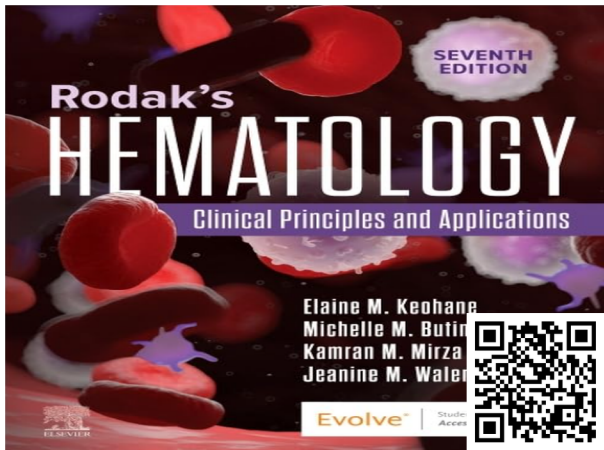


Rodak's Hematology 7th Edition PDF

Visit the link below to download the full version of the ebook

[DOWNLOAD NOW](#)



Scan to Download
or Type the Link

ebook.ac/rodak7e

r h
SEVENTH
EDITION

Rodak's

HIMMILIH

Clinical Principles and Applications

A
1
Elaine M. Keahane
Michelle M. Butina
Kamran M. Mirza
Jeanine M. Walenga



Evolve®

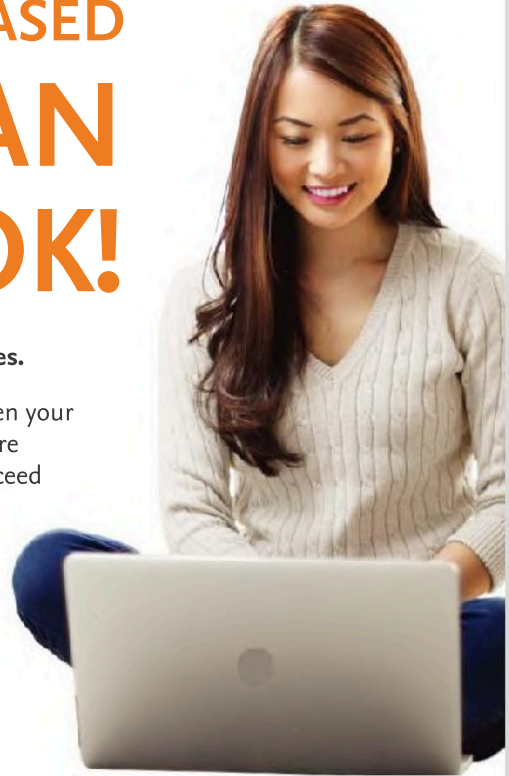
Student Resources on Evolve
Access Code Inside

Evolve[®]

YOU'VE JUST PURCHASED MORE THAN A TEXTBOOK!

Enhance your learning with Evolve Student Resources.

These online study tools and exercises can help deepen your understanding of textbook content so you can be more prepared for class, perform better on exams, and succeed in your course.

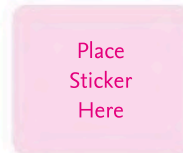


Activate the complete learning experience that comes with each NEW textbook purchase by registering with your scratch-off access code at

<http://evolve.elsevier.com/Rodak/>

If your school uses its own Learning Management System, your resources may be delivered on that platform. Consult with your instructor.

If you rented or purchased a used book and the scratch-off code at right has already been revealed, the code may have been used and cannot be re-used for registration. To purchase a new code to access these valuable study resources, simply follow the link above.



REGISTER TODAY!



You can now purchase Elsevier products on Evolve!
Go to evolve.elsevier.com/shop to search and browse for products.

