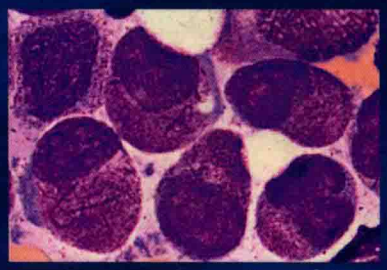
H. Löffler
J. Rastetter

Atlas of Clinical Hematology

Initiated by
L. Heilmeyer
and
H. Begemann

Fifth revised
Edition



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Atlas of Clinical Hematology

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and H. Begemann

Fifth Revised Edition

With 199 Figures, in 1032 separate Illustrations,
Mostly in Color, and 18 Tables

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H. Löffler · J. Rastetter

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Preface to the Fifth Edition

The first edition of the *Atlas of Clinical Hematology* was published over 40 years ago. The first four editions were coauthored by Herbert Begemann, who died unexpectedly in April of 1994. We wish to dedicate the fifth edition as a memorial to this dedicated physician and hematologist.

Since the fourth edition was published in 1987, hematology has undergone profound changes. New methods such as cytochemistry and immunophenotyping have been joined by cytogenetics and, more recently, molecular genetic techniques, which have assumed a major role in routine diagnostic procedures. This has been due in part to significant advances in methodology and new tools in molecular biology. When used in standardized protocols, these tools can furnish swift results that are relevant to patient care. Since the advent of cytogenetics and molecular genetics, we have formulated new definitions for clinical and biological entities. An example is promyelocytic leukemia with its two variants (M3 and M3v), the (15;17) translocation, and the PML/RARA fusion gene, which has been successfully treated for the first time with differentiation therapy. Another example is acute myelomonocytic leukemia with abnormal eosinophiles (M4Eo), inversion 16, and the MYH/11/CBFB fusion gene, which has a very good prognosis. The transmission of morphologic findings by electronic data transfer is also gaining importance in hematology, as it permits the immediate review of difficult findings by specialists. Several colleagues seated at their own desks and microscopes can communicate with one another instantaneously by computer monitor. These advances do not alter the fact that hematologists must still have a sound grasp of morphologic principles. Diagnostic problems often arise when modern counting devices and cell sorters, with their impressive capabilities, are used without regard for cellular morphology. There is no question that classical morphology has gained much from its competition and comparison with the new techniques, leading to significant diagnostic and prognostic advances.

While retaining the basic concept of the previous editions, we found it necessary to eliminate several chapters. Now that many hematologic centers and laboratories are equipped with fluorescence-activated cell sorters (FACS) for immunotyping, and given the availability of reliable commercial kits and precise staining instructions for immunocytochemistry, the chapter by B. R. Kranz has been omitted from the present edition. We have also dropped the methodology section and most of the electron micrographs supplied by Prof. D. Huhn. Both colleagues merit our sincere thanks. Ever since the first edition, Prof. W. Mohr of Hamburg has authored the chapter on blood parasites as the principal causative agents of tropical diseases, and we gratefully acknowledge his contribution. Following the death of Prof. Mohr, we have chosen to include this chapter owing to the special importance of tropical diseases in the modern world. We are grateful to Prof. R. Disko of Munich, who agreed to revise and update the chapter.

The chapters on chronic myeloproliferative diseases, and especially those dealing with myelodysplasias, acute leukemias, malignant lymphomas, and malignant mastocytoses, had to be extensively revised or rewritten. We have

added new sections and illustrations on therapy-induced bone marrow changes, cytologic changes in the cerebrospinal fluid due to leukemic or lymphomatous meningeal involvement, and NK cell neoplasias. We have also endeavored to give due attention to issues in pediatric hematology.

In compiling this revised fifth edition, in which over 90 % of the illustrations are new, we benefited greatly from our two decades of central morphological diagnostics for the ALL and AML studies in adults and the morphological consulting of the BFM treatment study on AML in children (H. L.). We thank the directors of these studies, Professors D. Hoelzer, T. Büchner, U. Creutzig, and J. Ritter, for their consistently fine cooperation. We also thank the Institute of Pathology of the University of Kiel, headed by Prof. Karl Lennert, and the current head of the Department of Hematologic Pathology, Prof. Reza Parwaresch, for preparing histologic sections of the tissue cores that we submitted.

