BOOK REVIEWS

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CLINICAL HEMATOLOGY, 5th ed. *Maxwell M. Wintrobe*, Philadelphia, Lea & Febiger, 1186 pp., $18.50.

The appearance of another edition (this time the fifth) of Wintrobe's well-known text on *Clinical Hematology* must be considered an event. This one, encased as it is in sturdy, blood red covers; in a much larger and very much heavier (6 lbs.) format; with two-columned pages and much larger print, is almost a revolution. Thus the book, which is about twice as large as the first edition of almost 20 years ago, reflects the great advance in the field of hematology and as Wintrobe says: "In many respects, only the skeleton is the same as before."

As always, one cannot help but be amazed at how much has been put into this book, distilled as it is from the author's wide experience and the careful culling of an enormous literature. Here, in a single volume, one can examine the whole broad, now almost boundless, expanse of hematology and find few if any lacunae.

The basic material—blood, bone marrow, cell production and survival, etc.—takes up the first 400 pages, after which comes the parade of the anemias, the polycythemias, the purpuras, the leukemias, etc. A welcome addition is the great increase in the number of the tables,—logically conceived, admirably constructed, highly instructive. One may cite as examples Table 11-1 "Causes of Pancytopenia" or Table 9-5 "Shot-Gun Therapy—Advantages and Disadvantages". Were it not for these tables, which pack so much information into so small a space, and for the increased length and breadth of the book, it might easily have become a two-volume affair. Perhaps it will when the next edition comes along!

A dissection of this volume reveals its essentially sensible construction and "no nonsense" discussion. Speculation and radical ideas are at a minimum, as perhaps they should be in this authoritative text. The "primary refractory anemias" always pose a bit of a problem, because each author has his own ideas of what this heading should include; and the reviewer for one would rather not use this term under any circumstances—since who knows but what is refractory today may be curable tomorrow. This has already happened in our life time to pernicious anemia, many forms of hemolytic anemia, including the autoimmune type, and occasional cases responding to pyridoxine. It is not clear from either the text or the tables exactly what Wintrobe has in mind regarding these "refractory anemias." Are they only the hypoplastic-aplastic group, do the "simple chronic anemias" go into this category, and are the "sideroblastic" refractory anemias to be put here? If so, what about the Di Guglielmo syndrome—which is described amongst the leukemias? Such are the difficulties of the careful and conscientious author. As a matter of fact, chapter and section headings are always a nuisance. For example, under the broad designation of the "normocytic anemias" are included such heterogenous entities as aplastic anemia, myelofibrosis with myeloid metaplasia, and all the various and sundry hemolytic anemias, including hereditary spherocytosis and thalassemia.

"Myelofibrosis" is also discussed in Chapter 11. Curiously, the commonly used designation of "myelofibrosis with myeloid metaplasia" is not used, and there is complete omission of the concept of the "myeloproliferative disorders" which has been so widely adopted in the past decade. Actually, this rather vague designation for a group of disorders is often as good a diagnosis as one can make. In proliferations of the bone marrow, which encompasses several different kinds of cells, nature often mixes things up so that the student of differential diagnosis finds it difficult to decide upon an exact nosologic entity. In this situation the rather didactic presentation of a text such as Wintrobe's fails to take note of this variability. Contrary to the interpretation of most workers in this field, Wintrobe holds to the "compensatory" theory for the myeloid metaplasia, rather than to a generalized

proliferative one. In fact there is no mention here of the commonly observed transition of typical polycythemia vera to myelofibrosis with myeloid metaplasia, and one also looks in vain for this in the chapter on polycythemia as well.

The hemolytic anemias have in themselves become an enormous field—as witness Dacie's need for expanding his original one volume work to two volumes and more recently to three. Wintrobe covers them in about 130 pages. Table 12-1 presents a very comprehensive classification of the hemolytic disorders, which are divided into two broad groups: I. Intracorpuscular Defects; and II. Extracorpuscular Causes. Under the latter are listed infectious, chemical, and physical agents, poisons, isoagglutinins, symptomatic types and "idiopathic acquired hemolytic anemia," but no indication whatever of immunologic (autoimmune) mechanisms. In the text, however, one is glad to find the statement that "autoimmune mechanisms appear to be the basis of all, or at least almost all, cases of idiopathic acquired hemolytic anemia." One partial misstatement is made in this chapter (p. 622): "The Coombs' antiglobulin test is used to demonstrate the presence of iso-immune mechanisms in a case of hemolytic anemia." The section dealing with hemoglobin abnormalities has been entirely re-written and brought up to date.

