

*Williams*  
***Hematology***  
*Fifth Edition*

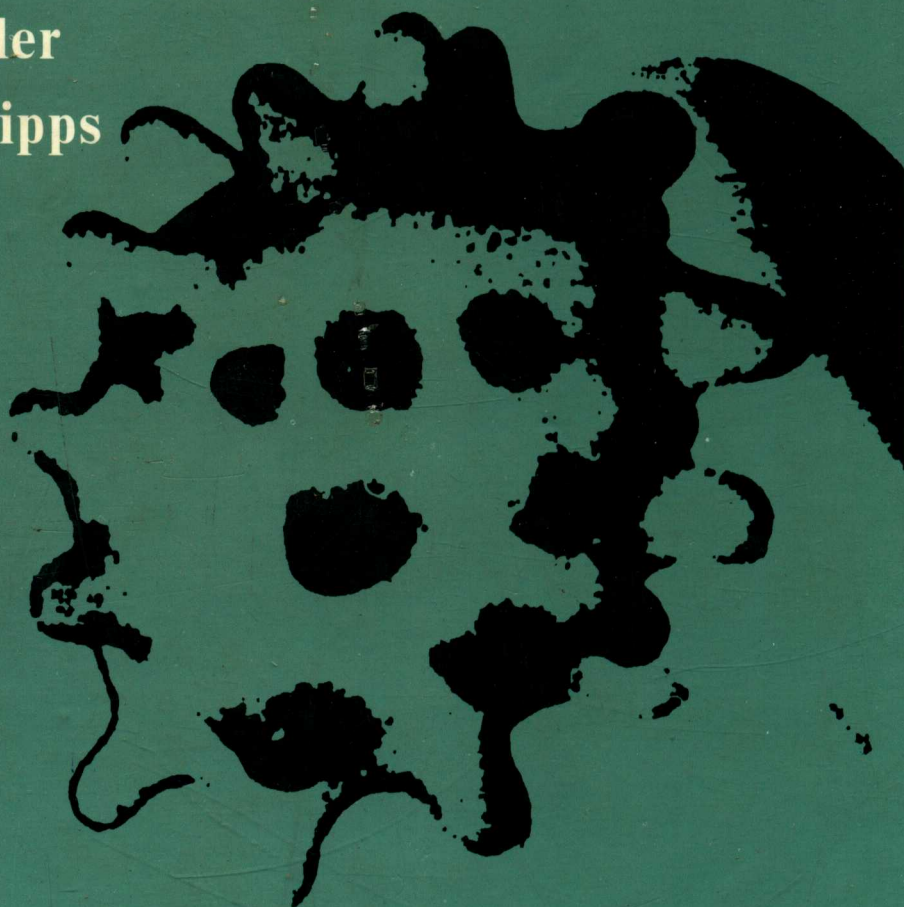
**威廉姆血液学**

Ernest Beutler

Marshall A. Lichtman

Barry S. Coller

Thomas J. Kipps



世界图书出版公司

# Williams *Hematology* Fifth Edition

EDITORS

**Ernest Beutler, M.D., Ph.D. (Hon)**

*Member and Chairman  
Department of Molecular and Experimental Medicine  
The Scripps Research Institute  
Clinical Professor of Medicine  
University of California, San Diego  
La Jolla, California*

**Marshall A. Lichtman, M.D.**

*Dean  
School of Medicine and Dentistry  
Hematology Unit  
University of Rochester Medical Center  
Rochester, New York*

**Barry S. Coller, M.D.**

*Murray M. Rosenberg Professor of Medicine  
Chairman  
Samuel Bronfman Department of Medicine  
The Mount Sinai Medical Center  
Mount Sinai School of Medicine  
New York, New York*

**Thomas J. Kipps, M.D., Ph.D.**

*Professor  
Department of Medicine  
University of California at San Diego  
La Jolla, California*

**McGraw-Hill**  
Health Professions Division

New York St. Louis San Francisco Auckland Bogotá Caracas Lisbon  
London Madrid Mexico City Milan Montreal New Delhi  
San Juan Singapore Sydney Tokyo Toronto

**McGraw-Hill**

A Division of The McGraw-Hill Companies



## Williams Hematology

Copyright 1995, 1990, 1983, 1977, 1972 by The McGraw-Hill Companies, Inc. All rights reserved. Printed in the United States of America. Except as permitted under the United States Copyright Act of 1976, no part of this publication may be reproduced or distributed in any form or by any means, or stored in a data base or retrieval system, without the prior written permission of the publisher.

234567890 DOW DOW 9876

ISBN 0-07-070386-8

This book was set in Times Roman by York Graphic Services, Inc. The editors were J. Dereck Jeffers and Mariapaz Ramos Englis; the editing assistant was Richard Kasmin; the production supervisors were Roger Kasunic and Robert Laffler; the cover designer was Edward Schultheis; the index was prepared by Irving Conde Tullar. R.R. Donnelley and Sons was printer and binder.

This book is printed on acid-free paper.

### Library of Congress Cataloging-in-Publication Data

Williams hematology / editors, Ernest Beutler ... [et al.]. — 5th ed.  
p. cm.

Rev. ed. of: Hematology. 4th ed. c1990.

Includes bibliographical references and index.

