

ion. Dr. Papaspyros is a very unusual person combining an unquenchable interest in clinical diabetes simultaneously with a great appreciation for the history of medicine. This volume demonstrates clearly that he has that unusual combination of discipline that allows him more than a single field of knowledge. He demonstrates most clearly what Wilder Penfield has called a Second Career.

The amount of labor and endless search that has gone into this publication can be appreciated only by one who has undertaken a similar endeavor. This edition brings up to date many of the interesting historical items concerning the development of some of the newer agents in the treatment of diabetes.

The format, paper stock and printing are of very first class but despite these admirable qualities this reviewer would be derelict in his responsibility if he did not point out that there are far too many spelling errors and this volume deserves a much more critical editing. It will be used for a long time as an excellent reference book by medical students, physicians, and other interested individuals and it can be recommended most highly for this reason.

MANUAL OF CLINICAL NUTRITION. By Robert S. Goodbart and Michael G. Wohl. \$5.50, 279 pp., Lea & Febiger, 1964.

The authors of this manual are two well-known people in the field of clinical nutrition. Any manual jointly authored by these physicians should command attention and respect as being an authoritative discussion of the subject. The authors point out in the preface that this is not a textbook on nutrition, but a manual designed to supplement the use of the expensive, detailed texts available.

The book is divided into two sections, the first of which is the estimation of nutritional status; the second is a discussion of nutrition in disease with special references to the principles of therapeutic dietetics.

In the first section on the estimation of nutritional status, the authors present a detailed compendium of the laboratory values of normal ranges for the concentrations of many of the nutrients and metabolic endproducts found in the circulating blood and in the urine. These tables of normal values will be of inestimable value to the physician as a daily reference.

The second part of the book, that is, the nutrition in disease, may be subject to some criticism. This is a matter of personal bias of this reader and his disagreement with the authors. However, this is not characteristic of this manual, but is characteristic of the field in general. The authors were extremely brave to undertake a pragmatic statement of many of the situations which are still somewhat subject to further elucidation. I find, however, that the authors' pragmatism is probably one of the major virtues of the book, much as I may disagree with some of the statements in detail. The general practitioner and the medical student should not be concerned with the theoretical disputes and problems in this general field. He should have available to him a definitive set of recommendations which have proven of value empirically, regardless of the theoretical background and origin. The authors have succeeded admirably in establishing this type of criteria. This book will serve as a desk reference for the general practitioner. To the medical student, it will undoubtedly

be used in the time prior to examination when he is attempting to fill the receptacles of his mind with specific, positive data.

NUTRITION IN HEALTH AND DISEASE. By Cooper, L. F., Barber, E. M., Mitchell, H. S., Rynbergen, H. J., and Greene, J. C. \$7.00, 615 pp., including 60 pages of tables, 14th Edition, 1963.

This volume is designed for use by dietitians, nutritionists, and instructors of nurses. It is deliberately not prepared for physicians or investigators. The book has long been considered a valuable and standard work in its field. This new fourteenth edition has been carefully brought up to date in many details. A fifth author has joined the group.

The data on food composition make use of the recently revised Agriculture Handbook No. 8, 1963. Points of view and emphases are comparably contemporary.

The typography, ninety-nine illustrations and arrangement of material are all acceptable and attractive. A glossary and numerous menus and recipes add to the utility of the work.

The volume can be recommended heartily for nurses and dietitians to use and for their training.

PROGRESS IN DIABETES RESEARCH, Proceedings of the First Symposium of the German Diabetes Committee (in German). Edited by Prof. K. Oberdisse and Prof. K. Jabnke. Georg Thieme Verlag, Stuttgart, West Germany, 1963. 176 pp.

