CLINICAL HEMATOLOGY

By

Maxwell M. Wintrobe, M.D., Ph.D., D.Sc. (Hon.)

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Fifth Edition, Thoroughly Revised
265 Illustrations in Black and White
50 Illustrations in Colour on 19 Plates

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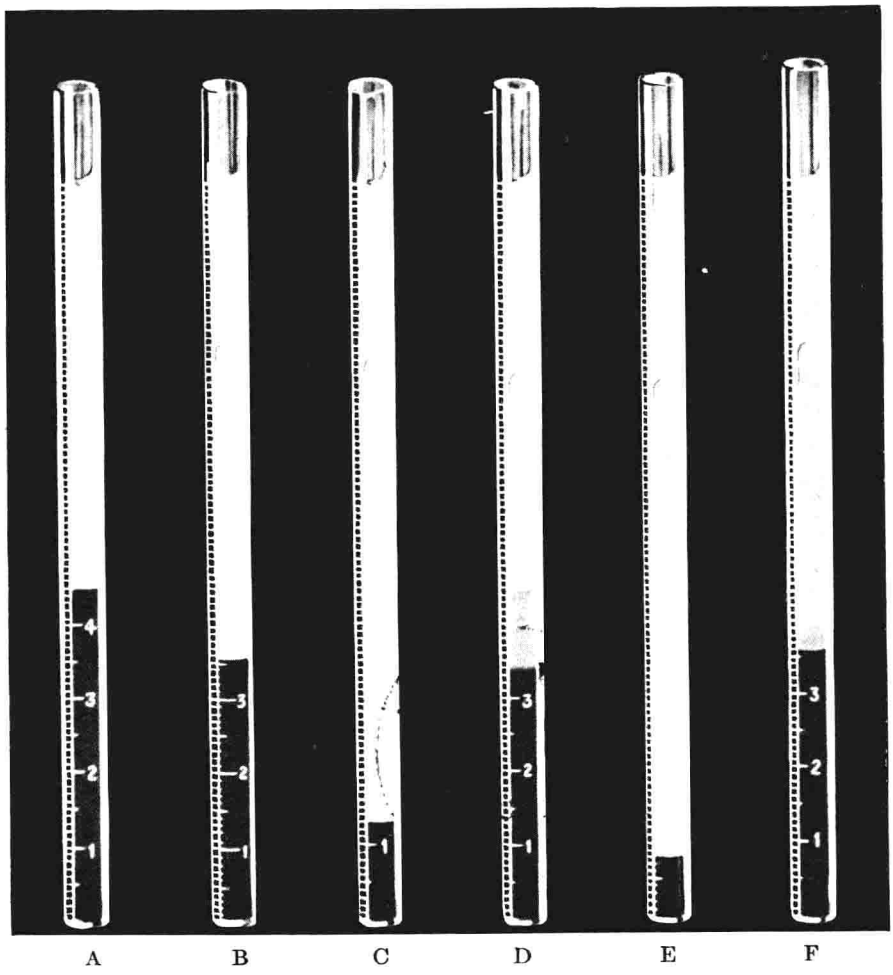
PLATE I



THE APPEARANCE OF CENTRIFUGED BLOOD IN VARIOUS CONDITIONS

(Oxalated venous blood was placed in hematocrit tubes and centrifuged at 3000 revolutions per minute for one-half hour.)

A. Normal blood.

B. Simple anemia due to chronic infection.

C. Chronic posthemorrhagic anemia. The blood plasma is very pale.

D. Chronic myelocytic leukemia. There is a thick layer of white corpuscles and platelets above the red corpuscles.

E. Pernicious anemia. Note the small amount of packed red corpuscles, the very narrow layer of leukocytes and platelets, and the coloring of the blood plasma due to increased bilirubinemia.

F. Infectious hepatitis and slight anemia. In this case the coloring of the blood plasma is due to biliary obstruction rather than to increased blood destruction. *(Wintrobe, Tice Practice of Medicine, courtesy of W. F. Prior Company.)*

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Preface to the Fifth Edition

THE fundamental contributions which have been and continue to be made in the field of hematology attest to the ingenuity and industry of the investigators and demonstrate the comprehensive character of the field. Once a discipline limited to morphology, hematology now has grown in depth and in breadth; in depth to the molecular level and in breadth to the fields of human genetics and anthropology. Many other disciplines are embraced within this range.