SEVENTH
EDITION

Rodak's

HEMATOLOGY

Clinical Principles and Applications

**SEVENTH
EDITION**

Rodak's

HEMATOLOGY

Clinical Principles and Applications

**Elaine M. Keohane, PhD, MLS(ASCP)
SH^{CM}**

Professor Emeritus, Clinical Laboratory and Medical
Imaging Sciences
School of Health Professions
Rutgers, The State University of New Jersey
Newark, New Jersey

**Michelle Montgomery Butina, PhD,
MLS(ASCP)^{CM}**

Associate Professor, Pathology, Anatomy, and
Laboratory Medicine
Vice Chair, Biomedical Laboratory Diagnostics
Program Director, Medical Laboratory Science
School of Medicine
West Virginia University
Morgantown, West Virginia

**Kamran M. Mirza, MD, PhD, FCAP,
FASCP, MLS(ASCP)**

Godfrey D. Stobbe Professor of Pathology Education
Clinical Professor of Pathology
Assistant Chair for Education Programs
Director, Division of Education Programs
Pathology
Michigan Medicine
Ann Arbor, Michigan

**Jeanine M. Walenga, PhD,
MLS(ASCP)^{HCM}**

Professor, Thoracic-Cardiovascular Surgery, Pathology,
and Physiology
Co-Director, Hemostasis and Thrombosis Research Unit
Stritch School of Medicine
Loyola University Chicago
Laboratory Director, Clinical Coagulation
Laboratory Director, Urinalysis and Medical Microscopy
Associate Director, Point of Care & Referred Testing
Pathology and Laboratory Medicine
Loyola University Health System
Maywood, Illinois



Elsevier
3251 Riverport Lane
St. Louis, Missouri 63043

RODAK'S HEMATOLOGY: CLINICAL PRINCIPLES AND APPLICATIONS,
SEVENTH EDITION

ISBN: 978-0-323-93650-7

Copyright © 2025 by Elsevier, Inc. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

Publisher's note: Elsevier takes a neutral position with respect to territorial disputes or jurisdictional claims in its published content, including in maps and institutional affiliations.

No part of this publication may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, recording, or any information storage and retrieval system, without permission in writing from the publisher. Details on how to seek permission, further information about the Publisher's permissions policies and our arrangements with organizations such as the Copyright Clearance Center and the Copyright Licensing Agency, can be found at our website: www.elsevier.com/permissions.

This book and the individual contributions contained in it are protected under copyright by the Publisher (other than as may be noted herein).

Notice

Practitioners and researchers must always rely on their own experience and knowledge in evaluating and using any information, methods, compounds or experiments described herein. Because of rapid advances in the medical sciences, in particular, independent verification of diagnoses and drug dosages should be made. To the fullest extent of the law, no responsibility is assumed by Elsevier, authors, editors or contributors for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products, instructions, or ideas contained in the material herein.

Previous editions copyrighted 2020, 2016, 2012, 2007, 2002, and 1995.

Senior Content Strategist: Kelly Skelton
Senior Content Development Specialist: Sarah Vora
Publishing Services Manager: Julie Eddy
Senior Project Manager: Rachel E. McMullen
Design Direction: Patrick Ferguson

Printed in India

Last digit is the print number: 9 8 7 6 5 4 3 2 1





Bernadette “Bunny” Beales Rodak, MS, MLS(ASCP)SH, Professor Emeritus of Pathology at Indiana University School of Medicine, died at the age of 70 on March 22, 2016. Bunny was the founding author and editor of *Hematology: Clinical Principles and Applications*, renamed *Rodak’s Hematology: Clinical Principles and Applications* in 2016. For over 20 years and through five editions, she dedicated countless hours to this indispensable text while mentoring five coeditors and more than 50 authors. Bunny considered the combination of this textbook and the *Clinical Hematology Atlas*, coauthored with friend and colleague **Jacqueline Carr** through five editions, to be her greatest contribution to medical laboratory hematology. Bunny’s work continues to inform and inspire a generation of medical laboratory practitioners and scholars as her textbook now offers its seventh edition.