ISBN 0-07-070386-8 (alk. paper)

I. Blood—Diseases. 2. Hematology. I. Beutler, Ernest, date.

II. Williams, William J. (William Joseph), date III. Title:  
Hematology.

[DNLM: 1. Hematologic Diseases. WH 100 W721 1995]

RC633.H43 1995

616.1'5—dc20

DNLM/DLC

for Library of Congress

94-34780

# Contributors

## Camille N. Abboud, M.D.

Associate Professor  
University of Rochester Medical Center  
Department of Medicine  
Hematology Unit  
Rochester, New York [4]

## Kazuhiko Adachi, Ph.D.

Research Associate Professor of Pediatrics  
University of Pennsylvania School of Medicine  
Philadelphia, Pennsylvania [L10]

## H. Richard Alexander, M.D.

Senior Investigator, Surgery Branch  
National Cancer Institute  
National Institutes of Health  
Clinical Assistant Professor of Surgery  
Uniformed Services of the Health Sciences  
Bethesda, Maryland [20]

## Richard Aster, M.D.

Professor of Medicine and Pathology  
The Medical College of Wisconsin  
President & CEO  
The Blood Center of Southeastern Wisconsin, Inc.  
Milwaukee, Wisconsin [129]

## Bernard M. Babior, M.D., Ph.D.

Adjunct Professor of Medicine  
Department of Medicine  
University of California, San Diego  
Head, Division of Biochemistry  
The Scripps Research Institute  
Department of Molecular and Experimental Medicine  
La Jolla, California [35, 45, 76]

## Dorothy Ford Bainton, M.D.

Professor of Pathology  
Department of Pathology  
Vice Chancellor of Academic Affairs  
University of California School of Medicine  
San Francisco, California [73]

*Note:* Numbers in brackets refer to chapters written or co-written by the contributors.

## Stephen M. Baird, M.D.

Professor of Clinical Pathology  
University of California-San Diego  
School of Medicine  
Chief, Pathology and Laboratory Medicine  
Veteran's Administration Medical Center  
San Diego, California [112]

## William P. Baldus, M.D.

Consultant  
Department of Internal Medicine  
Division of Gastroenterology  
Mayo Clinic  
Professor, Mayo Medical School  
Rochester, Minnesota [51]

## Peter M. Banks, M.D.

Professor, Department of Pathology  
Director, Anatomic Pathology  
The University of Texas  
Health Science Center at San Antonio  
San Antonio, Texas [109]

## Bart Barlogie, M.D.

Director, Division of Hematology/Oncology  
Department of Medicine  
University of Arkansas for Medical Sciences  
Little Rock, Arkansas [114]

## Kenneth A. Bauer, M.D.

Associate Professor of Medicine  
Harvard Medical School  
Chief, Hematology/Oncology Section  
Brockton-West Roxbury  
Department of Veteran's Administration Medical Center  
Associate Physician  
Beth Israel Hospital  
Boston, Massachusetts [123, 144, L43]

## Joel S. Bennett, M.D.

Professor of Medicine  
Hematology/Oncology Section  
University of Pennsylvania  
Philadelphia, Pennsylvania [133, L53]

## Robert F. Betts, M.D.

Professor of Medicine  
University of Rochester School of Medicine  
Rochester, New York [104]



**Ernest Beutler, M.D.**

Member and Chairman  
Department of Molecular and Experimental Medicine  
The Scripps Research Institute  
Clinical Professor of Medicine  
University of California, San Diego  
La Jolla, California [11, 25, 29, 33, 34, 36, 39, 44, 46, 50, 54,  
56-58, 62, 63, 72, 74, 75, 92, 151, L5, L6, L13-L17, L19,  
L20, L24, L30, L31]

**Steven M. Beutler, M.D.**

Assistant Clinical Professor of Medicine  
University of California at Irvine  
Irvine, California  
Director, Division of Infectious Diseases  
San Bernardino County Medical Center  
San Bernardino, California [17]

**Karl G. Blume, M.D.**

Professor of Medicine  
Director of Bone Marrow Transplantation Program  
Stanford University Medical School  
Stanford, California [18]

**Edwin G. Bovill, M.D.**

Professor and Chairman  
Department of Pathology  
University of Vermont College of Medicine  
Burlington, Vermont [121, L36, L42, L46-L50]

**Laurence A. Boxer, M.D.**

Professor, Department of Pediatrics  
Director, Pediatric Hematology/Oncology  
Mott Children's Hospital  
Ann Arbor, Michigan [77, 83]

**James K. Brennan, M.D.**

Assistant Professor of Medicine  
Hematology Unit, Department of Medicine  
University of Rochester Medical Center  
Rochester, New York [26]

**Brian S. Bull, M.D.**

Professor  
Department of Pathology and Laboratory Medicine  
Vice-President and Dean  
Loma Linda University School of Medicine  
Loma Linda, California [32]

**Samuel A. Burstein, M.D.**

Professor of Medicine  
University of Oklahoma HSC  
Oklahoma City, Oklahoma [118]

**Loni Calhoun, M.T. (A.S.C.P.), S.B.B.**

Senior Technical Specialist, Transfusion Medicine  
University of California-Los Angeles Medical Center  
Los Angeles, California [148]

**Jaime Caro, M.D.**

Professor of Medicine  
Thomas Jefferson University  
Cardeza Foundation for Hematologic Research and Division of  
Research  
Division of Hematology  
Philadelphia, Pennsylvania [42, L18]

**Dennis A. Carson, M.D.**

Professor  
Department of Medicine  
University of California-San Diego  
La Jolla, California [94]

**Bruce A. Chabner, M.D.**

Director  
Division of Cancer Treatment  
National Institutes of Health  
Bethesda, Maryland [15]

**Edward A. Clark, Ph.D.**

Professor  
Department of Microbiology and Immunology  
University of Washington  
Seattle, Washington [98]

**Alan S. Cohen, M.D.**

Chief of Medicine  
Director, Thorndike Memorial Laboratory  
Conrad Wesselhoef Professor of Medicine  
Boston University School of Medicine  
Boston, Massachusetts [117]

**Barry S. Coller, M.D.**

Murray M. Rosenberg Professor of Medicine  
Chairman, Samuel Bronfman Department of Medicine  
The Mount Sinai Medical Center  
Mount Sinai School of Medicine  
New York, New York [119, 132, L54]

**Philip C. Comp, M.D., Ph.D.**

Professor of Medicine  
Oklahoma University Health Science Center  
Oklahoma City, Oklahoma [L44]

**Daniel G. Connaghan, M.D.**

Associate Professor of Medicine  
Hematology Department  
Emory University Medical Center  
Atlanta, Georgia [136]