Acknowledgements

We are indebted to Prof. Brigitte Schlegelberger, Prof. Werner Grote (director of the Institute of Human Genetics, University of Kiel), Dr. Harder, and Mr. Blohm for providing the cytogenetic findings and schematic drawings. We limited our attention to important findings that have bearing on the diagnosis or confirmation of a particular entity.

A work of this magnitude cannot be completed without assistance. My secretary of many years, Mrs. Ute Rosburg, often freed me from distracting tasks so that I could gain essential time. Mrs. Margot Ulrich efficiently organized the processing of the photographic materials, while Mrs. Ramm-Petersen, Mrs. Meder, and Mrs. Tetzlaff were meticulous in their performance of cytologic, cytochemical, and immunocytochemical methodologies. My senior staff members in Kiel, Prof. Winfried Gassmann and Dr. Torsten Haferlach, helped with the examination and evaluation of many of the specimens pictured in the Atlas. My colleague Dr. Haferlach collaborated with the study group of Prof. Schlegelberger to introduce the FISH technique into routine clinical use. Finally, we thank Mrs. Monika Schrimpf and the entire staff at Springer-Verlag in Heidelberg as well as Ms. Judith Diemer at PRO EDIT GmbH for their thoughtful and effective support.

St. Peter and Munich
Summer 1999

Helmut Löffler · Johann Rastetter

Preface to the Fourth Edition

Hematology, the study of the blood and its disorders, has existed as a science for approximately one hundred years. During that period it has remained true to its goals. Despite many advances in the submicroscopic and biochemical realm, hematology has clung to its basic postulate that the majority of blood disorders are expressed in morphologically distinct cellular changes. Even modern hematology relies largely on the morphologic examination of cells, and the microscope continues to be its main diagnostic tool. Today we may describe hematology as the only morphologically oriented clinical science. It owes its existence chiefly to the development of staining methods that make it possible to assign morphologic structures to specific cellular functions and thus to specific pathologic states. The first step in this direction was the brilliant discovery of panoptic stains in the early part of this century by Pappenheim, Wright, and others. This was followed in the 1950 s and 1960 s by the development of numerous cytochemical procedures for the differentiation of diverse biochemical reactions and cell types. In the last decade, immunologic methods have been employed to identify cell type-specific antigens as a means of classifying lymphatic and other cells more precisely and more objectively. This has aided in the differentiation of many important hematologic disorders.

In this fourth edition of the *Atlas of Clinical Hematology,* we have attempted to update the text and bring it in line with recent developments. As before, the book is subdivided into a theoretical part and a pictorial part which illustrates the morphologic features of specific disorders using a combination of photomicrographs and watercolor paintings created by Hans and Thea Dettelbacher. The paintings convey a sense of depth to the microscopic image that will help the student appreciate and differentiate morphologic details. We have retained the chapter on electron microscopy, which we regard as a kind of connecting link between cell structures that are visible by light microscopy and the functional significance of those structures. Tropical medicine has become a subject of growing interest to hematologists and internists in our increasingly mobile population, and therefore the section on tropical medicine has been revised and expanded. Also, we have added new photomicrographs and have replaced a number of old ones with photographs of greater clarity.

The present edition features a new, comprehensive chapter on the light-microscopic demonstration of immunologic cell markers. It is divided into a methodologic and a cytologic section and deals extensively with the subtyping of normal and malignant lymphoid cells. This new and difficult chapter was authored by Bernd R. Kranz, who proved to be not only a leading expert in his field but also a cooperative, constructive coworker who offered many helpful suggestions going beyond his area of specialization. We express our sincere thanks for his contributions. We are also indebted to our co-authors Dieter Huhn and Werner Mohr, who worked with us on earlier editions and extensively revised and updated their chapters.