No wonder, then, that in spite of the overwhelming quantity of literature which has been published in the five years intervening since the publication of the fourth edition, the effort of reviewing and digesting the important contributions to the field of hematology has been well repaid. It may be added that, seen individually as they have been published, these sometimes have failed to impress one as much as they should; fitted together, some as bricks and stones and a few as keystones which serve to complete the bridge of knowledge which joins facts until then of uncertain significance, each observation stands out in a truer light. Vague details take shape and understanding advances. A comparison with the first edition of this work, published twenty years ago, gives some indication of the growth of the field and, incidentally, provides a glimpse of the advances in medicine as a whole in that interval. It is noteworthy how much has depended on the successive discovery of various techniques whereby some of the secrets of nature have been pried loose.

As before, the whole text has required careful review and much has needed modification, some of it very extensively. In many respects, only the skeleton is the same as before. Many sections have been completely rewritten and a number of new topics have been added, in keeping with the progress of hematology. Numerous new illustrations have been included and a number of older ones have been discarded This applies also to the color plates; here advantage has been taken of the development of color photomicrography. New tables have been designed and the bibliography has been completely revised.

Certain explanations may prove helpful. In preparing this book the writer has had in mind the beginning student, the discerning technician, the advanced postgraduate, the clinician, the teacher, and even the biochemist and the sophisticated hematologist. For this reason certain details will be found and some illustrations have been retained because it is thought that they have value for certain potential readers although they may not be useful to others. Here it may also be explained that this book is not designed primarily as a laboratory manual and that, for this reason, laboratory techniques are not all discussed in one section, in an appendix. The intent, rather, is to indicate the principles and objectives of a procedure, its value and its pitfalls. Details are given concerning the simpler procedures, many of which every physician should be able to carry out himself. In addition, enough detail has been provided concerning other techniques to allow the reader to gain a thorough understanding of the method. When possible, these techniques have been described in connection with the kind of information which they are designed to provide; in context rather than in appendix.

It probably needs only to be mentioned

that the bibliography, voluminous as it is, must necessarily represent only a small proportion of the papers which have been published. Omissions should not be construed as implying lack of appreciation of the worth of the papers not cited. In general, the attempt has been made to limit the bilbiographic references to the most recent ones dealing with the topic concerned, or to especially pertinent or historical ones. Additional references will be found in the papers quoted, some of which have been selected because of their value in this regard.

As in the past the author is greatly indebted to his associate, Dr. George E. Cartwright, for his criticism and advice. Dr. Paul Didisheim has been most helpful in the area of coagulation and the hemorrhagic disorders. The technical procedures which are described are those employed in our coagulation laboratory under his direction. Dr. Robert L. Hill also has been most generous of his time and help, especially in connection with the fascinating problems of the normal and abnormal hemoglobins. To Dr. Arthur Haut and his assistant, Miss Doris Kurth, the author is deeply indebted for their skill and many hours of labor in providing essentially all of the new illustrative material including, especially, the color photomicrographs.

A number of workers in the field of the hemoglobinopathies have graciously supplied information, some as yet unpublished, and have been helpful in many ways. The author is especially indebted to Dr. Hermann Lehmann, Dr. Richard T. Jones, Dr. E. M. Shooter and Dr. S. Park Gerald, as well as to Dr. Corrado Baglioni, Dr. A. O. W. Stretton and Dr. Phillip Sturgeon.

For proofreading the author thanks his wife, as well as Drs. Robert C. Edmondson, Otto P. Haab, G. Richard Lee and Dane R. Boggs. To them he is also indebted for many helpful suggestions.

Inexhaustible energy, infinite patience and sincere dedication are a few of the attributes of his secretary, Miss Alida Woolley, for which the author expresses appreciation. Last but not least, thanks are due to his associates in the Department of Medicine, as well as to his wife, for their understanding and indulgence.

It is a special pleasure to express the author's appreciation of the skill and the wholehearted and unstinting cooperation of the publishers, Lea and Febiger, and their staff, especially Mr. Victor J. Boland.

MAXWELL M. WINTROBE

Salt Lake City, Utah

Preface to the First Edition

As knowledge is gained and a subject is better understood, it should become more simple rather than more difficult. Yet hematology has appeared to the average physician to grow constantly more complex, in spite of the fact that great progress has been made in this field and a clearer concept of the factors governing hematopoiesis as well as of the disorders of blood formation has been evolved.

The introduction of new methods, the description of new disease syndromes and the application of new terms have contributed to the apparent complexity of the subject. The literature, moreover, has grown voluminous and the task of the physician who must keep abreast of many fields is overwhelming.