**David Chandler Dale, M.D.**

Professor of Medicine  
Department of Medicine  
University of Washington  
Seattle, Washington [81, 82]

**George L. Dale, Ph.D.**

Associate Professor  
Department of Medicine  
The Oklahoma University Health Sciences Center  
Oklahoma City, Oklahoma [120]

**Frederick R. Davey, M.D.**

Professor and Chair  
Department of Pathology  
SUNY Health Science Center  
Syracuse, New York [L23, L25-L28]

**Louis DePalma, M.D.**

Professor of Pediatrics and Pathology  
The George Washington University Medical Center  
Department of Laboratory Medicine  
Children's Hospital  
Washington, D.C. [67]

**Daniel Deykin, M.D.**

Professor of Medicine and Public Health  
Boston University School of Medicine  
Director  
Health Services Research & Development Services  
Chief, Cooperative Studies Program  
Department of Veterans Affairs  
Boston, Massachusetts [146]

**Steven D. Douglas, M.D.**

Professor  
Pediatrics and Microbiology  
Section Chief of Immunology  
Children's Hospital of Philadelphia  
Philadelphia, Pennsylvania [86, 93]

**Ann M. Dvorak, M.D.**

Professor of Pathology  
Department of Pathology  
Harvard Medical School  
Director, Electron Microscopy Laboratory  
Beth Israel Hospital  
Boston, Massachusetts [79]

**C. J. Eaves, Ph.D.**

Professor, Medical Genetics  
The Terry Fox Laboratory for Hematology/Oncology  
British Columbia Cancer Agency  
Vancouver, British Columbia, Canada [L4]

**Mayez A. El-Harake, M.D.**

Fellow, Hematology/Oncology Division  
University of Oklahoma Health Sciences Center  
Oklahoma City, Oklahoma [128, 129]

**Allan J. Erslev, M.D., D.Sc.**

Distinguished Professor of Medicine  
Cardeza Foundation for Hematologic Research  
Jefferson Medical College of Thomas Jefferson University  
Philadelphia, Pennsylvania [39-43, 48, 49, 59, 61, 69, 70, L7,  
L8, L18]

**Virgil F. Fairbanks, M.D.**

Consultant  
Department of Internal Medicine  
Division of Hematology  
Mayo Clinic  
Professor, Mayo Medical School  
Rochester, Minnesota [34, 46, 50, 51]

**Richard I. Fisher, M.D.**

Director, Oncology Institute  
Division of Hematology/Oncology  
Loyola University Stritch School of Medicine  
Maywood, Illinois [111]

**Louis Fiore, M.D.**

Assistant Professor of Medicine  
Boston University School of Medicine  
Hematology Section  
Boston Veterans Affairs Medical Center  
Boston, Massachusetts [146]

**Kenneth A. Foon, M.D.**

Director, Markey Cancer Center  
Professor and Chief  
Division of Hematology/Oncology  
Department of Medicine  
University of Kentucky  
Lexington, Kentucky [111]

**Charles W. Francis, M.D.**

Professor of Medicine  
Department of Medicine, Hematology Unit  
University of Rochester School of Medicine and Dentistry  
Rochester, New York [124, 142]

**Donald Gaffney, B.S.**

Laboratory Technician  
Department of Biochemistry  
University of Vermont  
Burlington, Vermont [121]

**Dennis K. Galanakis, M.D.**

Associate Professor  
Department of Pathology  
State University of New York  
Stony Brook, New York [L39]

**Stephen J. Galli, M.D.**

Professor of Pathology  
Harvard Medical School  
Director, Division of Experimental Pathology  
Beth Israel Hospital  
Boston, Massachusetts [79]

**Tomas Ganz, M.D., Ph.D.**

Professor of Medicine  
Department of Medicine  
University of California-Los Angeles School of Medicine  
Center for the Health Sciences  
Los Angeles, California [87, 88]

**Terri Gelbart, B.S.**

Research Assistant  
The Scripps Research Institute  
La Jolla, California [L17, L20]

**James N. George, M.D.**

Professor of Medicine  
Chief, Hematology/Oncology Section  
Department of Medicine  
University of Oklahoma Health Sciences Center  
Oklahoma City, Oklahoma [120, 127-130, L55]

**David Ginsburg, M.D.**

Professor of Internal Medicine and Human Genetics  
Investigator, Howard Hughes Medical Institute  
University of Michigan  
Ann Arbor, Michigan [138]

**Joan Cox Gill, M.D.**

Professor of Pediatrics  
Medical College of Wisconsin  
Blood Center of Southeastern Wisconsin  
Wautwatosa, Wisconsin [154]

**David W. Golde, M.D.**

Professor of Medicine  
Cornell University Medical College  
Professor of Molecular Pharmacology and Therapeutics  
Cornell University Graduate School of Medical Sciences  
Head, Division of Hematologic Oncology  
Memorial Sloan-Kettering Cancer Center  
New York, New York [16, 76]

**Harvey R. Gralnick, M.D.**

Chief, Hematology Service Clinical Center  
National Institutes of Health  
Bethesda, Maryland [136, 138]

**David Green, M.D.**

Professor of Medicine  
Northwestern University Medical School  
Chief of Medicine  
Rehabilitation Institute of Chicago  
Chicago, Illinois [139]

**Janine Breton-Gorius, M.D.**

Director of Research INSERM  
INSERM U · 91 Hôpital Henri Mondor  
Creteil, France [32, 118]

**Jack Hirsh, M.D.**

Hamilton Civic Hospitals Research Center  
Henderson General Division  
Hamilton, Ontario, Canada [L3]

**Robert S. Hillman, M.D.**

Professor of Medicine  
University of Vermont School of Medicine  
Burlington, Vermont  
Chief of Medicine, Maine Medical Center  
Portland, Maine [68]

**Wen-Zhe Ho, M.D.**

Research Assistant Professor  
Children's Hospital of Philadelphia  
Philadelphia, Pennsylvania [86]

**Maureane Hoffman, M.D., Ph.D.**

Assistant Professor of Pathology  
Duke University School of Medicine  
Durham, North Carolina [135]