In October 1962, the first symposium on diabetes took place in Düsseldorf, Germany, arranged by the German Diabetes Committee. There is no German Diabetes Association; this Committee is a subdivision of the German Society for Internal Medicine. Attendance was limited to fifty-three invited guests, mainly from Germany, but also from Switzerland (3), Belgium (1), England (1) and United States (1). The proceedings contain an abbreviated version of each of the invited papers, followed by a bibliography and discussion. Two papers are in English, and twenty-five are in German. This limits its usefulness for potentially interested non-German readers. The special topics discussed were: (1) Insulin in blood (eleven papers); (2) methods for determination of glucose in blood and urine (five papers); (3) organization of a diabetic outpatient department; (4) histology of the islets of Langerhans (six papers); and lastly, prediabetes and early detection of diabetes (four papers).

1. *Insulin in blood*

Renold and Steinke (Boston) present a summary of their work concerning measurement of serum insulin-like activity (ILA) employing the rat adipose tissue assay. Their data obtained with sera from early untreated and genetically selected prediabetic patients strongly suggests that in the early phase of diabetes a stage of relative, rather than absolute insulin deficiency exists. To explore the differential effectiveness of endogenous insulin on rat diaphragm and on rat adipose tissue, the authors present new data obtained in their laboratory by Rafaelsen who injected test doses of labeled glucose, with and without insulin intraperitoneally, and measured glucose incorporation into glycogen in diaphragm, heart, liver, epididymal and subscapular fat. Vallance-Owen (Newcastle-upon-Tyne) reviews insulin antagonists in general and the synalbumin factor in particular. Presence of this factor in the hereditary type of diabetes, but its absence

in hemochromatosis and diabetes associated with pancreatitis, suggest to him that the primary abnormality in essential diabetes is increased antagonism to insulin. Studies in relatives of patients with clinical diabetes support a dominant mode of inheritance of this factor. Pfeiffer (Frankfurt) reviews his work on the dynamics of insulin secretion, employing the fat pad assay for measurement of ILA. The stimulatory effect of glucose and tolbutamide on serum ILA was studied in the portal blood of dogs and in the peripheral blood of human subjects. The normal dog pancreas responds promptly by releasing insulin under glucose stimulus. There is a definite glucose dose insulin secretion relationship. Tolbutamide induces a response almost as marked as does glucose, however, the effect is not dose dependent. Whereas the normal human subject shows an increase in peripheral serum ILA most marked after glucose and less after tolbutamide, the maturity onset diabetic patient fails to respond to glucose, but shows elevated levels of serum ILA after tolbutamide. Of therapeutic importance is the observation that the diabetic patient has a prolonged refractory period following administration of tolbutamide which is absent in the normal subject. Froesch (Zurich) discusses his findings with assay of serum insulin by the rat adipose tissue assay measuring simultaneously glucose uptake and net gas production produced by serum alone and with added anti-insulin serum. He concludes that there are two forms of serum insulin-like activity, one suppressible by insulin antibody and one nonsuppressible. Values for suppressible ILA fall within the range reported by Yalow and Berson employing their immunoassay and represent approximately 7 per cent of total ILA. In alloxan diabetic rats both the suppressible and the nonsuppressible ILA disappear. The nonsuppressible ILA is probably not related to the insulin complex described by Antoniades, as Froesch's fraction does not change following glucose administration, whereas the insulin complex of Antoniades decreases, but both workers agree that the "free" or the "suppressible" ILA rises after glucose administration. Ditschuneit (Frankfurt) reports on serum ILA of prediabetes patients. He found elevated fasted levels and a decreased response to intravenous administered glucose, as did Renold and Steinke. Zone electrophoretic fractionation of serum collected fasting and thirty minutes following oral glucose loading revealed a shift of the majority of ILA from the beta globulin region to the alpha₁ globulin-albumin fraction. No such shift was seen in serum from prediabetics. Daweke and Bach (Düsseldorf) discuss three patients with insulin resistance and their treatment with intravenous crystalline zinc insulin in small doses. Adipose tissue obtained from one patient was studied *in vitro*—it showed less response to added crystalline insulin than did tissue obtained from control subjects. Hasselblatt (Göttingen) presents data on activation of serum insulin by *in vitro* addition of tolbutamide. These interesting observations have recently been published in *Metabolism*. Weinges (Hamburg) measured serum ILA by the fat pad assay in humans after glucagon administration. He detected a consistent increase thirty minutes following the injection. Kerp, Creutzfeld and Steinsilber (Freiburg) could not verify Hasselblatt's findings when they examined the effect of tolbutamide on insulin bound to insulin antibodies employing ultracentrifugal separation. On the other hand, Otto and Körner (Münster) support Hasselblatt's finding.

