin release by the rising level of blood glucose or amino acids.

The humoral system, which could also involve other gastrointestinal hormones, would provide a mechanism for facilitating the release of insulin to coincide with the onset of metabolite absorption.

*Cole, Harold S.; Bilder, Joan H.; Camerini-Davalos, Rafael; and Grimaldi, Richard D.* (Depts. of Pediat., Obstet., and Gynec., and the Diabetes Center, New York Med. Coll., New York, N.Y.): GLUCOSE TOLERANCE, INSULIN AND GROWTH HORMONE IN INFANTS OF GESTATIONAL DIABETIC MOTHERS. *Pediatrics* 45:394-403, March 1970.

*Verbatim summary.* Twelve control and nine gestational diabetic mothers and their infants were studied at birth. All infants received a three-hour oral glucose tolerance test completed during the first twenty-four hours of life. All mothers in both groups were obese, and the mean birth weights of the infants were not significantly different.

Glucose, serum insulin, and growth hormone values were obtained. The control infants showed a disposal of glucose similar to that of the IGDM. No evidence of hyperinsulinemia was observed in either group during the glucose tolerance test.

*Crespin, Stephen R.; Greenough, William B. III; and Steinberg, Daniel* (Molecular Disease Branch, National Heart Inst., NIH, Bethesda, Md.): STIMULATION OF INSULIN SECRETION BY INFUSION OF FREE FATTY ACIDS. *J. Clin. Invest.* 48:1934-43, October 1969.

*Verbatim summary.* The acute elevation of plasma free fatty acid (FFA) levels by direct infusion of sodium oleate into the plasma of conscious dogs was accompanied by the rapid onset of a two- to twelve-fold increase in plasma immunoreactive insulin, and, subsequently, a marked fall in plasma glucose, even in dogs receiving intravenous glucose throughout the infusion. The magnitude of both the insulin and glucose responses correlated with the mean FFA level during infusion. A large increase in plasma insulin and fall in glucose also occurred when glycerol was infused with oleate in order to simulate endogenous lipolysis more closely. Insulin levels in pancreaticoduodenal vein blood rose markedly during oleate infusion, while plasma ketone levels rose only slightly.

In contrast to the effects of oleate infusion, elevation of plasma FFA to correspondingly high levels by triolein ingestion and intravenous heparin produced only small increases in plasma insulin, which did not correlate well with the FFA level reached, and small increases in plasma glucose.

The results indicate that under certain conditions elevated FFA levels may be a potent stimulus of insulin secretion. This response is modified under other conditions such as during chylomicron removal under the influence of heparin. This effect may play a role in the regulation of lipolysis and ketone formation, but determination of the exact mechanism of FFA stimulation of the pancreas and its physiological significance will require further investigation.

*Cristol, R.; Cottet, J.; and Cloarec, M.* (Hôpital Saint Antoine, 75 Paris (12e) France): STUDY OF GLUCOSE REGULATION BY AN INTRAVENOUS TOLBUTAMIDE TEST IN CORONARY INSUFFICIENCY. *Presse Med.* 78:739-42, March 28, 1970.

*Verbatim summary.* The authors studied fifty-two coronary patients, including fifteen cases of myocardial infarction before the age forty-five, with an intravenous tolbutamide test. According to their criteria, 46 per cent had signs of latent diabetes and 19 per cent had signs of hypoglycemia.

A study of these findings in relation to age and weight did not show any statistically significant difference between prediabetic and normal subjects. There was however a slight

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difference regarding total lipids and triglycerides. These results are in agreement with those of other authors.

A mild disorder of glucose regulation should not henceforth be considered a high risk factor for the development of atheroma. This raises the problem of pathogenic links between atheroma, hyperlipemia and disorders of glucose regulation.

Better detection of such a disorder should lead to better prophylaxis.

*Dubois, Reuben S.; Roy, Claude C.; Fulginiti, Vincent A.; Merrill, Deborah A.; and Murray, Robert L.* (Dept. of Pediat., Univ. of Colorado Med. Center, Denver, Colo.): DISACCHARIDASE DEFICIENCY IN CHILDREN WITH IMMUNOLOGIC DEFICITS. *J. Pediat.* 76:377-85, March 1970.

*Verbatim summary.* Eighteen Caucasian patients with various immunologic deficiencies had gastrointestinal manifestations such as diarrhea, steatorrhea, partial villous atrophy, and lymphoid nodular hyperplasia. The levels of IgA in the saliva and in the duodenal juice correlated well with each other and also reflected the serum levels of IgA. Determinations of the jejunal disaccharidase activity revealed an isolated lactase deficiency with normal villi in three of the eighteen patients. Seven of the eight patients with deficiencies of cellular immunity and one with isolated IgA deficiency and normal cellular immunity, were found to have decreased lactase, sucrose, and maltase activity despite the presence of a normal villous pattern and of intact epithelial cells.