As for polycythemia, this is excellently covered, although the reviewer would disagree with the author in his outspoken advocacy for the use of radioactive phosphorus, and in the statment that such chemotherapeutic agents as Myleran require much closer supervision of the patient than with P^{32}. My own experience indicates that too many patients are given too much P^{32} and there is sometimes too little observation for possible after-effects such as anemia, acute leukemia, etc.

The purpuras (Chapter 17) are well described with "purpura hemorrhagica" ("ITP") being prominently and wisely discussed. The controversial questions of therapy with particular reference to ACTH and the corticosteroids and splenectomy are thoroughly aired. By and large, there is no great difference between Wintrobe's management of patients with acute and chronic ITP and our own. He realizes that "splenectomy . . . is not the infallible remedy that some have held." He believes that this operation is contraindicated in the acute cases. He finds a prominent place for the corticosteroids and one suspects that they are usually used as the first and often as the only agent, with splenectomy being left as the last resort measure "in those cases of ITP in which spontaneous remission has not occurred after six or more months of observation and the clinical manifestations are moderate or severe." The possibility of the development of systemic lupus after splenectomy is discussed; this question is certainly controversial. One misses a more or less comprehensive discussion of systemic lupus, not only as an autoimmune disorder—which would be asking too much, one realizes—but as a complex of hematologic and vascular disturbances.

The section on coagulation looks new and up to date; that on the hemorrhagic disorders might have been a bit more comprehensive; fibrinolytic disorders are covered rather cursorily and there seems to be an omission of the hemorrhagic state associated with hyperglobulinemic conditions.

Leukemias and related disorders are covered authoritatively and comprehensively in less than 200 pages, and again one wonders how so much could have been compressed into so little space. There is a sensible discussion of the spleen, splenomegaly and hypersplenism.

Thus one must finally conclude that this book has about everything for everybody wanting some information in the hematologic field. For the tyro, the work is authoritative and will not mislead; for the expert, the bibliography will give one a start in looking up the rare syndrome, and of course a chance to see "what Wintrobe says." Hematology must be ever in debt to Wintrobe for his careful and eminently useful presentation of this subject so that others may learn. The few criticisms uttered here are miniscule as compared with the broad sweep of this by now classic text.—*William Dameshek*

BIOLOGICAL APPROACHES TO CANCER CHEMOTHERAPY. Edited by *A. J. C. Harris,* London and New York, Academic Press, 1961, 431 pp., $14.00.

The symposium which this volume records was held under the auspices of UNESCO and the World Health Organization, in June 1960. Investigators representing a wide variety

of disciplines were invited apparently in the hope of stimulating fresh thoughts and fresh approaches to the design of new agents with selective effects on tumors. For the most part, one suspects that this diversity was somewhat overdone, that the circles of mutual understanding were small in relation to the area of the whole symposium. This view appears to be supported by the recorded discussion which either was meagerly reported or possibly was indeed meager.

The concept of the symposium reflects a philosophy which seems naïve—that somewhere within reach there is a unitary solution to the cancer problem—as expressed in the foreword: "The probability is that all of the necessary clues are available, and failure to solve the full problem results from the inadequacy of the intellectual effort so far put in." It seems much more likely to this reviewer that the conquest of cancer will be achieved in small increments, through hard and intelligent effort devoted for the most part to designs already in hand and not to those of several would-be architects whose plans have never been built and indeed cannot be because of ignorance of the strengths of materials, forces of stress and even of gravity.

The volume contains 31 articles of rather mixed value. Some obviously were designed as broad introductions to a field which was not expected to be familiar to the majority of the participants and several are clearly rehashes of material which has been presented on numerous occasions. A number of the papers deal directly with problems of cancer chemotherapy; the contributions of Bergel and Larionov are particularly notable for the combination of sound rationale with the empirical working-out which is characteristic of successful chemotherapy. R. T. Williams has given a succinct and down-to-earth summary of the metabolic fates which drugs may encounter in the host, and some suggestions as to possible ways in which known detoxicating mechanisms might be used to improve selective toxicity. Gorer puts forward evidence for the existence of isoantigens to tumors and De Somer and Zilber deal with specific tumor antigens. Klein has written a lucid and tightly-reasoned essay on the progressive changes in the composition of the cellular population of tumors, and attempts to follow such changes using as a marker the H-2 determined isoantigenic system of the mouse. Hormonal dependence and autonomy are discussed by Furth and Mühlbock. Luria and Harris deal with aspects of viral carcinogenesis and Alice Moore with viral carcinolysis. Magasanik has written a cogent essay on feedback mechanisms in biological synthesis to which are appended some rather feeble attempts to connect this with cancer chemotherapy.

