# ABSTRACTS

*Anderson, D. M.; and Elsley, F. W. H.* (Rowett Res. Inst., Bucksburn, Aberdeen): THE INTRAVENOUS GLUCOSE TOLERANCE TEST IN THE PIG. Quart. J. Exp. Physiol. 55:104-11, April, 1970.

*Verbatim summary.* After intravenous injection of 50 gm. glucose, the blood glucose concentration in sows declined very quickly from the high concentrations initially found. The blood glucose concentration always returned to the fasting concentration within the period eighteen to forty-five minutes after glucose injection. The rate at which the glucose was removed was a function of the total blood glucose concentration.

After the blood glucose concentration returned to the fasting concentration, the concentration continued to fall, concentrations of 5-10 mg./100 ml. being achieved regularly with no overt signs of hypoglycemia.

The time required for the blood glucose concentration to return to the fasting glucose concentration was found to be the most repeatable quantitative assessment of the test.

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*Berndt, W. O.; Miller, Michael; Kettyle, William M.; and Valtin, Heinz* (Depts. of Pharmacol. & Toxicol. & Physiol., Dartmouth Med. Sch., Hanover, N. H.): POTENTIATION OF THE ANTIDIURETIC EFFECT OF VASOPRESSIN BY CHLORPROPAMIDE. Endocrinology 86:1028-32, May 1970.

Chlorpropamide was administered intraperitoneally to rats of the Brattleboro strain with hypokalemic diabetes insipidus (DI). No effect of chlorpropamide could be observed on urine volume, osmolalities, sodium or potassium concentrations. When DI rats were pretreated with chlorpropamide two hours before the administration of a minimally effective dose of vasopressin the urine osmolality was increased, the urine volume decreased and both sodium and potassium concentrations of the urine were significantly increased when compared with control animals not given chlorpropamide. The effect of subthreshold doses of vasopressin tannate in oil was significantly enhanced by oral chlorpropamide in these animals. These studies showed that chlorpropamide has no direct antidiuretic effect on its own but is effective in potentiating the action of vasopressin in diabetes insipidus. C.R.S.

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*Brech, W. J.; Glennon, J. A.; and Gordon, E. S.* (Medizinische Klinik der Universitat Heidelberg, Heidelberg, Germany, and Dept. of Med., Univ. of Wisconsin, Madison, Wis.): INVESTIGATIONS OF KINETICS OF GLUCOSE METABOLISM. I. GLUCOSE POOL, GLUCOSE TURNOVER, AND CORI CYCLE IN NORMAL SUBJECTS. Klin. Wschr. 48:521-29, May 1, 1970.

*Verbatim summary.* The determination of glucose kinetics in vivo using the technic of a single injection of glucose-C-14 is based on a variety of assumptions the validity of which cannot totally be demonstrated. It is assumed that the body glucose is equally distributed in a single pool with one or more free interchangeable compartments, and that injected glucose mixes rapidly with the total glucose pool. Glucose kinetics are to be corrected for recycling glucose.

In the present communication glucose pool, glucose turnover and Cori cycle are described in six normal subjects and compared to results obtained from a patient with insulin-resistant diabetes mellitus. Three additional patients were investigated after two different diets, one high in fat, the other high in carbohydrates. It could be shown that the basic glucose metabolism in the overnight fasting individuum is not influenced by such dietary manipulations.

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*Brech, W. J.; Glennon, J. A.; and Gordon, E. S.* (Medizinische Klinik der Universitat Heidelberg, Heidelberg, Germany, and Dept. of Med., Univ. of Wisconsin, Madison, Wis.): INVESTIGATIONS OF KINETICS OF GLUCOSE METABOLISM. II. GLUCOSE POOL, GLUCOSE TURNOVER, AND CORI CYCLE IN OBESITY. Klin. Wschr. 48:529-36, May 1, 1970.

*Verbatim summary.* Kinetic studies of glucose metabolism were performed in eighteen obese patients. The size of the glucose pool was directly related to body weight as it was in the case in normal subjects, but significantly smaller per kilogram of body weight. However, these calculations seemed not to be valid since in obesity the proportions of the body are—due to the accumulation of fat—distorted in such a way that they cannot be compared to normal. For this reason, the lean body weight has been determined and was used as a basis for calculating the metabolic data. Then, the glucose pool was normal in obesity; the glucose turnover was, however, significantly reduced.