*Fenichel, R. L.; Purse, R. M.; Alburn, H. E.; and Edgren, R. A.* (Res. Div., Wyeth Labs., Philadelphia, Pa.): EFFECTS OF ORAL CONTRACEPTIVES AND THEIR COMPONENTS ON GLUCOSE TOLERANCE IN RATS. *Acta Endocr.* 62:438-48, November 1969.

*Verbatim summary.* Treatment of adult female rats with norgestrel, ethynyl oestradiol and their combination (Ovral) at doses approximating one and twenty-five-fold multiples of the human dose protected them against the combined diabetogenic influence of a glucose load and the hyperglycemic effect of reduced insulin B-chain. Norgestrel and Ovral appeared to be antidiabetogenic since they reversed the B-chain-induced hyperglycemia. Various steroidal contraceptives and certain of their components failed to modify B-chain-induced hyperglycemia in spayed rats sensitized with a high fat, high protein diet.

Normal intact female rats treated with norgestrel, ethynyl oestradiol and their combinations and given glucose tolerance tests produced glucose responses higher than those of controls, but since these groups showed recovery to or toward control blood glucose levels, insulin mobilization was apparently normal. In a second experiment, Ovral and various contraceptive formulations failed to produce significant alterations in glucose tolerance.

None of these studies suggested a diabetogenic effect of the contraceptive steroids employed; in fact, the first study with reduced insulin B-chain suggested an antidiabetogenic effect for Ovral.

*Fineberg, S. E.; Merimee, T. J.; Rabinowitz, D.; and Edgar, P.* (Evans Div. of Clin. Res., and Boston City Hosp., Boston Univ. Sch. of Med., Boston, Mass.; Johns Hopkins Sch. of Med., Div. of Endocr., Baltimore, Md.): INSULIN SECRETION IN ACROMEGALY. *J. Clin. Endocr.* 30:288-92, March 1970.

A comparative study of insulin release was made in nine acromegalics and thirty-nine normal controls subjects who had normal fasting plasma glucoses. Both hyperglycemic and nonhyperglycemic stimuli were used to provoke insulin secretion. Nondiabetic acromegalic patients responded to every stimulus investigated with hyperinsulinism. Decreased carbohydrate tolerance was present only with the glucose tolerance test. The authors conclude that carbohydrate intolerance alone was not sufficient even in the glucose tolerance test to account for increased insulin release, and that the capacity of the pancreatic beta cell to release insulin is increased with prolonged exposure to excessive quantities of human growth hormones. T.J.M.

*Glick, Z.; Baile, C. A.; and Mayer, J.* (Dept. of Nutrition, Harvard Sch. of Public Health, Boston, Mass.): INSULINOTROPIC AND POSSIBLE INSULIN-LIKE EFFECTS OF SECRETIN AND CHOLECYSTOKININ-PANCREOZYMIN. *Endocrinology* 86: 927-31, April 1970.

Intravenous secretin and cholecystokinin-secretin (C-P) caused four to five-fold increases in serum IRI in monkeys within two minutes. Only C-P caused an increase in serum IRI in rats while secretin produced no change. Serum glucose levels decreased in monkeys following the rise in IRI; in neither species did serum glucose increase so that the IRI response was not related to glucose fluxes. Isolated fat cells from epididymal fat pads of rats did not respond with increases in glucose uptake when secretin or C-P were added to the incubation media. These results indicate that secretin and C-P exert their influences on serum glucose through the release of insulin and not through a direct insulin-like activity. C.R.S.

*Gries, F. A.; and Oberdisse, K.* (II Medizinische Klinik und Poliklinik und Diabetes-Forschungs-Institut der Universität Düsseldorf, Düsseldorf, Germany): *Deutsch. Med. Wschr.* 95: 727-34, April 1970.

*Verbatim summary.* Ketoacidosis and secondary hyperlipidemia in decompensated cases of diabetes are largely due to an abnormal metabolism in the fatty tissues where, as a result of insulin deficiency, there is an increased mobilization of fats and inhibition of storage of circulating lipids. Secondary hyperlipidemia is a cause of diabetic vascular complications. The effectiveness of metabolic control in diabetics should be judged not only by blood sugar levels but also serum lipid levels. Various primary disorders of fat metabolism have recently been demonstrated as responsible for favoring the manifestation of a genetic diabetic predisposition. Essential hyperlipidemia of types III, IV and V (after Fredrickson) are associated with an abnormal carbohydrate metabolism in about four fifths of cases, together with relative insulin resistance and hyperinsulinism. Obesity is the factor most important clinically in favoring the manifestation of diabetes. If there is relative insulin resistance glucose tolerance remains normal only as long as hyperinsulinism is maintained. The clinical signs of diabetes in obese persons can largely be explained by the abnormal metabolism of fat cells.