Bunny authored numerous influential publications and conducted countless professional presentations. She chaired the American Society for Clinical Laboratory Science (ASCLS)

Hematology and Hemostasis Scientific Assembly and went on to coordinate all of the ASCLS Scientific Assemblies. She was editor-in-chief of the ASCLS *Clinical Laboratory Science* journal and led an online expert team to answer consumer laboratory-related questions. She was a member of the ASCLS Education and Research Fund, which in 2016, endowed the Bernadette “Bunny” Rodak Memorial Scholarship. In 2013, the ASCLS awarded her their coveted Robin H. Mendelson Memorial Award, recognizing her achievements and contributions to medical laboratory science worldwide.

While an acknowledged innovator and role model, Bunny was readily available to students and colleagues. She put everyone at ease and, being humble, never revealed her long history of community service. All her acquaintances attest to her kind and helpful spirit. Bunny’s colleagues miss her gracious smile and are honored to continue her work.

The Former and Current Editors

To my students for being great teachers, to my mentors for their guidance and support, and to Camryn, Riley, Harper, Stella, Jackie, Alana, Ken, and Jake for grounding me in the important things in life.

EMK

To my mentors, Kathryn Doig and Lynn Maedel, for sharing your inquisitiveness, enthusiasm, and vast knowledge of blood cells; your support and encouragement inspired me to take this exciting journey, and I am eternally grateful.

MMB

To John Anastasi and James Vardiman, for opening my eyes to the mystery, wonder, and beauty of hematopathology.

KMM

To my teachers, both formal and informal, for all this fascinating knowledge in the clinical laboratory sciences, which made possible my interesting career.

JMW

REVIEWERS

David Alter, MD, DABCC, MPH
Director of Clinical Chemistry
Associate Professor
Pathology and Laboratory Medicine
Emory University
School of Medicine
Atlanta, Georgia

C. L. Freeman, PhD, MLS(ASCP)BB
Program Director
Medical Laboratory Technology
Fayetteville Technical Community College
Fayetteville, North Carolina

Amy Kapanka, MS, MLS(ASCP)SC
Program Director
Medical Laboratory Technology
Professor
Hawkeye Community College
Waterloo, Iowa

Emily Kaufman, MLS(ASCP)^{CM}
Generalist Medical Laboratory Scientist
Formerly at Cleveland Clinic Akron General
Akron, Ohio

Angela Njoku, MS, MLS(ASCP)
Adjunct Professor
Clinical Laboratory Technology
St. Louis Community College
St. Louis, Missouri

Malissa S. Norfolk, MBA, MLS(ASCP)^{CM} SH^{CM}
Medical Laboratory Science
College of Nursing and Health Science
University of Massachusetts Dartmouth
Dartmouth, Massachusetts

CONTRIBUTORS

Nicholas C. Brehl, MEd, MLS(ASCP)^{CM}
Assistant Professor of Clinical Pathology and
Laboratory Medicine
Director, Health Professions Programs,
Medical Laboratory Science Program
Indiana University School of Medicine
Indianapolis, Indiana

**Michelle Montgomery Butina, PhD,
MLS(ASCP)^{CM}**
Associate Professor, Pathology, Anatomy,
and Laboratory Medicine
Vice Chair, Biomedical Laboratory
Diagnostics
Program Director, Medical Laboratory
Science
School of Medicine
West Virginia University
Morgantown, West Virginia

Karen S. Clark, BS, MLS(ASCP)^{SH}
POC Supervisor, Pathology
Baptist Memorial Hospital Memphis
Memphis, Tennessee

**Stephanie B. Cochrane, EdD, MS,
MLS(ASCP)^{CM}**
Lecturer, Clinical Laboratory and Medical
Imaging Sciences;
Clinical Coordinator, Medical Laboratory
Science Program
School of Health Professions
Rutgers University
Newark, New Jersey

Magdalena Czader, MD, PhD
Professor, Pathology and Laboratory
Medicine
Indiana University School of Medicine
Indianapolis, Indiana

Phillip J. DeChristopher, MD, PhD
Medical Director, Transfusion Medicine
Professor, Pathology and Laboratory
Medicine
Loyola University Health System
Maywood, Illinois