2. *Methods for determination of glucose in blood and urine*

Schmidt (Mannheim) compares the glucose oxidase with the hexokinase method for measurement of blood glucose. With the oxidase method 2-deoxy-D-glucose may interfere. In urine the hexokinase method appears superior to the glucose method due to presence of urinary chromogens. Haussler (Frankfurt) discusses the AutoAnalyzer and presents a modification by which the number of samples per hour can be increased from forty to sixty. Fuhr (Hamburg), Maibauer (Berlin) and Jahnke (Düsseldorf) discuss available methods for glucose determination and the advantages of the AutoAnalyzer.

3. *Organization of a diabetic outpatient department*

Under the chairmanship of Constam (Zurich), this vivid discussion centered on not so much what could be accomplished by such a department but rather if one should be established at all. Constam himself, Mehnert, Steigerwaldt and Reinwein spoke in favor of an outpatient department specializing in diabetes where careful group instruction can take place, the clinical laboratory can be employed to its full extent, clinical research, especially with regard to new drugs can be easily carried out on a large number of patients and consultation with other services is available. They also expressed their opinion that such a clinic seldom takes patients away from the family doctor, as the majority of patients are actually referred by their family physician who realizes he has not the time for careful instruction and evaluation and/or may have had insufficient training to cope with a difficult diabetic patient. The speakers opposed to such a view cited in their favor that most diabetic patients are easy to handle as office patients and do not need elaborate work-ups, that the care given to patients in a diabetic clinic varies and lacks continuity as the medical house staff changes, and also that the patients are not treated and respected as individuals but rather as cases. Finally, quite a few patients resent attending such a clinic since it becomes generally known they are suffering from diabetes.

4. *Histology of the islets of Langerhans*

This chapter is considered by the reviewer to be very valuable as it summarizes the present status of histology and histochemistry in diabetes and contains information previously available only in scattered reports. A detailed summary is not given, as in summer of 1963 an international symposium on pancreatic islets took place in Sweden, the proceedings of which will be published in English soon.

Ferner (Heidelberg) and Seifert (Münster) review our new concepts on ultrastructure. Gepts (Brussels) presents data collected in Boston and Philadelphia from twenty-two cases of juvenile diabetics who died within six months of onset. Compared to juvenile patients of longstanding diabetes whose pancreas shows absence of beta cells, the pancreases in his group showed markedly decreased numbers of islets although the beta cells are characterized by stigmata of maximal secretory hyperfunction. Bander (Frankfurt) comments that in human pancreas mitosis of beta cells has not been observed. However, in rat islets mitosis takes place following administration of tolbutamide. Goessner (Tübingen) presents a comprehensive review of enzyme histochemistry in the islet cells with special reference for the presence of acid phosphatase, glucose-6-phosphatase, adenosintriphosphatase, glucose-6-P-dehydrogenase and glycerol-P-dehydrogenase.

5. *Prediabetes and early detection of diabetes*

There was no standard definition for prediabetes. Clinical criteria rather than genetic ones were selected, for example, women with a history of repeated abortions and/or large babies, etc. Unfortunately Dr. Hoet could not attend this session. Westwerdt (Hamburg) discusses it from the obstetrical point of view. Oberdisse (Düsseldorf) reports his experience with the cortisone glucose tolerance test in women with a history consistent with prediabetes. Otto and Mauren (Münster) measured pulse waves in young diabetic patients and in normal children and found no difference. Therefore, they doubt if this method will have any value in detection of prediabetic patients. Jahnke reports on glucose tolerance test alone and with steroid preparation and on the sodium tolbutamide test in patients over forty years of age. Of seventy-three unselected patients examined by all three tests, glucose tolerance test was abnormal in half, cortisone-glucose tolerance test abnormal in one third, tolbutamide test abnormal in 10 per cent.