**Sandra J. Horning, M.D.**

Associate Professor of Medicine  
Division of Oncology  
Stanford University School of Medicine  
Stanford, California [110]

**Leon W. Hoyer, M.D.**

Adjunct Professor of Genetics  
George Washington University  
Washington, D.C. [140]  
Director, Holland Laboratory  
American Red Cross Biomedical Services  
Rockville, Maryland

**Mae B. Hultin, M.D.**

Professor of Medicine, Division of Hematology  
State University of New York  
Health Sciences Center  
Stony Brook, New York [L37, L41, L45]

**Eric A. Jaffe, M.D.**

Professor of Medicine  
Cornell University Medical College  
New York, New York [125]

**Ann A. Jakubowski, M.D., Ph.D.**

Assistant Professor, Department of Medicine  
Memorial Sloan-Kettering Cancer Center  
New York, New York [16]

**Jolyon Jesty, M.D.**

Professor of Medicine  
Division of Hematology School of Medicine  
Health Sciences Center  
State University at Stony Brook  
Stony Brook, New York [122]

**Petr Jarolim, M.D., Ph.D.**

Assistant Professor of Medicine  
Tufts University School of Medicine  
St. Elizabeth's Medical Center  
Boston, Massachusetts [52]

**Marshall E. Kadin, M.D.**

Associate Professor of Pathology  
Department of Hemopathology  
Beth Israel Hospital  
Harvard Medical School  
Boston, Massachusetts [108]

**A. Barry Kay, M.D., Ph.D.**

National Heart & Lung Institute  
Department of Allergy and Clinical Immunology  
London, England [78, 84]

**Neil E. Kay, M.D.**

Professor of Medicine  
Department of Internal Medicine  
Division of Hematology/Oncology  
University of Kentucky Medical Center  
Lexington, Kentucky [93]

**Haewon C. Kim, M.D.**

Associate Director of Pediatrics  
Division of Hematology  
The University of Pennsylvania School of Medicine  
Medical Director, Transfusion/Apheresis Service  
Children's Hospital of Philadelphia  
Philadelphia, Pennsylvania [L9-L12]

**Thomas J. Kipps, M.D., Ph. D.**

Professor, Department of Medicine  
University of California, San Diego  
San Diego, California [6, 14, 96, 97, 100, 101, 106, 107, 115,  
116, L21, L22, L29]

**Diane M. Komp, M.D.**

Professor of Pediatrics  
Department of Pediatrics  
Yale University School of Medicine  
New Haven, Connecticut [91]

**Wanda Kuhl, B.A., B.S.**

Scientific Associate  
The Scripps Research Institute  
La Jolla, California [L31]

**Stephen A. Landaw, Ph.D.**

Professor of Medicine and Associate Professor of Radiology  
SUNY-Health Science Center  
Associate Chief of Staff  
Research and Development  
Veteran's Administration Medical Center, Syracuse  
Syracuse, New York [L2]

**Che-Leung Law, M.D., Ph.D.**

Research Assistant Professor  
Department of Microbiology  
University of Washington  
Seattle, Washington [98]

**Michelle M. LeBeau, Ph.D.**

Associate Professor  
Department of Medicine, Hematology/Oncology  
The University of Chicago  
Chicago, Illinois [12]

**Tucker W. LeBien, Ph.D.**

Professor  
Department of Laboratory Medicine and Pathology  
University of Minnesota Medical School  
Minneapolis, Minnesota [95]

**John P. Leddy, M.D.**

Professor of Medicine and of Microbiology  
Chief, Clinical Immunology/Rheumatology Unit  
Department of Medicine  
University of Rochester  
Rochester, New York [64-66]

**Robert I. Lehrer, M.D.**

Professor of Medicine  
Department of Medicine  
University of California-Los Angeles School of Medicine  
Center for the Health Sciences  
Los Angeles, California [87, 88]

**Alexandra M. Levine, M.D.**

Professor of Medicine  
Chief, Division of Hematology  
University of Southern California School of Medicine  
Los Angeles, California [103]

**Arnold J. Levine, Ph.D.**

Hary C. Weiss Professor in the Life Sciences  
Department of Molecular Biology  
Lewis Thomas Laboratory  
Princeton, New Jersey [13]

**Marshall A. Lichtman, M.D.**

Professor and Dean  
School of Medicine and Dentistry  
Hematology Unit  
University of Rochester Medical Center  
Rochester, New York [4, 23, 26-28, 30, 80, 85, 89-91, 113]

**Howard A. Liebman, M.D.**

Associate Professor of Medicine and Pathology  
University of Southern California School of Medicine  
Los Angeles, California [103]

**Johnson M. Liu, M.D.**

Clinical Associate  
Hematology Branch  
National Heart, Lung, and Blood Institute  
National Institutes of Health  
Bethesda, Maryland [19]

**Gwynn D. Long, M.D.**

Assistant Professor of Medicine  
Stanford University Medical Center  
Stanford, California [18]

**Joseph Loscalzo, M.D., Ph.D.**

Professor, Department of Medicine and Biochemistry  
Director, Whitaker Cardiovascular Institute  
Vice Chairman, Department of Medicine  
Chief, Cardiovascular Medicine  
Boston University School of Medicine  
Boston, Massachusetts [143, 147]

**Thomas P. Loughran, Jr., M.D.**

Professor of Medicine and Microbiology and Immunology  
SUNY Health Sciences Center at Syracuse  
Chief of Hematology  
Veterans Administration Medical Center  
Syracuse, New York [108]

**Naomi L. C. Luban, M.D.**

Professor of Pediatrics and Pathology  
Director, Blood Bank & Hematology  
Department of Laboratory Medicine  
The George Washington University Medical Center  
Washington, D.C. [67]

**Lucio Luzzatto, M.D.**

Chairman  
Department of Human Genetics  
Memorial Sloan-Kettering Cancer Center  
New York, New York [L8]