*Howland, R. J.; and Nowell, N. W.* (Dept. of Zoology, Univ. of Hull, Hull, England): THE CONTROL OF BLOOD SUGAR IN THE LABORATORY RAT AND GOLDEN HAMSTER. *Acta Endocr.* 62:283-88, October 1969.

*Verbatim summary.* Further investigations of blood sugar

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control in the Wistar albino rat (*Rattus norvegicus*) and the golden hamster (*Mesocricetus auratus*), kept in the laboratory at 21° C. have been made. Concentrations of plasma insulin in the fasting and the glucose loaded animal were determined, and it was shown that the hamster maintains a lower plasma insulin concentration than the rat, and secretes less insulin in response to glucose loading. It is concluded that the high fasting blood sugar level and poor glucose tolerance of the hamster result from a relative lack of insulin in this animal.

*Kaess, H.; Schlierf, G.; and Von Mikulicz-Radecki, J. G.* (Dept. of Med., Univ. of Heidelberg Med. Sch., Heidelberg, West Germany): EFFECT OF INTRADUODENAL INSTILLATION OF HYDROCHLORIC ACID ON PLASMA INSULIN LEVELS OF PATIENTS WITH PORTOCAVAL SHUNTS. *Metabolism* 19:214-18, March 1970.

Rises in plasma insulin concentrations were observed in six of eight patients with portocaval shunts following the intraduodenal instillation of hydrochloric acid. Since secretin is known to be released by this procedure and since plasma insulin levels rise after the administration of secretin it is suggested that the insulin release occurring after intraduodenal acidification is mediated by endogenous secretin liberation. In normal subjects the plasma insulin response to this procedure is apparently obliterated by hepatic insulin clearance and by the dilution of hepatic vein plasma in the peripheral circulation. C.R.S.

*Kamm, D. E.; and Asher, R. R.* (Dept. of Med., Univ. of Rochester Sch. of Med., Rochester Gen. Hosp., Rochester, New York; Dept. of Med., Harvard Med. Sch., Peter Bent Brigham Hosp., and the Joslin Diabetes Foundation, Boston, Mass.): RELATION BETWEEN GLUCOSE AND AMMONIA PRODUCTION IN RENAL CORTICAL SLICES. *Amer. J. Physiol.* 218:1161-65, April 1970.

*Verbatim summary.* The relation between ammonia and glucose production was examined in renal cortical slices from rats with metabolic acidosis or alkalosis. In studies with slices from normal or adrenalectomized animals incubated with either glutamine or glutamic acid, a linear correlation between glucose and ammonia production was observed with both parameters increasing during acidosis and decreasing during alkalosis. In experiments with normal animals, the ratio of the increase in ammonia production to the increase in glucose production during acidosis was 5.22:1 with glutamine as substrate and 2.14:1 with glutamic acid as substrate. In experiments with adrenalectomized animals, these ratios were 6.0:1 and 2.96:1. These findings suggest that: (a) most of the glutamine or glutamic acid that gives rise to ammonia in renal cortex is also converted to glucose, (b) the relation between glucose and NH<sub>3</sub> production is not dependent on the presence of the adrenal gland, and (c) a large part of the increase in renal ammonia production during acidosis is metabolically linked to renal gluconeogenesis.

*Kattermann, R.; and Kobberling, J.* (Div. Gastroenterology and Metabolic Disorders and Sect. of Clin. Chem., Dept. of Med., Univ. of Göttingen, Göttingen, Germany): SERUM LIPIDS IN FIRST-DEGREE RELATIVES OF DIABETICS. *German Med. Monthly* 15:47-52, January 1970.

