THE RED CELL

PRODUCTION, METABOLISM, DESTRUCTION: NORMAL AND ABNORMAL

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FOREWORD

Two challenges to the student and teacher of medicine have been made sharply by Vannevar Bush,* physicist and statesman of science:

"(i) Medicine is largely empirical in spite of scientific progress in biochemistry and physiology: it has new and powerful tools but understands and controls them only vaguely: and its progress toward logical processes is slow because of the appalling complexity of its subject matter.

"(ii) The library, as we know it, can not cope with the task before it. Science has become bogged down in its own products, inhibited like a colony of bacteria by its own exudations. . . . The pile is mounting daily, science is becoming polyglot, duplication is rife: synthesis, crossing many fields, becomes increasingly difficult and more and more necessary. In such a morass, how are the great syntheses of the future to be brought to light?"

In preparing the following monograph, John W. Harris has had the courage to prepare a synthesis in a field of great complexity and bring it to the desk of the second-year student of medicine and to the teacher. Both find this monograph to be challenging in depth, filled with detail but rich in principles that are dynamic and applicable to the understanding of physiologic and pathologic processes. Observations of the clinical investigator have been coupled with those of biologic scientist, biophysicist, chemist, and physicist.

The advancement of knowledge in medicine is evident from inspection of this monograph with its 2,074 references. For example, the bursting new knowledge of abnormal hemoglobins had its origin only 13 years ago in the report by Linus Pauling and his colleagues on sickle cell anemia, a molecular disease. They gave the clues to both the biochemical and genetic differences in hemoglobin formation. The chapter on this field of globin synthesis is brief but has 225 references, 180 of which were pub-

* *For Man to Know*, Atlantic Monthly, pp. 37, 32, August 1955.

lished from 1955 to date. Probably no field of medicine offers more opportunity for student and teacher to synthesize principles of genetics, hemoglobin chemistry, biophysical behavior of hemoglobin molecules, and the consequences of such abnormalities as sickle cell hemoglobin in producing symptoms of pain and dangerous thromboses in the patient, anemia, and abnormalities in organs where thromboses occur.

The problems facing the student, teacher, and author have much in common. There is mutual desire to understand the scientific basis of medicine to help in the care of patients. The complex fields are greatly simplified when a principle is clearly defined, understood, and applied. The author who will study, correlate, and clarify principles makes a major contribution to us, especially when he presents the evidence to support his concepts. The hurried and harried reader may be required to omit the details, avoid the historic development of concepts, and go crashing toward the summary statements. This is the dilemma of enormous advances in knowledge.

John W. Harris has derived this monograph for students showing his faith in them and in their ability and desire to learn principles and the bases of the principles. In fact, this document has inspired the development of a program of cooperative research in teaching hematology in which several medical schools are participating. The question is raised, "Can the student take the responsibility to learn on his own initiative from the study of problems?" Obviously, any student and any faculty member is challenged to learn from the monograph by Harris.

From the practical point of view, the author has insisted that the dollar-cost of this volume be kept to a minimum to meet the needs of the student's pocketbook and the rapid obsolescence of any report in a rapidly advancing field.

Thomas Hale Ham, M.D.

PREFACE

The various sections of this work were developed for use in the second-year course of hematology at Western Reserve University School of Medicine and have been so used in approximately their present form for the past 3 years. They have been titrated for concepts and factual content so that under the conditions employed the ready grasp of the good student is somewhat exceeded while the outstanding student takes them in stride and supplements with source materials.

The attempt is made to report the current status of the body of knowledge relative to the various topics considered in such a way that the experimental approaches employed in reaching conclusions are illustrated and sufficient data are supplied to support the conclusions and indicate their limits of accuracy and dependability. It is entirely organized around and limited to the red cell—development, synthesis of component parts, function, metabolism, and destruction (normal and abnormal)—and is intended to extend into a specific model system (hematology) the student's knowledge of biochemistry, physiology, pathology, etc. Brief clinical descriptions are presented to provide frames of reference into which the illustrative pathophysiology and disease mechanisms can be placed and retained for subsequent clinical application. The bibliographies supplied are fairly extensive and selected to allow ready penetration beyond the outlines here reported; as such they have sometimes been cited with less regard for priority than for aptness of documentation, illustration, and usefulness in leading the inquirer further along a search.

To enable the student to take the responsibility for learning on his own initiative, so-called "Case Development Problems" have been employed as simple learning devices* in association with this text. A group of these

* Harris, J. W., Horrigan, D. L., Ginther, J. R., and Ham, T. H.: Pilot study in teaching hematology with emphasis on self-education by the student, J. Med. Educ. 37:719, 1962.

problems has been published by The Commonwealth Fund and is available as an inexpensive supplement.*

Credit for what is accurate must go largely to the following workers, who most helpfully reviewed various sections: Drs. Franklin G. Ebaugh, Jr., Clement A. Finch, Clifford W. Gurney, Ernst R. Jaffé, Wallace N. Jensen, Robert F. Schilling, Rudi Schmid, and Scott N. Swisher. Their corrections and suggestions are gratefully acknowledged. For any remaining inaccuracies, omissions, and misleading statements, the blame is wholly mine.

Special thanks are given to Mrs. Marie K. Gubics for her invaluable aid and unfailing patience in preparing the manuscript, not only in the several preliminary forms in which it has been used for teaching, but also for publication. David B. Harris was of material help in preparing the index. Mrs. Dorothy S. Obré and Roger A. Crane of The Commonwealth Fund have contributed greatly in the process of bringing the book to its final form.

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* Harris, J. W., and Horrigan, D. L.: Case Development Problems in Hematology: Series 1, The Red Cell, Problems 1–8, Harvard University Press, Cambridge, Mass., 1963.

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