We thank our colleagues Heimpel of Ulm, Kaiserling of Tübingen, Lopes-Cardozo of Leiden, Müller-Hermelink of Würzburg, and Sepp of Munich for

supplying specimens and photomicrographs of rare disorders or special cell forms. We are grateful to Mr. Jorg Kuhn, who mastered the difficult task of supplementing the watercolor illustrations done for the first edition by Hans and Thea Dettelbacher. Mr. Kuhn proved to be a talented and sensitive artist, and his contribution is gratefully acknowledged.

Despite her other professional obligations, Dr. Gudula Wernekke-Rastetter has again provided an outstanding subject index. We thank her for turning our atlas into a useful reference work.

If this book recaptures the visual impact of the earlier editions, the credit belongs to Springer-Verlag and its staff as well as to the Dreher Reproduction Service in Stuttgart and Stürtz Printers in Würzburg. All contributed to the success of our book, and all demonstrated great technical expertise and understanding. Everyone with whom we worked took pains to implement our wishes as regards the finished appearance of the volume. Working with them was always a pleasant and satisfying experience. We express our sincere thanks to Dr. H. Götze, Mrs. T. Deigmöller, Mrs. U. Pfaff, Dr. J. Wieczorek, and Mr. K. Söll, to name but a few of the many persons who contributed to the success of this book. Finally we would like to express our sincere thanks to our translator, T. C. Telger.

It is the hope of the editors and authors that this fourth edition of our atlas will enjoy the same enthusiastic critical and consumer response that greeted the first three editions.

Munich, Summer 1989 Herbert Begemann · Johann Rastetter

Preface to the First Edition

So far the diagnostic advances of smear cytology have found only limited applications in medical practice. This is due largely to the fact that available illustrative materials have been too stylized to give the novice a realistic introduction to the field. In the present atlas we attempt to correct this situation by portraying the great morphologic variety that can exist in individual cells and in pathologic conditions. In so doing, we rely mainly on artist's depictions rather than photographs. On the one hand the "objectivity" of color photos, though much praised, is inherently questionable and is further degraded by the process of chemographic reproduction. An even greater drawback of photomicrographs is their inability to depict more than one plane of section in sharp detail. By contrast, a person looking through a microscope will tend to make continual fine adjustments to focus through multiple planes and thus gain an impression of depth. A drawing can recreate this impression much better than a photograph and so more closely approximates the subjective observation. We have avoided depicting cells in black and white; while there is merit in the recommendation of histologists that students' attention be directed toward structure rather than color, this is rarely practicable in the cytologic examination of smears. The staining methods adopted from hematology still form the basis for staining in smear cytology. For this reason most of the preparations shown in this atlas were stained with Pappenheim's panoptic stain. Where necessary, various special stains were additionally used. For clarity we have placed positional drawings alongside plates that illustrate many different cell types, and we have used arrows to point out particular cells in films that are more cytologically uniform.

We were most fortunate to have our color plates drawn by an artist, Hans Dettelbacher, in whom the faculties of scientific observation, technical precision, and artistic grasp are combined in brilliant fashion. We express our thanks to him and to his equally talented daughter Thea, who assisted her father in his work. Without their contribution it is doubtful that the atlas could have been created.

We are also grateful to a number of researchers for providing scientific help and specimens, especially Prof. Dr. Henning and Dr. Witte of Erlangen, Dr. Langreder of Mainz, Prof. Dr. Mohr of the Tropical Institute of Hamburg, Dr. Moeschlin of Zurich, Dr. Undritz of Basel, and Dr. Kuhn of our Freiburg Clinic. We also thank our translators, specifically Dr. Henry Wilde of our Freiburg Clinic for the English text, Dr. Rene Prevot of Mulhouse for the French text, and Dr. Eva Felner-Kraus of Santiago de Chile for the Spanish text. We must not fail to acknowledge the help provided by the scientific and technical colleagues at our hematology laboratory, especially Mrs. Hildegard Trappe and Mrs. Waltraud Wolf-Loffler. Finally, we express our appreciation to Springer Verlag, who first proposed that this atlas be created and took the steps necessary to ensure its technical excellence.

Freiburg, Spring 1955 Ludwig Heilmayer · Herbert Begemann

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