Kathryn Doig, PhD, MLS(ASCP)^{CM}^{SH}^{CM}
Professor Emeritus, Biomedical Laboratory
Diagnostics
Michigan State University
East Lansing, Michigan

George A. Fritsma, MS, MLS
Proprietor, The Fritsma Factor, Your
Interactive Hemostasis Resource
Precision BioLogic Inc.
Dartmouth, Nova Scotia, Canada
Clinical Associate Professor, Laboratory
Medicine
University of Alabama at Birmingham
Birmingham, Alabama
Clinical Associate Professor, Biomedical
Laboratory Diagnostics
Michigan State University
East Lansing, Michigan
Clinical Associate Professor, Clinical
Laboratory and Medical Imaging
Sciences
School of Health Professions
Rutgers University
Newark, New Jersey

Bertil Glader, MD, PhD
Professor, Pediatric Hematology/Oncology
Professor, Pathology
Stanford University
Stanford, California

Kathryn E. Golab, MLS(ASCP)^{CM}^{SH}^{CM}
Clinical Laboratory Utilization Specialist
Wisconsin Diagnostic Laboratories
Milwaukee, Wisconsin;
Resident, Doctor of Clinical Laboratory
Science Program
School of Health Professions
Rutgers University
Newark, New Jersey

Karen Golemboski, PhD, MLS(ASCP)
Professor, Medical Laboratory Science
Bellarmine University
Louisville, Kentucky

Brandy Gunsolus, DCLS, MLS(ASCP)^{CM}
Pathology Utilization, Pathology
Augusta University Medical Center
Augusta, Georgia
Adjunct Associate Professor, Clinical
Laboratory and Medical Imaging
Sciences
School of Health Professions
Rutgers University
Newark, New Jersey

Teresa G. Hippel, BS, MLS(ASCP)^{SH}
Quality Reviewer, Diagnostic Laboratories
Vanderbilt University Medical Center
Nashville, Tennessee

S. Renee Hodgkins, PhD, MLS(ASCP)
Clinical Associate Professor, Clinical
Laboratory Sciences
Director, Doctorate in Clinical Laboratory
Science Program
University of Kansas Medical Center
Kansas City, Kansas

**Debra A. Hoppensteadt, PhD,
MLS(ASCP)^{SH}**
Professor, Pathology, and Pharmacology
Loyola University Chicago
Maywood, Illinois

Cynthia L. Jackson, PhD, HCLD(ABB)
Director, Molecular Genomic Pathology
Laboratory
Lifespan Academic Medical Center
Professor, Pathology
Warren Alpert School of Medicine at Brown
University
Providence, Rhode Island

Walter P. Jeske, PhD
Professor, Cardiovascular Research Institute
Stitch School of Medicine
Health Sciences Division
Loyola University Chicago
Maywood, Illinois

**Constantine E. Kanakis, MD, MSc,
MLS(ASCP)**
Resident Physician, Pathology and
Laboratory Medicine
Loyola University Medical Center
Adjunct Instructor
Medical Laboratory Science Graduate
Program
Loyola Parkinson School of Health Sciences
and Public Health
Maywood, Illinois

**Elaine M. Keohane, PhD, MLS(ASCP)
SH^{CM}**
Professor Emeritus, Clinical Laboratory and
Medical Imaging Sciences
School of Health Professions
Rutgers University
Newark, New Jersey

Ameet R. Kini, MD, PhD
Professor, Pathology and Laboratory
Medicine
Stitch School of Medicine
Loyola University Chicago
Maywood, Illinois

Kristen N. Krum, MD, MS
Assistant Professor, Pathology
Loyola University Medical Center
Maywood, Illinois

Clara Lo, MD
Clinical Associate Professor, Pediatric
Hematology-Oncology
Stanford University
Palo Alto, California

Naveen Manchanda, MD
Associate Professor of Clinical Medicine
Internal Medicine
Indiana University School of Medicine
Indianapolis, Indiana

Steven Marionneaux, PhD, MLS(ASCP)
Medical and Scientific Affairs Adviser
Cellavision, Inc.
Lund, Sweden
Adjunct Assistant Professor, Clinical
Laboratory and Medical Imaging
Sciences
School of Health Professions
Rutgers University
Newark, New Jersey