In obese diabetic patients glucose pool size was expanded due to an elevation of pool concentration rather than to an increased pool volume. Total glucose turnover was normal (12 gms./hr.). This suggests that the higher glucose concentration in the diabetic pool may represent a compensatory mechanism to shift a normal glucose turnover across an increased metabolic threshold.

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*Burton, Robert A.; and Raskin, Neil H.* (Dept. Neurol. Sch. of Med., Univ. of California, San Francisco, Calif.): ALIMENTARY (POSTGASTRECTOMY) HYPOGLYCEMIA. Arch. Neurol. 23:14-17, July 1970.

*Verbatim summary.* Hypoglycemia occurring one-and-one-half to three hours postprandially in a patient who has undergone a gastrectomy is probably alimentary in type. It previously has been unclear whether recurrent seizures may be the manifestation of this disorder. Two patients are presented with episodic neurologic dysfunction, which included convulsions, whose underlying disorder proved to be alimentary hypoglycemia. The neurological disturbance ceased in each case upon the institution of a high-protein, low-carbohydrate diet.

The patient who has undergone gastrectomy may be vulnerable to episodic neurologic syndromes, which are sometimes bizarre in character. Appropriate glucose tolerance testing may establish a diagnosis. Dietary treatment is generally effective.

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*Cohen, Margo P.; and Foglia, Virgilio G.* (Inst. of Physiol. Univ. of Buenos Aires, Buenos Aires, Argentina): EFFECT OF PANCREATECTOMY, HYPOPHYSECTOMY, AND HYPOPHYSECTOMY-PANCREATECTOMY ON SULFATE UPTAKE IN RAT AORTAS. Proc. Soc. Exp. Biol. Med. *133*:1275-78, April 1970.

*Verbatim summary.* The effect of partial pancreatectomy, hypophysectomy, and hypophysectomy plus pancreatectomy on the incorporation of S-35 sulfate into the aortic mucoplysaccharides of rats was studied. There was a marked peak in sulfate-35 uptake four hours after the injection of the label in pancreatectomized and in hypophysectomized animals, and the appearance of this peak preceded the development of hyperglycemia in the pancreatectomized animals. In hypophysectomized-pancreatectomized animals, this peak was abolished. The findings suggest that insulin has an important role in vivo in the regulation of sulfate metabolism in vascular connective tissue. The results are discussed in relation to a possible interraction between growth hormone and insulin in the regulation of sulfate uptake and incorporation.

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*Dietschy, John M.; and Wilson, Jean D.* (Dept. of Intern. Med., Univ. of Texas, Southwestern Med. Sch., 5323 Harry Hines Boulevard, Dallas, Tex. 75235): REGULATION OF CHOLESTEROL METABOLISM (FIRST OF THREE PARTS). New England J. Med. *282*:1128-38, May 14, 1970.

A three part summary on current concepts of the physiologic regulation of cholesterol absorption, synthesis and degradation in the intact animal is presented. Emphasis is placed upon the regulatory mechanism and their interaction.

Discussed in the first part are historical explanations of cholesterol turnover in the two-exchange pool model and a proposed three-pool model; the latter model providing a convenient frame work for examination of interlocking feedback systems controlling cholesterol metabolism.

Synthesis and absorption of cholesterol is discussed in detail. Studies of cholesterogenesis in various tissues of lower animals and man as measured under in vitro conditions indicate marked variations exist in relative rates at which tissue slices from different organs incorporate acetate into sterols. In adult animals the liver and gastro-intestinal tract have the highest rates of synthesis per unit weight of tissue. Sterol synthesis occurs at much lower rates in other tissues.

Three physiologic variables are considered to be regulating mechanisms in control of cholesterogenesis in tissues; the amount of cholesterol in the diet; caloric intake of the animal; and the functioning integrity of the enterohepatic circulation of bile acids. B.R.B.

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*Dietschy, John M.; and Wilson, Jean D.* (Dept. of Intern. Med., Univ. of Texas, Southwestern Med. Sch. 5323 Harry Hines Boulevard, Dallas, Tex. 75235): REGULATION OF CHOLESTEROL METABOLISM (SECOND OF THREE PARTS). New England J. Med. *282*:1179-83, May 21, 1970.

The second part of the series on regulation of cholesterol metabolism is concerned with mechanisms of cholesterol absorption especially with quantitation in the intact animal.

Although evidence indicates cholesterol input into the circulation is derived from exogenous absorption and endogenous synthesis principally in the liver and gastrointestinal tract, the complete role of these various components in the intact animal remains to be resolved. B.R.B.