First degree relatives of overt maturity-onset diabetics were studied to determine the relationship between glucose and lipid metabolism in diabetic individuals with an inherited

predisposition to diabetes. Out of 728 subjects, 289 were found to be clearly lean or obese and to have definitely normal or abnormal glucose tolerance as defined by limits of the blood glucose response to a 75-gm. oral glucose tolerance test. Sixty-nine of these people were randomly grouped as follows: Group 1: lean, normal glucose tolerance; Group 2: obese, normal glucose tolerance; Group 3: lean, abnormal glucose tolerance; and Group 4: obese, abnormal glucose tolerance. Four parameters of lipid metabolism were measured in fasting blood (free fatty acids, free glycerol, triglycerides, and cholesterol) and in Group 1 were found to be no different than values in a group of normal subjects. Elevations of various parameters were found in the other groups as follows: Group 2, free glycerol and triglyceride; Group 3, all four parameters; and Group 4 all parameters except cholesterol. It was concluded that (a) despite a genetic predisposition for diabetes, lipid metabolism was normal in lean subjects with normal glucose tolerance; (b) obesity or glucose intolerance are associated with lipid abnormalities in genetic prediabetics and each of these abnormalities should be managed with early dietary restriction in hopes of delaying the onset of overt diabetes and of later arteriosclerotic complications. J.E.V.

*Lazarus, N. R.; Tanese, T.; Gutman, R.; and Recant, L.* (Depts. of Physiol. and Med., Veterans Administration Hosp. and Georgetown Univ., Washington, D.C.): SYNTHESIS AND RELEASE OF PROINSULIN AND INSULIN BY HUMAN INSULINOMA TISSUE. *J. Clin. Endocr.* 30:273-81, March 1970.

Insulinoma tissue was found to synthesize both insulin and proinsulin in vitro and to release these hormones into the incubation medium. Glucose, cyclic AMP, and theophylline, which caused the release of insulin, likewise had a similar effect on proinsulin. Trypsin treatment of an intermediate form produced material that migrated as insulin and C-peptide on polyacrylamide electrophoresis.

Before removal of the tumor and performing of in vitro studies, tolbutamide administered intravenously caused a rise of plasma insulin with the major portion of the insulin being "big insulin." The authors suggest that certain insulinomas are capable of releasing large amounts of proinsulin into the circulation. T.J.M.

*Levin, S. R.; Booker, J.; Smith, D. F.; and Grodsky, G. M.* (Metabolic Res. Unit and Dept. of Biochem. and Biophysics, Univ. of California Med. Center, San Francisco, Calif.): INHIBITION OF INSULIN SECRETION BY DIPHENYLHYDANTOIN IN THE ISOLATED PERFUSED PANCREAS. *J. Clin. Endocr.* 30:400-01, March 1970.

Diphenylhydantoin (Dilantin) is known to induce hyperglycemia after administration to man and animals. To investigate the mechanisms involved in the production of hyperglycemia by Dilantin, rat pancreases were extirpated and perfused with 75 µg./ml. of this drug. The insulin response to glucose was compared in Dilantin perfused and control organs. Dilantin completely inhibited the insulin response to glucose. The mechanism for this effect is not known. T.J.M.

*Mahler, Richard J.; and Szabo, Olga* (Sect. of Endocr., Dept. of Med., New York Med. Coll., New York, N.Y.): STUDIES OF THE MECHANISMS OF CARBOHYDRATE INTOLERANCE PRODUCED BY FASTING. *Metabolism* 19:271-79, April 1970.

Abnormal oral glucose tolerance tests were obtained in nor-

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mal dogs following a three-day fast. Reduction of elevated FFA in these dogs was achieved by administration of nicotinic acid alone or with actinomycin D as well as by tolbutamide administration. These measures failed to improve glucose tolerance in the animals despite increased availability of insulin and FFA suppression. These results suggest that the abnormal carbohydrate utilization accompanying starvation is independent of hormonal action and lipolysis and may be due to impairment of hepatic glucose removal. C.R.S.

*Pi-Sunyer, F. Xavier; Campbell, Robert G.; and Hashim, Sami, A.* (Dept. of Med., St. Luke's Hosp. Center & Inst. of Nutrition Sciences, Columbia Univ., New York, N.Y.): EXPERIMENTALLY INDUCED HYPERKETONEMIA AND INSULIN SECRETION IN THE DOG. *Metabolism* 19:263-70, April 1970.

During the infusion of varying amounts of beta-hydroxybutyrate in dogs over one hour, the serum ketones rose while serum glucose fell in response to an early rise in serum IRI. With rapid infusions of ketone prompt responses in IRI were elicited in direct ratio with the amount of ketone injected. The gradients of portal to arterial blood IRI content were 2-3 to 1 following ketone administration. A relationship between the degree of hyperketonemia, insulin response and hypoglycemia has been demonstrated in dogs. The hyperketonemia encountered during lipolytic states may provide a feedback effect mediated by insulin which inhibits further release of FFA. C.R.S.

*Plevin, S. N.; Balodimos, M. C.; and Bradley, R. F.* (Joslin Diabetes Foundation, Inc., New England Deaconess Hosp., and Dept. of Med., Harvard Med. Sch., Boston, Mass.): PERINEPHRIC ABSCESS IN DIABETIC PATIENT. *J. Urol.* 103: 539-43, May 1970.