Peter Maslak, MD
Chief, Immunology Laboratory Service
Laboratory Medicine
Attending Physician, Leukemia Service
Internal Medicine
Memorial Sloan Kettering Cancer Center
Professor of Clinical Medicine
Internal Medicine
Weill Cornell Medical College
New York, New York

Susan A. McQuiston, MS, JD
Instructor, Biomedical Laboratory
Diagnostics
Michigan State University
East Lansing, Michigan

Shashi Mehta, PhD
Associate Professor, Clinical Laboratory and
Medical Imaging Sciences
School of Health Professions
Rutgers University
Newark, New Jersey

**Kamran M. Mirza, MD, PhD, FCAP,
FASCP, MLS(ASCP)**
Godfrey D. Stobbe Professor of Pathology
Education
Clinical Professor of Pathology,
Assistant Chair for Education,
Director, Division of Education Programs
Pathology
Michigan Medicine
Ann Arbor, Michigan

Tara Cothran Moon, PhD, MLS(ASCP)^{CM}
Professor, Clinical Laboratory Science
University of North Carolina at Chapel Hill
Chapel Hill, North Carolina

**Yukari Nishizawa-Brennen, PhD,
MLS(ASCP)^{CM}^{SC}^{CM}, MT(Japan)**
Assistant Professor, Biomedical Laboratory
Diagnosis Program
Michigan State University
East Lansing, Michigan

**Catherine N. Otto, PhD, MBA,
MLS(ASCP)^{CM}^{SH}^{CM}, DLM^{CM}**
Professor (Retired), Clinical Laboratory and
Medical Imaging Sciences
School of Health Professions
Rutgers University
Newark, New Jersey

Ruth Perez, MS, MLS(ASCP)
Program Director, Medical Laboratory
Science
Clinical Laboratory and Medical Imaging
Sciences
School of Health Professions
Rutgers University
Newark, New Jersey

Tim R. Randolph, PhD, MLS(ASCP)
Professor, Clinical Health Sciences
Doisy College of Health Sciences
Saint Louis University
St. Louis, Missouri

Mark A. Russell, MD
Hematopathology Fellow, Pathology and
Laboratory Medicine
Loyola University Medical Center
Maywood, Illinois

Kathleen M. Sakamoto, MD, PhD
Professor, Pediatrics
Stanford University
Stanford, California

Mayukh Kanti Sarkar, PhD, MLS(ASCP)
Project Manager, Regulatory Affairs –
Hemostasis
Sysmex America Inc.
Lincolnshire, Illinois

Natasha Marie Savage, MD
Associate Professor, Pathology
Medical College of Georgia at Augusta
University
Augusta, Georgia

Gail H. Vance, MD
Sutphin Professor of Cancer Genetics,
Medical and Molecular Genetics
Professor, Pathology and Laboratory
Medicine
Indiana University School of Medicine
Indianapolis, Indiana

Carolina Vilchez, MS, MLS(ASCP)H
Clinical Educator, William O. Green, Jr. M.D.
Medical Laboratory Science Program
The Valley Hospital
Ridgewood, New Jersey

Jeanine M. Walenga, PhD, MLS(ASCP)H^{CM}
Professor, Thoracic-Cardiovascular Surgery,
Pathology, and Physiology
Co-Director, Hemostasis and Thrombosis
Research Unit
Stritch School of Medicine
Loyola University Chicago
Laboratory Director, Clinical Coagulation,
Urinalysis and Medical Microscopy
Associate Director, Point of Care & Referred
Testing
Pathology and Laboratory Medicine
Loyola University Health System
Maywood, Illinois

PREFACE

The science of *clinical laboratory hematology* involves the analysis of normal and pathologic peripheral blood cells, hematopoietic (blood-producing) tissue, and hematopoietic cells in nonvascular body cavities such as cerebrospinal and serous fluids. Laboratory hematology also includes the analysis of the cells and coagulation proteins essential to clinical hemostasis. Hematology laboratory assay results are critical for diagnosis, prognosis, and monitoring treatment of primary and secondary hematologic and hemostatic disorders. Similarly, hematology and hemostasis test results are used to establish safety in the perioperative period, monitor treatments during surgical procedures, and monitor transfusion needs in trauma patients.