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*Dietschy, John M.; and Wilson, Jean D.* (Dept. of Intern Med., Univ. of Texas, Southwestern Med. Sch., 5323 Harry Hines Boulevard, Dallas, Tex. 75235): REGULATION OF CHOLESTEROL METABOLISM (THIRD OF THREE PARTS). New England J. Med. *282*:1241-49, May 28, 1970.

Neutral sterol output, bile acid output, enterohepatic circulation of bile acids, control of bile acid production and bile acid-bile acid feedback are reviewed in the last article on cholesterol metabolism regulation.

Four approaches used to assess over-all cholesterol balance and turnover in the intact animal were discussed and limitations existing in each technique presented. The techniques involved were chemical balance method; isotope balance methods; estimations based on analysis of radioactive cholesterol die-away curves in serum; and various combinations of these methods.

Current concepts in the over-all regulation of cholesterol metabolism are summarized and presented schematically.

Six areas of cholesterol metabolism are suggested as needing further exploration. These areas are feedback control mechanisms, defining the degree of feedback control in the liver; need for the identification of the rate limiting factors of cholesterol absorption in man; identification of the biosynthetic sources of circulating cholesterol; investigation of the origin and mechanisms of fecal neutral sterol secretions and studying factors controlling bile acid formation. B.R.B.

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*Feigin, Ralph D.; and Haymond, Morey W.* (Div. of Infectious Diseases, Dept. of Pediat., Washington Univ. Sch. of Med., St. Louis Children's Hosp., St. Louis, Mo.): CIRCADIAN PERIODICITY OF BLOOD AMINO ACIDS IN THE NEONATE. Pediatrics *45*:782-91, May 1970.

Circadian variation of blood amino acids is well established in the adult. In the present study a similar pattern was sought in forty-six full term infants ranging in age from one to 120 hours. Blood samples were obtained every four hours for one day. Total amino acid concentrations were highest between 1200 and 2000 hours and lowest at 0400 hours. Rhythmicity was observed as early as the first day of life. Individual amino acids varied with total levels to some extent but exceptions were not uncommon. The pattern of circadian rhythm was similar to that observed in adults except that the rise in levels between 0400 and 0800 hours was more brisk in the neonate. Possible biologic determinants for this rhythmicity are discussed, but specific factors have yet to be defined. Practical applications of this method for early detection of subclinical infection and screening for inborn errors of amino acid metabolism are discussed also. R.K.K.

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*Garnett, Jacqueline; Garnett, E. S.; Mardell, R. J.; and Barnard, D. L.* (Dept. of Nuclear Med., McMaster Univ., Hamilton, Canada): URINARY CALCIUM EXCRETION DURING KETOACIDOSIS OF PROLONGED TOTAL STARVATION. Metabolism *19*:502-08, July 1970.

Obese patients subjected to starvation for periods of up to fourteen weeks were found to excrete large amounts of calcium with the mean daily calcium excretion reaching levels of 560 mg. The calciuria was regarded as derived from the

labile bone pool. The calcium loss was of no significance in combatting metabolic acidosis in the ketotic fasting patient. C.R.S.

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*Like, Arthur A.* (Elliot P. Joslin Res. Lab. Dept. of Path. Harvard Med. Sch., Peter Bent Brigham Hosp. and the Joslin Diabetes Foundation, Boston, Mass.): THE UPTAKE OF EXOGENOUS PEROXIDASE BY THE BETA CELLS OF THE ISLETS OF LANGERHANS. Amer. J. Path. 59:225-46, May 1970.

The coated and smooth vesicles and smooth tubules of Golgi origin which are visible intracellularly under the electron microscope are assumed to have the capacity to transport protein. These organelles may transport insulin to the beta cell surface for secretion, bypassing the storage form in the beta granule.

It was postulated that intracellular transport of insulin toward the cell surface might create a directional gradient preventing absorption of proteins by the cellular vesicles and tubules and that demonstration of a failure of cells to absorb protein would provide evidence to support the hypothesis.

Horseradish peroxidase, an enzyme with a molecular weight of about 40,000, was injected into rats to serve as an ultrastructural protein marker with the use of electron microscopy. Both normal and hyperglycemic (diabetic) animals were studied. Staining of capillary lumens was seen forty seconds after injection and maximum staining in the extracellular space was seen after fifteen to thirty minutes. Peroxidase staining was not detected in the beta-granule-containing sacs close to the cell membrane and was only slowly taken up by vesicles and tubules.