**Kenneth G. Mann, Ph.D.**

Professor and Chairman  
Biochemistry Department  
University of Vermont  
Burlington, Vermont [121]

**Victor J. Marder, M.D.**

Professor of Medicine  
Hematology Unit, Department of Medicine  
University of Rochester School of Medicine & Dentistry  
Rochester, New York [124, 142]

**Jose Martinez, M.D.**

Professor of Medicine  
Associate Director for Research Education  
Cardeza Foundation for Hematologic Research  
Department of Medicine  
Jefferson Medical College of Thomas Jefferson University  
Philadelphia, Pennsylvania [60]



**S. P. Masouredis, M.D., Ph.D.**

Professor Emeritus  
Department of Pathology  
University of California, San Diego School of Medicine  
La Jolla, California [151]

**Alvin M. Mauer, M.D.**

Professor of Medicine  
College of Medicine  
Chief, Division of Hematology/Oncology  
The University of Tennessee Health Science Center  
Memphis, Tennessee [105]

**Jeffrey McCullough, M.D.**

Professor, Department of Laboratory Medicine and Pathology  
University of Minnesota Hospital  
Minneapolis, Minnesota [150]

**Jan M. McDonagh, Ph.D.**

Associate Professor  
Department of Pathology  
Beth Israel Hospital  
Harvard Medical School  
Boston, Massachusetts [137]

**Jay E. Menitove, M.D.**

Professor of Internal Medicine  
Deputy Director, Medical Services  
Hoxworth Blood Center  
University of Cincinnati  
Cincinnati, Ohio [154]

**Joseph P. Miletich, Ph.D.**

Professor of Medicine and Pathology  
Laboratory Medicine  
Washington University  
St. Louis, Missouri [L33–L35, L38, L40, L51, L52]

**Robert R. Montgomery, M.D.**

Professor of Pediatrics and Pathology  
The Medical College of Wisconsin  
Vice-President and Director of Research  
Blood Research Institute  
The Blood Center of Southeastern Wisconsin  
Milwaukee, Wisconsin [154]

**Michael W. Morris, B.S., M.S.**

Associate Professor of Medical Technology  
College of Health Related Professions  
Manager, Department of Pathology  
SUNY Syracuse Health Science Center  
Syracuse, New York [2, L1]

**Scott Murphy, M.D.**

Professor of Medicine  
Cardeza Foundation for Hematologic Research  
Thomas Jefferson University  
Philadelphia, Pennsylvania [153]

**Douglas A. Nelson, M.D.**

Professor Emeritus  
Department of Pathology  
SUNY Health Science Center  
Syracuse, New York [2, 3, L1, L23, L25]

**Yale Nemerson, M.D.**

Professor  
Department of Medicine  
Mt. Sinai School of Medicine  
New York, New York [122]

**W. Stephen Nichols, Jr., M.D.**

Director, Division of Molecular Pathology  
Department of Pathology and Laboratory Medicine  
Cedars-Sinai Medical Center  
Los Angeles, California [6]

**Arthur W. Nienhuis, M.D.**

St. Jude Professor of Pediatrics and Medicine  
St. Jude's Research Hospital  
Director  
St. Jude's Children's Hospital  
Memphis, Tennessee [19]

**Jacob Nusbacher, M.D.**

Visiting Professor of Medicine  
Sackler School of Medicine  
Tel Aviv University  
Ramat Aviv, Israel  
Director, Blood Bank  
Meir Hospital  
Kfar-Saba, Israel [152, 155]

**Frank A. Oski, M.D.**

Given Professor  
Director, Department of Pediatrics  
Pediatrician-in-Chief  
The Johns Hopkins Hospital  
The Johns Hopkins University School of Medicine  
Baltimore, Maryland [47]

**Charles H. Packman, M.D.**

Professor of Medicine, Hematology Unit  
University of Rochester School of Medicine and Dentistry  
Rochester, New York [64–66]

**Jiri Palek, M.D.**

Professor of Medicine  
Chairman, Department of Biomedical Research  
Chief, Division of Hematology/Oncology  
St. Elizabeth's Medical Center  
Boston, Massachusetts [37, 52, 53]

**Richard B. Patt, M.D.**

Associate Professor of Anesthesiology and Neuro-Oncology  
Deputy Chief, Pain and Symptom Management Section  
University of Texas M.D. Anderson Cancer Center  
Houston, Texas [21]

**Richard Payne, M.D.**

Associate Professor of Neurology  
Chief, Pain and Symptom Management Section  
University of Texas M.D. Anderson Cancer Center  
Houston, Texas [21]

**Lawrence D. Petz, M.D.**

Professor of Pathology and Laboratory Medicine  
Director, Transfusion Medicine  
University of California-Los Angeles Medical Center  
Los Angeles, California [148]

**Peter J. Quesenberry, M.D.**

Professor of Medicine  
 University of Massachusetts Medical Center  
 Director, Cancer Center  
 Worcester, Massachusetts [22]

**Helen M. Ranney, M.D.**

Professor Emeritus  
 Department of Medicine  
 University of California, San Diego  
 Alliance Pharmaceuticals Corporation  
 San Diego, California [38]

**Emily G. Reisner, Ph.D.**

Associate Clinical Professor  
 Department of Pathology  
 Director, Hematology Laboratory Service  
 Duke University Medical Center  
 Durham, North Carolina [149]

**Harold R. Roberts, M.D.**

Sarah Graham Kenan Professor of Medicine  
 Chief, Division of Hematology  
 Director, Center for Thrombosis and Hemostasis  
 School of Medicine  
 University of North Carolina  
 Chapel Hill, North Carolina [135]

**Bruce A. Robbins, M.D.**

Vice Chairman  
 Department of Pathology  
 Head, Division of Laboratory Medicine  
 Sections of Clinical Immunology & Immunopathology  
 Director, Immunopathology Training Program  
 Scripps Clinic and Research Foundation  
 La Jolla, California [107]

**Fred S. Rosen, M.D.**

James L. Gamble Professor of Pediatrics  
 Harvard Medical School  
 Boston, Massachusetts [102]