Rodak's Hematology: Clinical Principles and Applications systematically presents basic to advanced concepts to provide a solid foundation of healthy and pathologic states upon which readers can develop their skills in interpreting and correlating laboratory findings in anemias, hematologic malignancies, benign leukocyte disorders, and hemorrhagic and thrombotic conditions. It provides key features for accurate identification of normal and pathologic cells in blood, bone marrow, and body fluids. The focus, level, and detail of hematology, hematopathology, and hemostasis procedures, including their sources of error, along with the related clinical applications, interpretations, and testing algorithms are a highlight of this text.

The current practice of clinical laboratory hematology has been enhanced by profound changes as reflected in the numerous updates in the seventh edition of *Rodak's Hematology: Clinical Principles and Applications*. The seventh edition includes many improvements in the figures, tables, and boxes; significant updating of all chapters to include state-of-the-art content; major revisions in the chapters on automated blood cell analysis, acute leukemias, and hematology and hemostasis in selected populations (the last-mentioned including a new section on transgender populations); addition of a new chapter on patient safety; and addition of the thromboinflammatory reaction induced by COVID-19. Further, Michelle Montgomery Butina and Kamran M. Mirza are new coeditors, joining continuing editors, Elaine M. Keohane and Jeanine M. Walenga. Meticulous editing and attention to overall presentation of the material in the book add to the value of the seventh edition. Chapter highlights and new content are described below.

ORGANIZATION

Rodak's Hematology: Clinical Principles and Applications, seventh edition, is organized into 7 parts, 43 printed chapters, 4 e-chapters, and reference intervals for common laboratory assays conveniently located after the Index at the end of the book. Expanded appendices can be downloaded from the Evolve website allowing for easy access and searches of key abbreviations, formulas, glossary terms, and answers to case studies and review questions.

PART I: INTRODUCTION TO HEMATOLOGY

Chapter 1 previews the science of clinical laboratory hematology. **Chapter 2** is new to the seventh edition and provides an overview of patient safety in hematology and hemostasis to ensure that the total testing process is safe, timely, efficient, equitable, patient centered, and effective. **Chapter 3** provides comprehensive, updated coverage of quality assurance for laboratory testing, with enhanced sections on method evaluation, assay validation, multisite validation, and system-wide comparability.

PART II: BLOOD CELL PRODUCTION, STRUCTURE, AND FUNCTION

Chapters 4 and 5 include photomicrographs and figures to describe general cell structure and an updated section on selected cell processes, along with the morphologic and molecular details of hematopoiesis. **Chapters 6, 10, and 11** discuss erythropoiesis, leukopoiesis, and megakaryopoiesis using numerous photomicrographs to demonstrate ultrastructure and microscopic morphology. **Chapters 7 and 8** examine mature red blood cell metabolism, membrane and hemoglobin structure and function, and red blood cell senescence and destruction. Discussion of iron kinetics and laboratory assessment in **Chapter 9** has been updated with new figures and coverage of systemic and cellular regulation of iron. **Chapter 11** also includes a description of the function of platelets, detailing the primary hemostatic mechanisms of platelet adhesion, aggregation, and activation with updated information on the platelet proteome and the role of platelets in the inflammatory response.

PART III: LABORATORY EVALUATION OF BLOOD CELLS

Chapter 12 describes traditional (manual) clinical hematology laboratory procedures such as microscopy-based cell counts and hemoglobin and hematocrit determinations as well as point-of-care technology. **Chapter 13** includes updated descriptions, principles of operation, and figures of the major, state-of-the-art automated blood cell analyzers. It also describes new analyzer parameters and their clinical use. The digital data management capabilities of these analyzers have revolutionized the way blood specimens for the complete blood count, differential count, and morphology assessment are analyzed and how test results are reported and interpreted. **Chapter 14** describes peripheral blood film examination and the differential cell count correlation to the complete blood count. **Chapter 15** follows up with bone marrow aspirate and biopsy collection, preparation, examination, and reporting.

