Statement on Treatment of Diabetes

The Thirtieth Annual Meeting of the American Diabetes Association, held in St. Louis, ended on June 14. At the last scientific session on that date, several investigators reported results of studies on the long-term treatment of diabetes. Three papers were presented from the United States, two of which were reports from the University Group Diabetes Program (UGDP), which has received widespread publicity in the public press recently. There were also extensive discussions of studies conducted in England and Sweden. After these presentations, there was considerable discussion.

At a press conference that followed the scientific session, a statement giving the Association's position was read by Dr. Robert C. Hardin, retiring President. The statement to the press is reprinted in full below:

"The American Diabetes Association commends those persons who have reported studies concerning the effects of therapy on the course of diabetes and its complications at this Annual Meeting.

"New data have been presented, some of which raise questions about the efficacy and safety of oral therapy. However, it is difficult to generalize from these unpublished data. Careful evaluation of the complete data and further study will be necessary to reach final conclusions.

"At this point, the evidence does not appear to warrant abandoning the presently accepted methods of treatment of diabetes—diet, diet with oral agents, or diet and insulin as indicated."

"Status of Problem of Usage of Tolbutamide: Preliminary Statements" appeared on pages 467-68 of the June 1970 issue of this Journal. It included the statement of the Food and Drug Administration of May 22 and that of the Chairman of the University Group Diabetes Program (UGDP) of May 21.

BOOK REVIEWS

CLINICAL ENDOCRINOLOGY, *R. Hall, B.Sc., M.D., M.R.C.P., J. Anderson, M.B., B.S., M.R.C.P., and G. A. Smart, B.Sc., M.D., F.R.C.P., $15.00, 418 pages, Philadelphia, J. B. Lippincott Co., 1969.*

This book is aimed at senior medical students and postgraduate students working for a higher examination in medicine and surgery. The authors have retained the conventional arrangement dealing with each gland and have included chapters dealing with pregnancy, obesity, disorders of growth, and hormonal syndromes associated with neoplasms not derived from endocrine glands. They have avoided the use of frequent references, listing a few key articles and reviews at the end of each chapter.

The book summarizes a wide area of knowledge and the authors have attempted to keep up to date. Many of the references quoted were published in 1968. A short section on calcitonin and its possible use in man is included, as are sections on the Alexander-Harden regime for distinguishing drug-responsive from relapse-prone thyrotoxic patients treated with antithyroid drugs, and on the effects of oral contraceptives on fat and carbohydrate metabolism.

In condensing this large subject into a small text and aiming for a wide audience, the authors ran the risk of undocumented statements. The serious student will occasionally be frustrated by these. For example, in table 5.11 on page 90 the distinction is made that atrial fibrillation is a general sign of hyperthyroidism and that cutaneous vasodilatation and a systolic murmur due to increased blood flow are especially common in the elderly. The authors insert many tables, some of which are unnecessary. For example, the information in table 15.4, page 286 that lists the dosage of insulin used in diabetic acidosis could easily be described in the text.

The section on the parathyroids is good, but others are uneven. The bibliography is generally adequately selected and, as might be expected, has many British references. The authors should give the title of each reference to help the reader who wishes to pursue a subject.

The book is printed well, has the advantage of uniformity of style, and is easy to read. It is recommended for the student of nursing or pharmacy who wishes a review of this rapidly growing field and who does not have the time or desire to study a more complete text.

DUNCAN'S DISEASES OF METABOLISM. Vol. I: Genetics and Metabolism. Vol. II: Endocrinology and Nutrition. *Sixth Edition. Philip K. Bondy, M.D., (Ed.); $39.00, 1413 pages, 594 illustrations. Philadelphia, W. B. Saunders Co., 1969.*

The extensive revision and reorganization by Bondy and

his associates for the sixth edition has produced a most useful review of metabolic disease. "Metabolic disease" is an expanding term, since, as the editor points out, almost all disease is a result of disordered metabolism. In the selection of topics, however, those mentioned in the subtitles of the two volumes indicate conventional choices.

Chapters summarizing biochemical aspects of the various subjects, written by specialists in their fields, are appropriately placed. For example, a chapter on intermediary metabolism precedes that reviewing disorders of carbohydrate metabolism. After a brief summary of certain aspects of intermediary metabolism, Bondy discusses the physiology of insulin, glucagon and other hormones influencing carbohydrate metabolism. He then goes on to describe the clinical aspects of disordered carbohydrate metabolism. Among the various topics are normal values for the plasma glucose determined by automated equipment, uncertainties about the inheritance of diabetes and the pros and cons of strict regulation of the blood sugar. In reviewing these subjects, as in the sections on the management of diabetes, the complications, treatment of ketoacidosis and the oral agents, the author's approach is balanced and logical.