**Robert D. Rosenberg, M.D., Ph.D.**

William B. Castle Professor of Medicine  
 Harvard Medical School  
 Chief, Molecular Medicine Unit  
 Beth Israel Hospital  
 Professor of Biochemistry  
 Department of Biology and Whitaker College  
 Massachusetts Institute of Technology  
 Cambridge, Massachusetts [123]

**Janet D. Rowley, M.D.**

Professor, Department of Medicine  
 Section of Hematology/Oncology  
 The University of Chicago  
 The Pritzker School of Medicine  
 Chicago, Illinois [12]

**Shigeru Sassa, M.D., Ph.D.**

Associate Professor  
 Head, Biochemical Hematology  
 The Rockefeller University  
 New York, New York [71]

**Andrew I. Schafer, M.D.**

WA and Deborah Moncrief Professor and Vice Chairman  
 Department of Medicine  
 Baylor College of Medicine  
 Houston, Texas [31]

**Paul Schneiderman, M.D.**

Associate Clinical Professor of Dermatology  
 College of Physicians & Surgeons  
 Columbia University  
 New York, New York [134]

**Elias Schwartz, M.D.**

Professor and Chairman  
 Department of Pediatrics  
 Physician-in-Chief  
 The Children's Hospital of Philadelphia  
 Philadelphia, Pennsylvania [L9-L12]

**George B. Segel, M.D.**

Professor of Pediatrics and of Medicine  
 Director, Division of Pediatric Genetics  
 University of Rochester Medical Center  
 Rochester, New York [8]

**Uri Seligsohn, M.D.**

Professor of Hematology  
 Sackler School of Medicine  
 Tel Aviv University  
 Chairman, Department of Hematology  
 Director, Institute of Thrombosis and Hemostasis  
 Chaim Sheba Medical Center  
 Tel-Hashomer, Israel [141]

**Richard K. Shadduck, M.D.**

Clinical Professor of Medicine  
 Director, Western Pennsylvania Cancer Institute  
 University of Pittsburgh School of Medicine  
 Western Pennsylvania Hospital  
 Pittsburgh, Pennsylvania [24]

**Vijay S. Sharma, Ph.D.**

Professor of Medicine in Residence  
 Department of Medicine  
 University of California-San Diego  
 La Jolla, California [38]

**Sanford J. Shattil, M.D.**

Professor of Medicine  
 Hematology/Oncology Division  
 University of Pennsylvania  
 Philadelphia, Pennsylvania [133]

**Joseph E. Smith, D.V.M., Ph.D.**

Professor, Department of Pathology and Microbiology  
 Kansas Veterinary Medical Center  
 Kansas State University  
 Manhattan, Kansas [10]

**James E. Smolen, Ph.D.**  
Research Scientist and Associate Professor  
Division of Hematology/Oncology  
Department of Pediatrics  
University of Michigan  
Ann Arbor, Michigan [77]

**Elizabeth Steinhaus, M.D.**  
Staff Fellow  
Surgery Branch  
National Cancer Institute  
National Institutes of Health  
Bethesda, Maryland [20]

**Russell P. Tracy, Ph.D.**  
Associate Professor  
Department of Pathology  
University of Vermont College of Medicine  
Burlington, Vermont [L36, L42, L46-L50]

**Giorgio Trinchieri, M.D.**  
Professor and Chair  
Immunology Program  
The Wistar Institute  
Philadelphia, Pennsylvania [99]

**Ara A. Vaporciyan, M.D., Ph.D.**  
Professor and Chair  
Department of Surgery  
University of Texas Health Science Center  
Houston, Texas [7]

**Christopher E. Walsh**  
Clinical Associate  
Hematology Branch  
National Heart, Lung, and Blood Institute  
National Institutes of Health  
Bethesda, Maryland [19]

**Peter A. Ward, M.D.**  
Professor and Chair  
Department of Pathology  
The University of Michigan Medical School  
Ann Arbor, Michigan [7]

**A. J. Wardlaw, M.D.**  
Department of Respiratory Medicine  
Glenfield General Hospital  
University of Leicester School of Medicine  
Leicester, England [78, 84]

**J. Anthony Ware, M.D.**  
Associate Professor of Medicine  
Cardiovascular Division  
Harvard Medical School  
Beth Israel Hospital  
Boston, Massachusetts [119]

**D. J. Weatherall, M.D.**  
Regius Professor of Medicine  
Institute of Molecular Medicine  
University of Oxford  
John Radcliffe Hospital  
Headington, Oxford, England [55]

**Harvey J. Weiss, M.D.**  
Professor of Medicine  
Columbia University College of Physicians and Surgeons  
Chief, Division of Hematology/Oncology  
St. Luke's-Roosevelt Hospital Center  
New York, New York [145]

**Leon P. Weiss, M.D.**  
Professor of Cell Biology  
School of Veterinary Medicine  
Professor of Hematology  
University of Pennsylvania School of Medicine  
Philadelphia, Pennsylvania [5]

**William J. Williams, M.D.**  
Edward C. Reifenshtein Professor of Medicine  
Department of Medicine  
State University of New York  
Health Science Center  
Syracuse, New York [1-3, 9, 126, 131, L1, L32]

**Wyndham Wilson, M.D.**  
Special Assistant to the Director  
Division of Cancer Treatment  
National Cancer Institute  
Bethesda, Maryland [15]

# Preface

*Williams Hematology* is designed to provide comprehensive, readable coverage of clinical hematology, while bringing to the reader the scientific underpinnings required for the rational practice of our subspecialty. After publication of the first edition in 1972, the rapid progress in the field necessitated the publication of new editions every five to seven years. The five years that have passed since the fourth edition of *Williams Hematology* were marked by accelerated progress in many areas in the field of hematology, including blood formation, the functioning of the immune system, and hemostasis and thrombosis. This progress has been translated into new and more powerful diagnostic tests and treatments for blood diseases.