PART IV: ERYTHROCYTE DISORDERS

Chapter 16 provides an overview of the anemias and describes cost-effective diagnostic approaches that integrate patient history, physical examination, and symptoms, with laboratory results for hemoglobin, red blood cell indices, reticulocyte count, and abnormal red blood cell morphology. **Chapters 17 to 19** describe disorders of iron and DNA metabolism and bone marrow failure. Algorithms help the reader to distinguish types of microcytic and macrocytic anemias. **Chapters 20 to 23** discuss hemolytic anemias due to intrinsic or extrinsic defects. **Chapter 20** also includes detailed figures that explain extravascular and intravascular hemolysis and hemoglobin catabolism. **Chapters 24 and 25** provide updates in pathophysiology, diagnosis, and treatment of the hemoglobinopathies and thalassemias, including the use of Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) technology.

PART V: LEUKOCYTE DISORDERS

The chapters in this section begin with nonmalignant disorders, followed by an introduction to hematologic neoplasms, three chapters discussing diagnostic methodologies, and finally chapters discussing the major categories of hematologic neoplasms.

Chapter 26 is updated with many excellent photomicrographs and summary boxes of nonmalignant leukocyte disorders manifested by the abnormal distribution or morphology of white blood cells. These include bacterial and viral infections, various systemic disorders, and benign lymphoproliferative disorders. **Chapter 27** provides an introduction to hematologic neoplasms, including sections on classification, molecular pathogenesis, and general categories of treatment options. **Chapter 28** describes flow cytometry and its diagnostic applications, including numerous scatterplots of normal and leukemic conditions. **Chapter 29** covers molecular diagnostics, with many figures on basic molecular biology, real-time polymerase chain reaction (PCR), microarrays, and DNA sequencing, including next-generation sequencing. Molecular diagnosis has augmented or in many instances replaced long-indispensable laboratory assays. **Chapter 30** provides details on traditional cytogenetic procedures for detection of quantitative and qualitative chromosome abnormalities and more sensitive methods such as fluorescence in situ hybridization (FISH) and genomic hybridization arrays. **Chapters 31 to 34**, with significant updating according to the 2022 World Health Organization classification, provide the latest pathophysiologic models for acute lymphoblastic and myeloid leukemias and myeloproliferative, myelodysplastic, and mature lymphoid neoplasms, with numerous full-color photomicrographs and illustrations. The chapters discuss traditional monitoring of leukemias and lymphomas at the cellular level; detection of minimal residual disease at the molecular level; and new targeted molecular, immunologic, and cellular therapies, which have dramatically improved survival.

PART VI: HEMOSTASIS AND THROMBOSIS

The chapters of this section begin with the mechanisms of normal hemostasis followed by the hemorrhagic disorders, thrombotic disorders, and anticoagulant therapies. Disorder-specific laboratory testing accompanies the clinical discussion of the disorder in each chapter. Routine coagulation tests and instrumentation are discussed in the chapters at the end of this section.