To bring together the accumulated information in the field of hematology in a systematic and orderly form, to sift the important from the less significant, to describe the newer methods which are of practical value and to make note of those which are less essential, to outline details of differential diagnosis, to describe the indications for and methods of treatment, and to make clear as far as present knowledge permits the nature of the underlying physiological disturbances, are the objects of this book.

To fulfill these objects a book must be comprehensive, complete and authoritative. To this end thousands of publications have been consulted. This information has been so organized that it should be readily accessible. In addition, a bibliography of some 2400 references is provided in order that the interested reader may obtain still more information if he so wishes. The bibliographies are found at the end of each chapter and the text of the chapter serves as an index to the contents of each bibliography. Monographs and articles furnishing more complete bibliographies are so designated.

Emphasis is placed on the importance of accurate diagnosis as a prerequisite to efficacious treatment. The use of therapeutic measures without discrimination and the administration of "shotgun" antianemic remedies indicate the need for a clear understanding of the indications for liver, iron, vitamins and other substances. The effective employment of these and other therapeutic agents is discussed in detail.

Laboratory procedures of value in diagnosis are in the main quite simple and can be carried out in the office of the average physician. They are considered in detail. A departure from the usual custom has been made, however, in that the technical methods are not all grouped in a single section but are described in the various chapters of which they logically form a part. This is done because the objects and principles of a laboratory test must be thoroughly understood if it is to be well performed and correctly interpreted. Only those procedures which do not come within the scope of the various specific chapters are described in the chapter on methods. The vital importance of technical precision is stressed and the limits of accuracy of various procedures are indicated.

There is in this book no departure from accepted terminology. Instead, an attempt is made to give a clear interpretation of the terms now employed. Furthermore, no glossary of hematological terms has been prepared. It is believed that the meaning of a name or descriptive phrase is best expressed in the text where

it is used. The index serves as the key to the definitions of the various terms.

In a book on hematology adequate illustration is essential. Nevertheless the cost must not be prohibitive to the student and physician. The excellent illustrations which have been published by a number of writers prove that much of the essential detail of cells, including even the leukocytes, can be demonstrated in engravings without the aid of color. For these reasons colored plates have been used sparingly in this book and serve to amplify rather than to displace illustrations in black and white. This saving in expense has permitted the inclusion of many illustrations of clinical features which have been neglected in most books on hematology.

Although it forms no part of clinical hematology, an Appendix giving the blood findings in 46 species of animals, including non-mammals, as well as a bibliography of literature on comparative hematology, is included in this book because I have been called upon to supply such information frequently and know that it is not readily accessible elsewhere. Many of the blood determinations have been made in our own laboratories.

Photographs, drawings and roentgenograms of patients have been used freely for illustration, through the courtesy of Dr. Warfield T. Longcope, my chief, to whom I am also indebted for the opportunity to study all of the cases with hemopoietic disorders on the medical service and to use the records which have been accumulated with great care over a period of many years. Dr. Edwards A. Park has very kindly allowed me the privilege of seeing many patients in the Department of Pediatrics.

It is with pleasure that I express my gratitude to those students of the Department of Art as Applied to Medicine of the Johns Hopkins University who have prepared many of the drawings which are reproduced here. Thanks are due particularly to Miss Laura Ornstedt, Miss Dagmar Haugen, Miss Marjorie Hoag and Miss C. M. Shackleford. I am also indebted to W. F. Prior Company, Inc., for permission to reproduce a number of the plates prepared under my direction which appear in Tice's Practice of Medicine.

I am particularly grateful to Dr. Oliver P. Jones for his helpful advice and criticism and to my many associates at the Johns Hopkins Hospital for the same reasons, including especially Dr. J. William Pierson and his staff in the Department of Roentgenology, Dr. Alan M. Chesney, Dr. Arnold Rich, and Dr. Harry Eagle. Thanks are due also to Dr. Edward A. Gall, Dr. Jacob Furth and Dr. Samuel Richman, and to the authors and publishers of articles from which illustrations have been reproduced. These are acknowledged in the text. The hundreds of investigators who have generously furnished reprints of their papers have made my task very much easier and I have thought of their kindness many times as this book was being written.

My wife has been my chief assistant in the preparation of the manuscript and in the reading of proofs, and my debt to her for this and for her patience and encouragement is great. Mrs. Norma Strobel, my secretary, Dr. Conrad Acton and the members of my laboratory staff gave valuable assistance in the preparation of the manuscript and charts. The staff of Messrs. Lea & Febiger have been both patient and skilful in their work of publication.

M. M. WINTROBE

BALTIMORE, MARYLAND

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