It was concluded that beta cells which are actively secreting insulin in response to sustained hyperglycemia are not primarily absorptive cells and that the numerous vesicular and tubular profiles may be responsible for insulin secretion under these conditions. J.E.V.

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*Manchester, K. L.* (Dept. of Bioch., Univ. Coll. London, London, England): THE CONTROL BY INSULIN OF AMINO ACID ACCUMULATION IN MUSCLE. Biochem. J. 117:457-65, April 1970.

This work extends the list of amino acids whose uptake by isolated muscle is enhanced by insulin. Additional amino acids previously not verified as affected by insulin were B-alanine and y-aminobutyric acid. The original intent of this work was to find an alternative explanation of why uptake of several amino acids appeared after insulin only in the presence of puromycin, though not in its absence. To avoid complications associated with puromycin, cyclohexamide was used.

The authors found that the above phenomenon did not require an explanation, since amino acids stated to be unaffected by insulin in the absence of an inhibitor of protein synthesis, showed a response to insulin without the inhibitor. The quantitative response to insulin also did not change significantly when an inhibitor (cyclohexamide) was used. For those who wish to obtain an up-to-date list of those amino acids whose transport is altered by insulin (with ample references included), tables appearing in the article are more than sufficient. T.J.M.

*Miller, Myron; and Moses, Arnold M.* (Veterans Administration Hosp., & Dept. of Med., State Univ. of New York, Upstate Med. Center, Syracuse, N.Y.): POTENTIATION OF VASOPRESSIN ACTION BY CHLORPROPAMIDE IN VIVO. Endocrinology 86:1024-27, May 1970.

The antidiuretic activity of chlorpropamide was studied using Brattleboro rats homozygous for hereditary hypokalemic diabetes insipidus (DI). An absence of antidiuretic effect was observed in these animals as well as in normal rats and those heterozygous for DI. When the homozygous DI rats were treated with chlorpropamide the antidiuretic effect of small doses of vasopressin was found to be significantly enhanced when compared to the effect of vasopressin injected into rats not pretreated with chlorpropamide. Potentiation of the effect of small amounts of endogenous vasopressin appeared to be the mechanism of chlorpropamide effect upon DI. In the presence of large amounts of vasopressin, the potentiating effects of chlorpropamide cannot be distinguished. The drug does not appear to have a direct effect on the renal tubular concentrating mechanism and is inactive in the absence of vasopressin. An increase in urinary sodium excretion was observed with large doses of chlorpropamide. C.R.S.

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*Ozawa, Hitoshi* (Dept. of Biochem., Coll. of Physicians and Surgeons, Columbia Univ., New York, N.Y.): REACTION OF INSULIN WITH ETHYL GLYCINATE AND 1-ETHYL-3-(3-DIMETHYLAMINOPROPYL) CARBODIIMIDE. Biochemistry 9:2158-63, May 12, 1970.

This study demonstrates that all the carboxyl groups of insulin can be made to react with ethyl glycinate and a water-soluble carbodiimide under appropriate conditions. The reactivities of all the groups do not appear the same, however, and some specificity can be introduced at high pH and shorter reaction times. The most reactive groups appear to be one or both of the glutamic acid residues in the B chain. D.R.C.

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*Sando, H.; Kanazawa, Y.; and Kuzuya, T.* (Third Dept. of Intern. Med., Faculty of Med., Univ. of Tokyo, Tokyo, Japan): EFFECT OF BONITO INSULIN ON ENDOGENOUS INSULIN SECRETION IN DOGS. Amer. J. Physiol. 218:1357-62, May 1970.

A number of in vivo and in vitro experiments have been conducted to determine whether insulin secretion from the pancreas is influenced by the blood insulin level. With use of a guinea pig antisera against bonito or pork insulin, insulin mixtures could be assayed differentially. Intravenous infusion of bonito insulin (0.5-3mμ/kg./min.) produced a significant fall in dog insulin concentration in the pancreatic vein, but this was associated wth a parallel, consistent fall of the arterial glucose concentration. When the fall in glucose was prevented by the infusion of glucose, bonito insulin had no effect upon dog insulin concentration in the pancreatic vein. The interested reader might refer to an older work by Best and Haist (J. Physiol., London, 1961). In the latter, long term therapy with protamine zinc insulin reduced the insulin content of the pancreas. Is there a chronic effect of insulin upon insulin secretion, or is this also mediated by a chronically lower blood sugar? T.J.M.

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