

Williams
Hematology
Fifth Edition

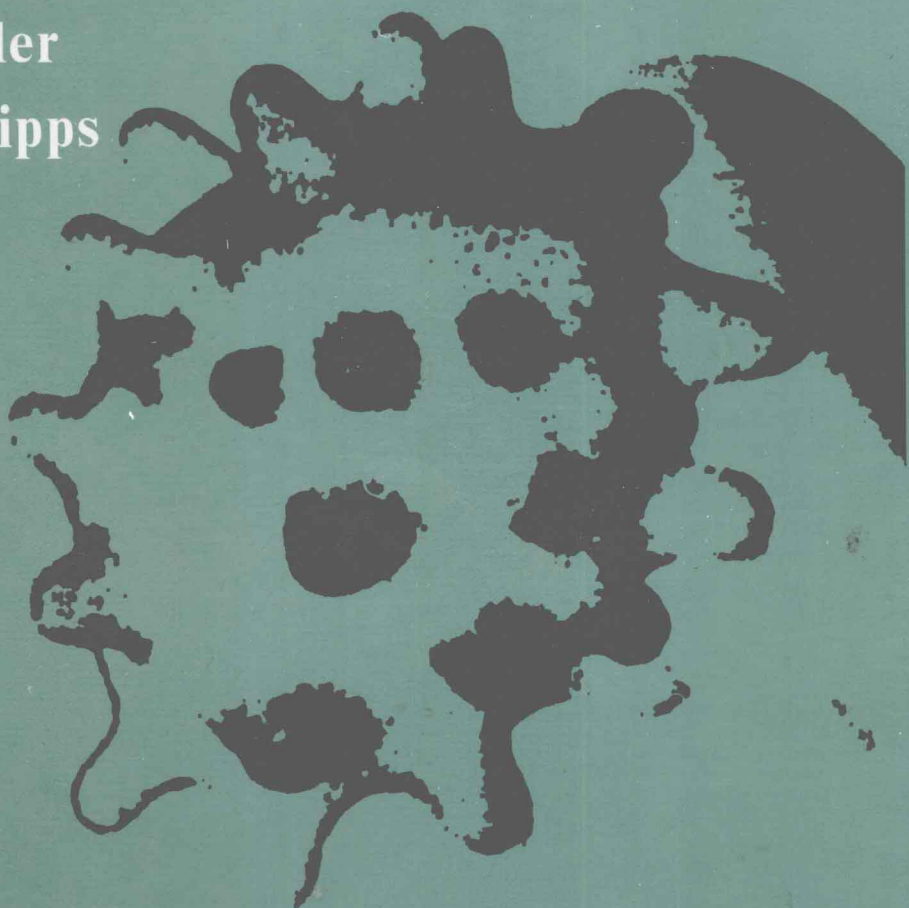
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Williams *Hematology* Fifth Edition

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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 multi-authored 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. Sickel, 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.

Project

Throughout the production of *Williams Hematology* we have maintained close contact with our contributors. In fact, we have had a number of meetings with them. Although it is not possible to list all the names of the contributors, we are grateful to all of them for their contributions. Many chapters have been revised and improved. We are particularly grateful to those who have provided us with clinical and laboratory data. This volume has been planned to serve as a reference work for the hematologist and the clinician. We have provided a balance of basic and clinical information. The question has been asked as to why we have not included the laboratory techniques and interpretation of over 2000 tests.

SI Unit Conversion Table

Constituent ^a	Traditional units	Multiplication factor ^b	SI units ^c
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 ⁶	number per liter
Fibrinogen ^d (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 ^f (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 ⁶	number per liter
Mean corpuscular			
hemoglobin	pg	1.0	pg
Mean corpuscular			
hemoglobin concentration	%	1.0	g per dl
Mean corpuscular volume	μm ³	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 ⁶	number per liter
Prophobilinogen (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 ⁶	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
Urophorphyrin (U)	μg per day	1.2	nmol per day
Vitamin B ₁₂ (S)	pg per ml	1.0	ng per liter
	pg per ml	0.738	pmol per liter

^aThe following abbreviations are used: B = blood; S = serum; P = plasma; U = urine.

^bConventional units multiplied by this factor will yield SI units.

^cThe following units are used:

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

^dThe molar concentration is calculated assuming a molecular weight of 340,000.

^eHemoglobin 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.

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