The fifth edition of *Williams Hematology* represents a major revision of the text. There are 30 new chapters dealing with subjects such as signal transduction, the use of venous access devices, pain management, cell surface markers, and gene transfer. In keeping with our long-standing policy, the authorship of many chapters has been rotated; 105 chapters have new authors in the fifth edition. Two of the four editors who participated in all four of the previous editions have retired from their editorial responsibilities. Both have made enormous contributions to the success of this text. We continue to refer to the book as "*Williams Hematology*" as a well-deserved tribute to Dr. William J. Williams who carried the primary responsibility for initiating the writing of this text and shepherding it through all previous editions. We are fortunate to have enlisted two new editors with broad expertise in hematology and special knowledge in two rapidly changing fields. Dr. Thomas Kipps' understanding of immunology and that of Dr. Barry Collier of hemostasis and thrombosis have allowed us to strengthen these areas of the book.

Throughout the revisions of *Williams Hematology* we have maintained comprehensive coverage without expanding the text beyond the limits of one volume. Although 95 experts have contributed to this edition, each chapter has been reviewed by all of the editors. Many chapters have been revised extensively to avoid duplication and provide integration with other chapters and to ensure the proper balance and organization of clinical and basic science content. In this way we have attempted to avoid problems sometimes associated with multiauthored textbooks. Our goal has been to create a comprehensive text that is not redundant and we also organized the text so that it is useful to the clinician and basic researcher. Extensive, up-to-date references are provided to allow the reader to explore topics in greater detail. This volume has been planned to take into account the marked increase in knowledge of the hematologic malignancies, immunohematology, and hemostasis and thrombosis. We have provided a balanced and comprehensive source of information about disorders of blood cells and of coagulation proteins. The appendix has been recast as a laboratory section that provides the principles, general techniques, and interpretation of over sixty tests

used for the diagnosis or management of hematologic diseases. We believe that this will be especially useful to the reader since information of this sort, as it is applied to hematology, is difficult to find in one place in this format. The detailed directions for performing tests may be found in the previous edition and in several laboratory manuals that are now available. Thus, we have made the coverage of hematology in this text comprehensive to include clinical, basic scientific, and laboratory descriptions. We have organized the material to provide the reader with a well-integrated textbook, not with a collection of exhaustive reviews.

The production of such a text has required the cooperation of our many contributors. We are grateful to them for providing us with the chapters that have made possible this comprehensive work. In this edition we have revised and expanded the color plates. Most of the blood, marrow, and lymph node photomicrographs were prepared by Jean A. Shafer, B.S., M.S., Assistant Professor of Medicine (Hematology) and of Pathology at the University of Rochester School of Medicine and Dentistry. Joshua Z. Sichel, M.D., Assistant Professor of Pathology, University of Rochester School of Medicine and Dentistry, provided the lymph node sections and the photomicrographs of Plates IX-6 and XVII-4 to XVII-10. Janet Rowley, M.D., and Michelle M. LeBeau, M.D., provided the photomicrographs for Plate XVIII. Paul Schneiderman, M.D., provided the photomicrographs for Plate XIX-1 to XIX-42. Virgil Fairbanks, M.D., provided the photomicrograph for Plate XIX-43 and Karl G. Blume, M.D., provided Plate XIX-44 and XIX-45.

Several colleagues were helpful to us in reviewing and criticizing parts of the text. We thank Dr. Ronald Nagel of the Albert Einstein College of Medicine, Dr. Daniel Salomon of the Scripps Research Institute, Dr. Jeffrey L. Kutok of the SUNY at Stony Brook, Dr. Jonathan Miller of the SUNY Health Science Center at Syracuse, and Dr. Jacob M. Rowe of the University of Rochester School of Medicine and Dentistry, Rochester, for their contributions in this regard. Organizing and tracking the production of the many chapters of this text and troubleshooting whenever necessary was an awesome task, and we are grateful to Mrs. Jane Verenini for having performed it and for having coordinated the production of *Williams Hematology* in La Jolla. We also thank Saralee LaVigueur, Audrey Majors, Shirley Murray, Maria Polintan, Lisa Preedom, Suzanne Rivera, Elizabeth Kearney Spreng, and Jane Uhle for their attention to detail and their assistance in bibliograph searches, record-keeping, typing, proofreading, and communications with the publisher, editors, and authors. Last but not least, it is the families of the editors and their infinite patience that made this edition possible.

Department of Pathology

The University of Michigan Medical School

Ann Arbor, Michigan 48106



### SI Unit Conversion Table

Constituent <sup>a</sup>	Traditional units	Multiplication factor <sup>b</sup>	SI units <sup>c</sup>
δ-Aminolevulinic acid (U)	mg per day	7.63	μmol per day
Bilirubin			
Direct (S)	mg per dl	17.1	μmol per liter
Total (S)	mg per dl	17.1	μmol per liter
Calcium (S)	mg per dl	0.25	mmol per liter
Coproporphyrin (U)	μg per day	1.5	nmol per day
Erythrocyte count (B)	number per μl	10 <sup>6</sup>	number per liter
Fibrinogen <sup>d</sup> (Factor I) (P)	mg per dl	0.01	g per liter
	mg per dl	0.029	μmol per liter
Folic acid (S)	ng per ml	1.0	μg per liter
	ng per ml	2.27	nmol per liter
Haptoglobin (S)	mg per dl	0.01	g per liter
Hematocrit (B)	%	0.01	ratio
Hemoglobin <sup>1</sup> (B)	g per dl	1.0	g per dl
Iron (S)	μg per dl	0.179	μmol per liter
Iron-binding capacity (S)	μg per dl	0.179	μmol per liter
Leukocyte count (B)	number per μl	10 <sup>6</sup>	number per liter
Mean corpuscular hemoglobin	pg	1.0	pg
Mean corpuscular hemoglobin concentration	%	1.0	g per dl
Mean corpuscular volume	μm <sup>3</sup>	1.0	fl
Packed cell volume (B)	%	0.01	ratio
Phosphorus (S)	mg per dl	0.323	mmol per liter
Platelet count (B)	number per μl	10 <sup>6</sup>	number per liter
Prothrombinogen (U)	mg per day	4.42	μmol per day
Protoporphyrin (erythrocyte)	μg per dl	0.018	μmol per liter
Reticulocyte count (B)	%	0.01	ratio
	number per μl	10 <sup>6</sup>	number per l
Transferrin (S)	mg per dl	0.01	g per l
Urea nitrogen (B)	mg per dl	0.36	mmol per liter
Uric acid (S)	mg per dl	0.0595	mmol per liter
Uroporphyrin (U)	μg per day	1.2	nmol per day
Vitamin B <sub>12</sub> (S)	pg per ml	1.0	ng per liter
	pg per ml	0.738	pmol per liter

<sup>a</sup>The following abbreviations are used: B = blood; S = serum; P = plasma; U = urine.