*Verbatim summary.* Eleven cases of perinephritis or perinephric abscess have been found in diabetic patients. The rarity of this disease is evident from the low prevalence of .02 per cent in the hospitalized diabetics.

The typical patient was a diabetic woman with abdominal pain, fever and urinary tract infection. Definitive diagnosis was frequently difficult. An abdominal mass or positive renal roentgenograms helped in establishing the diagnosis.

The use of antibiotics has been associated with a decreased prevalence of perinephritis and has changed the clinical picture and the course of this infection. However, precipitation of ketoacidosis and progressive diabetic nephropathy are problems which complicate the management.

The importance of prompt diagnosis is stressed to decrease mortality rates primarily by surgical incision and drainage of the abscess.

*Reid, R. A.* (Dept. of Biology, Univ. of York, York, England): DIABETES AND CONGENITAL ABNORMALITIES. *Lancet* 1:1030-31, May 16, 1970.

Congenital abnormalities are disproportionally common in children of diabetic mothers. Since the frequency decreases when good diabetic control is maintained throughout pregnancy it is likely that a metabolic factor is responsible. Analogy may be made to the effects of high exogenous glucose content on metabolism of certain strains of yeast. High glucose levels depress aerobic respiration and in addition induce changes in

mitochondrial biogenesis which are characterized by atypical form and reduced numbers of mitochondria. If such a pattern were to be manifest in the cells of the embryo of the diabetic mother, there might be a failure of groups of cells to meet their normal spatiotemporal commitments and teratogenesis might occur. Reversion to normal blood glucose might widen the energy gap by reducing the rate of glycolysis before the mitochondrial complement is completely restored. Thus fluctuating levels of blood glucose could induce even greater risk of fetal deformity than consistently high levels. T.G.S.

*Stauffer, U. G.; Hitzig, W. H.; and Zabler, P.* (Universitäts-Kinderklinik Zurich, Theodor-Kocher-Institut der Universität Bern, and Zentrallaboratorium des Blutspendedienstes der Schweizerischen Roten Kreuzes, Zurich and Bern, Switzerland): HYPERLIPEMIA IN MALIGNANT DISEASE. *Klin. Wschr.* 48:111-16, Jan. 15, 1970.

*Verbatim summary.* In two children hyperlipemia was detected during malignant disease (in case 1 acute monocytic leukemia, in case 2 reticular lymphosarcoma starting from the omentum maius). In both cases the first hint was a milky opalescence of serum taken in the fasting state. The fractionation by paper electrophoresis and thin layer chromatography disclosed two different types of hyperlipemia resembling the hereditary disorders described by Fredrickson as type I (in case 1) and type V (in case 2). Type I is due to insufficient production of lipoprotein lipase ("clearing factor"), whereas the "mixed" type V of hyperlipemia presents with an increase of lipid fractions from both exogenous sources and endogenous production.

The combination of malignant disease with hyperlipemia has been described in very rare instances in adults, but to our knowledge never in children. A chance combination is unlikely. The possible connections are very hypothetical. Case 1 in addition was combined with paraproteinemia which is as well extremely rare in childhood.

*Thorell, Jan I.; and Persson, Bengt* (Univ. of Lund, Isotope Lab. at Malmö Gen. Hosp., & Dept. of Pediat., Karolinska Inst. at Crown Princess Lovisa's Children's Hosp., Stockholm, Sweden): TRANSIENT STIMULATION OF INSULIN RELEASE BY FRUCTOSE IN NEWBORN PIGS. *Endocrinology* 86:897-98, April 1970.

Newborn pigs responded to intravenous fructose with a rise in plasma insulin accompanied by a fall in blood glucose. The changes in immunoreactive insulin and hypoglycemia were correlated quantitatively. The results are consistent with the view that hypoglycemia occurring in transient fructose intolerance in the newborn may be provoked by insulin. C.R.S.

*Vallet, H. L.; Prasad, M.; and Goldbloom, R. B.* (Dept. of Pediat., Faculty of Med., Dalhousie Univ., Halifax, Nova Scotia, Canada): CHLORPROPAMIDE TREATMENT OF DIABETES INSIPIDUS IN CHILDREN. *Pediatrics* 45:246-53, February 1970.

In nine of ten children with diabetes insipidus, intramuscular pitressin therapy could be discontinued and polyuria controlled with chlorpropamide alone for periods as long as twelve months. Symptomatic hypoglycemia occurred in five patients. This was alleviated in each instance by reducing the dosage without seriously limiting the antidiuretic effect. R.K.K.