Despite the rather quarrelsome attitude of this reviewer, in the end it has to be conceded that there is much of value in the volume, both for the casual reader who wants a quick once-over of the field but also in spots for the worker who is seriously interested in cancer chemotherapy. One thing is sure, the meeting must have been fun and stimulating for the participants.—*G. H. Hitchings*

RADIOISOTOPE TECHNIQUES IN CLINICAL RESEARCH AND DIAGNOSIS. *N. Veall and H. Vetter*, London, Butterworth & Co., Ltd., 417 pp., $10.00.

This is an excellent treatment of the subject matter exactly as the title implies. The authors have combined their experience in physics and medicine, and the result is a very clear and instructive book. The various chapters, and particularly the one on iron metabolism, are very complete and useful to the worker in hematology. The method of treatment of the material is very reminiscent of the series, *Methods in Research* (Yearbook of Chicago Publishers). There is an outstanding coverage of dynamic systems in general and specifically circulation studies.

Therapy has been covered in a very superficial way and could have been left out entirely since this coverage compares unfavorably with the remainder of the book.

The printing and illustrations are clear and informative. Constant reference to distant pages is very distracting and the number should be reduced drastically to make this very readable book even more so. I hope that in any future editions, a thorough discussion of liquid scintillation counting will be added. Carbon^{14} and H^{3} compounds cover a vast field but methods have been well worked out and are important in clinical research.

This book is a useful source for the clinician and research worker and is highly recommended.—*Joseph S. Burkle*

HEMOPHILIC DISEASES IN DENMARK. *Knud-Erik Sjølin*, Springfield, Ill., Charles C Thomas, 1961, 349 pp., 86 figures, 112 pedigrees, $8.50.

This book describes the results of an ambitious project in which the author studied 78 families, including virtually all the patients in Denmark with known disorders of blood thromboplastin formation. The qualitative clotting defect in each subject was investigated, the symptomatology described, and the modes of inheritance traced in detail.

The monograph opens with a summary of present knowledge concerning blood clotting, arranged in chronological fashion. The hematological characteristics of hemophilia are then defined as a triad: 1. Prolonged (or normal) clotting time. 2. Normal prothrombin time. 3. Delayed conversion of prothrombin to thrombin. The fact that hemophilic tissue shows normal thromboplastic activity is emphasized. Methods of investigating blood coagulation defects are outlined, with critiques (some prejudiced) of each.

The patients in the series were studied in the laboratory by a recalcified clotting time, a thrombin generation test, the Quick one-stage prothrombin time and a platelet count. Attempts to correct the defects were made by adding various reagents to the patient's plasma in the thrombin generation test. Some of the materials added were: adsorbed bovine plasma, normal human serum, heated readsorbed serum, and platelet suspensions. In addition, the effect of freezing some of these reagents before adding them in the test is described. The author places heavy emphasis on the results of the thrombin generation tests and devotes a full chapter to a discussion of their interpretations and the various additives that modify them.

One hundred forty-eight patients were classified according to their clotting defects. Sixty-one had AHF deficiency, 27 were diagnosed as PTC deficiency, 11 were stated to lack Hageman factor, 3 were PTA deficient and a circulating anticoagulant was found once. The remainder of those studied showed slight or combined defects. When the Danish results were compared with other large series, a number of discrepancies were noted by the author. The reasons given were: 1. It is easier to trace mild cases in a small country (?); 2. "the thrombin generation test is the most physiological method of demonstrating defects of the plasma thromboplastin, using the patient's plasma alone as substrate." In rebuttal one might propose the paper of Aggeler, Hoag, Wallerstein and Whissell (Am. J. Med. 30: 84, 1961) on the mild hemophilias where complete "profiles" were carried out in each patient.

The remainder of the book is concerned with clinical management of the patients, studies on carriers, "sporadic hemophilia", problems of the future, and finally, 156 pages of pedigrees and individual case reports. The chapter on pedigrees is preceded by a summary of the entire book.

Readers of this book will admire its magnitude, but its value especially to workers in the field would be enhanced if more "conventional" methods of study had been employed. For instance, what would the 11 cases of Hageman factor deficiency show in the thromboplastin generation test, and what would their prothrombin consumption be? Cases of Hageman factor deficiency are usually not associated with the symptomatology described by the author. The number of combined defects found by the author is notably higher than one would expect. In general, it will be difficult to compare the results of other studies with those here reported because of the methodology employed.

A few typographical errors are noted and on occasion the prose is somewhat difficult to follow.—*Aaron J. Marcus*