<sup>b</sup>Conventional units multiplied by this factor will yield SI units.

<sup>c</sup>The following units are used:

fl = femtoliter (10 <sup>-15</sup> liter)	fmol = femtomole	fg = femtogram
pl = picoliter (10 <sup>-12</sup> liter)	pmol = picomole	pg = picogram
nl = nanoliter (10 <sup>-9</sup> liter)	nmol = nanomole	ng = nanogram
μl = microliter (10 <sup>-6</sup> liter)	μmol = micromole	μg = microgram
ml = milliliter (10 <sup>-3</sup> liter)	mmol = millimole	mg = milligram
dl = deciliter (10 <sup>-1</sup> liter)		

<sup>d</sup>The molar concentration is calculated assuming a molecular weight of 340,000.

<sup>e</sup>Hemoglobin is not usually expressed in molar terms because of uncertainty regarding the polymeric state of the molecule. If the unit molecular weight is assumed to be 16,000, the multiplication factor is 0.62 to convert g per dl to mmol per liter [2]. If a molecular weight of 64,500 is assumed, the conversion factor is 0.155 [3].

SOURCES:

1. Baron DN, Broughton PMG, Cohen M, Lansley TS, Lewis SM, Shinton NK: The use of SI units in reporting results obtained in hospital laboratories. *J Clin Pathol* 27:590, 1974.
2. Young DS: "Normal laboratory values" (case records of the Massachusetts General Hospital) in SI units. *N Engl J Med* 292:795, 1975.
3. Lehmann HP: Metrication of clinical laboratory data in SI units. *Am J Clin Pathol* 65:2, 1976.

# Contents

Contributors .....	xxv
Preface .....	liii
SI Unit Conversion Table .....	xxxv

## PART I Clinical Evaluation of the Patient

CHAPTER 1	
Approach to the patient .....	1
<i>William J. Williams</i>	
CHAPTER 2	
Examination of the blood .....	8
<i>William J. Williams / Michael W. Morris / Douglas A. Nelson</i>	
CHAPTER 3	
Examination of the marrow .....	15
<i>William J. Williams / Douglas A. Nelson</i>	

## PART II General Hematology

CHAPTER 4	
Structure of the marrow .....	25
<i>Camille N. Abboud / Marshall A. Lichtman</i>	
CHAPTER 5	
Structure of the spleen .....	38
<i>Leon Weiss</i>	

CHAPTER 6	
Structure and function of other lymphoid tissues .....	43
<i>W. Stephen Nichols, Jr. / Thomas J. Kipps</i>	

CHAPTER 7	
The inflammatory response .....	48
<i>Ara A. Vaporciyan / Peter A. Ward</i>	

CHAPTER 8	
Hematology of the newborn .....	57
<i>George B. Segel</i>	

CHAPTER 9	
Hematology in the aged .....	72
<i>William J. Williams</i>	

CHAPTER 10	
Comparative hematology .....	77
<i>Joseph E. Smith</i>	

### PART III

#### Molecular Hematology

CHAPTER 11	
Genetic principles and molecular biology .....	89
<i>Ernest Beutler</i>	

CHAPTER 12	
Cytogenetics .....	98
<i>Michelle M. LeBeau / Janet D. Rowley</i>	

CHAPTER 13	
Principles of cell regulation .....	107
<i>Arnold J. Levine</i>	

CHAPTER 14	
The cluster of differentiation (CD) antigens .....	113
<i>Thomas J. Kipps</i>	

### PART IV

#### Therapeutic Principles

CHAPTER 15	
Pharmacology and toxicity of antineoplastic drugs .....	143
<i>Bruce A. Chabner / Wyndham Wilson</i>	

CHAPTER 16	
Therapeutic use of cytokines .....	155
<i>Ann A. Jakubowski / David W. Golde</i>	
CHAPTER 17	
Treatment of infections in the immunocompromised host .....	166
<i>Steven M. Beutler</i>	
CHAPTER 18	
Allogeneic and autologous marrow transplantation .....	172
<i>Gwynn D. Long / Karl G. Blume</i>	
CHAPTER 19	
Gene therapy .....	195
<i>Christopher E. Walsh / Johnson M. Liu / Arthur W. Nienhuis</i>	
CHAPTER 20	
The use of venous access devices .....	200
<i>Elizabeth Steinhaus / H. Richard Alexander</i>	
CHAPTER 21	
Pain management .....	203
<i>Richard B. Patt / Richard Payne</i>	

## PART V

### The Hemopoietic Stem Cell

CHAPTER 22	
Hemopoietic stem cells, progenitor cells, and cytokines .....	211
<i>Peter J. Quesenberry</i>	
CHAPTER 23	
Classification and clinical manifestations of the hemopoietic stem cell disorders .....	229
<i>Marshall A. Lichtman</i>	
CHAPTER 24	
Aplastic anemia .....	238
<i>Richard K. Shadduck</i>	
CHAPTER 25	
Paroxysmal nocturnal hemoglobinuria .....	252
<i>Ernest Beutler</i>	
CHAPTER 26	
Myelodysplastic disorders .....	257
<i>Marshall A. Lichtman / James K. Brennan</i>	