In summary, although much of the material presented has been published elsewhere or is in press, it represents a good synopsis of the fast-moving subject of diabetes research.

DIE ZUCKERKRANKHEIT. By F. Bertram and H. Otto. (In German.) \$7.40, 164 pp. Georg Thieme Verlag, Stuttgart, West Germany, 1963.

Like Joslin, the German diabetologist Bertram published, during his lifetime, a "manual" for diabetic patients (eleven editions) and a textbook on diabetes (four editions). Professor Bertram died in 1960. A former associate, H. Otto, has taken on the task of continuing this tradition and has been responsible for the fifth edition of the textbook. As the fourth edition was issued in 1947, important changes have been made, most of them by Bertram. This volume contains chapters on: physiology and experimental diabetes (twenty five pages); pathology (three pages); classification, symptomatology and complications of diabetes (fifty pages), and treatment (seventy pages). There are several excellent colorplates illustrating diabetic retinopathy and necrobiosis. The bibliography consists of 110 titles, of which one is of 1963, one of 1962, and less than ten are of 1961. There is a good subject index.

This book is primarily intended for the German-speaking physician interested in handling diabetic patients. Therefore, its main emphasis lies on clinical aspects and treatment of diabetes drawing from a large personal experience and the literature. This practical orientation probably explains why in the section on physiology there is no mention of assays of insulin in blood, results of which have deepened our understanding of diabetes as well as of the mechanism of action of certain oral hypoglycemic agents. In discussing experimental diabetes in the animal world, it is erroneously stated that

there exists no spontaneous or hereditary diabetes. The chapter on pathology is meager and does not mention any results obtained with electronmicroscopy. The discussion of factors responsible for diabetes centers of course on heredity, obesity, pregnancy, infection, etc., but there is also a discussion on the diabetogenic effects of nicotine, alcohol, ingestion of canned food, etc., under the heading of harmful effects of civilization. For diagnosis of diabetes by oral glucose tolerance test, it is suggested that not the full glucose load of 100 gm. be given but rather 1 gm. of glucose per kilogram of body weight. Unfortunately, no data are presented comparing both doses. Furthermore, it is urged that capillary rather than venous blood glucose be measured during a glucose tolerance test, possibly a misprint. For assessment of diabetic ketoacidosis no mention is made of the easy serum acetone test.

The treatment of diabetes is presented in detail, discussing diet, the various types of insulin and oral agents such as tolbutamide and phenformin. (Chlorpropamide is not commercially available in Germany.) It is urged that the diet be low in fat, never exceeding 70 gm. and to make up calories by carbohydrates, up to 400 gm. if necessary. No data are shown to support the beneficial effect of such a diet on prevention or delay of late complications. There is an intriguing statement alleging lack of late complications in patients with severe brittle diabetes, and again no follow-up studies are presented. For diabetic patients on insulin, the following are the suggested guidelines for blood glucose values: fasting under 180 mg. per 100 ml., following meals not above 250 mg. per 100 ml., and the total twenty-four-hour urinary glucose excretion not to exceed 20 to 30 gm. This seems to be dictated by fear of insulin reactions. Patients on dietary regimen alone or diet with oral agents should be regulated in such a way as to have close to normal blood glucose values.

To initiate a diabetic on insulin, the following rule of thumb is suggested: one unit of insulin for each 2 gm. of urinary glucose. The over-all mortality rate for diabetic acidotic coma is given as 10 to 15 per cent. There is much worry about the psychic well-being of diabetic patients. In this vein, patients are not encouraged to test their urine for sugar or acetone so they are not reminded of their diabetic condition. But aren't they reminded when taking insulin or following a diet?

The above comments are presented to point out certain points of controversy, here as well as abroad, and to challenge our thoughts. In most aspects of management of diabetic patients, the authors are following established principles and their results appear not to be strikingly different.

This book is clinically oriented and contains much practical information for the physician interested in clinical diabetes. It offers no outstanding features attractive to the reader familiar with the available American texts on diabetes.