The chapter on Disorders of Carbohydrate Metabolism goes on to discuss hypoglycemia and its causes, including the various types of glycogen storage disease. Other chapters are equally or even more comprehensive. Recent Developments, a section which follows the index in each volume, permits the authors to bring their chapters up to date at each printing.

The book is made up of a series of authoritative monographs, in most instances lucid and thorough, each followed by an extensive bibliography. It will be of great value in undergraduate and graduate training in the field of metabolism and endocrinology, and a most useful addition to the library of the clinician or investigator in this area.

ABSTRACTS

Andreani, Domenico; Cinotti, Giulio Alberto; and Stirati, Giovanni (Faculty of Med., Catholic Univ., and Second Med. Clin.; Univ. of Rome, Rome, Italy): CHLORPROPAMIDE IN IDIOPATHIC DIABETES INSIPIDUS. Metabolism *18*:874-77, October 1969.

Chlorpropamide administered in doses of 250 to 500 mg. daily was effective in reducing the urine output to normal in four patients with idiopathic diabetes insipidus. Hydrochlorthiazide and ethacrynic acid were less effective than chlorpropamide. During treatment with this agent, concentrating capacity of the kidney was regained, water clearance reached negative values and water loading did not result in the production of a normally diluted urine. The administration of sodium chloride to 10 mg. daily did not increase the diuresis. In one patient hypoglycemic episodes occurred on 500 mg. daily which disappeared when the dose was decreased to 250 mg. It has been concluded that chlorpropamide acts as an ADH-like substance. C.R.S.

Beckmann, Rüdiger (Biochemische Abteilung der Chemie Grünenthal GmbH, Stolberg/Rheinland): ABSORPTION, DISTRIBUTION IN THE ORGANISM AND ELIMINATION OF METFORMIN. Diabetologia *5*:318-24, 1969.

Verbatim summary. Twenty-four hours after oral administration of metformin-C-14 to mice (100 mg./kg.), an average of 72.2 per cent of the administered activity was recovered in the urine and 8.4 per cent in the feces. Under the same test conditions the rat eliminated 66.8 per cent of the administered dose in the urine and 18.4 per cent with the feces. Less than 1 per cent of the radioactivity was found in the bile. Unchanged metformin was the only radioactive substance which appeared in the urine of rats and mice. The investigation comparing the distributions of buformin-C-14 and of metformin-C-14 in the body organs gave a similar picture for both biguanides. The highest biguanide concentrations were found in the kidneys, adrenals, pancreas and liver. Serum concentrations amounted to an average of 1.2 μg./ml. after oral administration of 50 mg. buformin-C-14/kg. and 6.2 μg./ml. after 150 mg. metformin-C-14/kg. Healthy human volunteers eliminated an average of 63 per cent of the administered dose in the urine within thirty-six hours. Metformin was not metabolized by the human being. From the rate of elimination in the urine, the biological half-life of the biguanide was found to be 2.8 hours. Compared with other biguanides the weak hypoglycemic activity of metformin in both animals and diabetics cannot be explained by low absorption. It is due to the weak intrinsic activity of this biguanide as such.

Bennett, Leslie L.; Curry, Donald L.; and Grodsky, Gerold M. (Dept. of Physiol., The Metabolic Res. Unit, and Dept. of Biochem., Univ. of California Med. Center, San Francisco, Calif.): CALCIUM-MAGNESIUM ANTAGONISM IN INSULIN SECRETION BY THE PERFUSED RAT PANCREAS. Endocrinology *85*:594-96, September 1969.

Isolated rat pancreas perfused with a detran-electrolyte medium will consistently release insulin following a glucose pulse if the perfusing medium contains calcium (Ca) at 2.5 mEq./L. The secretory stimulation is attenuated if magnesium (Mg) is added to a concentration of 2.5 mEq./L. and abolished at a magnesium concentration of 5.0 mEq./L. Insulin secretion resumes if calcium concentration is also increased to 5 mEq./L. but is abolished again if magnesium is raised further to 15 mEq./L. These observations support the view that magnesium and calcium compete for the same active site on the cell or granule membrane and that the facilitating effect of calcium upon secretion is blocked by magnesium. C.R.S.

Chazan, Bernard I.; Kuwabara, Toichiro; Balodimos, Marios C.; and Beetham, William P. (The Elliott P. Joslin Res. Lab., Dept. of Med., Harvard Med. Sch., the Joslin Clinic, the New Eng. Deaconess Hosp., the Diabetes Found., and the Howe Lab. of Ophthalmic Path., Massachusetts Eye and Ear Infirmary, Boston, Mass.): THE REACTIVITY AND ULTRASTRUCTURE OF CONJUNCTIVAL MICROANEURYSMS IN DIABETES. Presented