Chapter 35 describes in detail the plasma- and cell-based coagulation models including the interactions between primary hemostasis, secondary hemostasis, and fibrinolysis. **Chapters 36 to 38** detail the hemorrhagic disorders including the diagnosis, management, and current therapies of acquired coagulopathies such as the acute coagulopathy of trauma and shock and inherited coagulopathies such as the hemophilias with a significant update on von Willebrand disease. Two chapters are devoted to quantitative and qualitative platelet defects as the cause of bleeding, with new and revised tables and figures. **Chapter 39** describes the known mechanisms associated with venous thrombosis, pulmonary embolism, and arterial thrombosis. Detailed discussions of antiphospholipid syndrome, disseminated intravascular coagulation, and heparin-induced thrombocytopenia, with its related vaccine-induced thrombocytopenia-thrombosis, are also provided. Thrombosis management in terms of prophylaxis and treatment, with current updates, is discussed in **Chapter 40**. The classical anticoagulants warfarin, heparin, and low-molecular-weight heparins are covered, along with new intravenous and oral thrombin and factor Xa inhibitor anticoagulants. Methods for monitoring each anticoagulant as used in various clinical settings as well as methods for monitoring the different classes of antiplatelet drugs are provided. **Chapter 41** details coagulation specimen collection and handling and covers the traditional coagulation laboratory assays that assess platelet function, coagulation factors, and fibrinolytic parameters, including clot-based and chromogenic assays. Updates for new thrombin generation and viscoelastometry (VET) tests are included. **Chapter 42** reviews the latest coagulation analyzers and point-of-care instrumentation for coagulation testing.

PART VII: HEMATOLOGY AND HEMOSTASIS IN SELECTED POPULATIONS

Chapter 43 underwent a major revision and provides valuable information on the hematology and hemostasis laboratory findings in the pediatric, pregnant, and geriatric populations as well as a new section on transgender populations, all correlated with information from previous chapters.

E-CHAPTERS

Four chapters that round out the details of good laboratory practice particular to hematology and hemostasis testing are provided in an online format. **Chapter E1** provides the laboratory safety requirements to maintain a safe working environment to

prevent accidents and mitigate exposure to biological, chemical, electrical, and fire hazards. **Chapter E2** describes the most up-to-date requirements for blood specimen collection from venipuncture and skin puncture. **Chapter E3** describes the principles, care, and use of microscopes, including light, phase contrast, polarized light, darkfield, and fluorescent microscopy. **Chapter E4** describes methods for analyzing normal and pathologic cells of cerebrospinal fluid, joint fluid, transudates, and exudates.

READERS

Rodak's Hematology: Clinical Principles and Applications is designed for medical laboratory scientists, medical laboratory technicians, and students and faculty of undergraduate and graduate educational programs in the clinical laboratory sciences and pathology. This text is also a helpful study guide for pathology and hematology-oncology residents and fellows and a valuable shelf reference for hematologists, pathologists, and hematology and hemostasis laboratory managers.

TEXTBOOK FEATURES

The outstanding value and quality of *Rodak's Hematology: Clinical Principles and Applications* reflect the educational and clinical expertise of its current and previous editors and authors who are each well known nationally, experienced, and respected in their field of expertise. The text is enhanced by nearly 700 full-color digital photomicrographs, figures, and line art. Detailed text boxes and tables clearly summarize important information. Reference intervals for common hematology, body fluid, and hemostasis laboratory assays are conveniently located after the Index at the end of the book.

Each chapter contains the following for enhanced pedagogical features:

- **Learning objectives** at all taxonomy levels in the cognitive domain
- One or two **case studies**, with open-ended discussion questions at the beginning of the chapter that stimulate interest and provide opportunities for application of chapter content in real-life scenarios
- A bulleted **summary** at the end of each chapter that provides a comprehensive review of essential material
- **Review questions** at the end of each chapter that correlate to chapter objectives and are in the multiple-choice format used by certification examinations

The Evolve website has multiple features **for the instructor**:

- A **test bank** that contains multiple-choice questions with rationales and cognitive levels
- **Instructor's manuals** for every chapter that contain key terms, objectives, outlines, and study questions
- **Learning objectives with taxonomy levels** to supplement lesson plans
- **Case studies** that have been updated and feature discussion questions and photomicrographs when applicable

- **PowerPoint presentations** for every chapter that can be used “as is” or as a template to prepare lectures
- An **image collection** that provides electronic files of all the chapter figures that can be downloaded into PowerPoint presentations

The Evolve website has important features for **the student and instructor**:

- **E- Chapters** on safety in the hematology laboratory, blood specimen collection, care and use of the microscope, and body fluid analysis
- Appendices that include an updated list of major abbreviations, commonly used formulas, answers to case studies and review questions, and an expanded glossary
- **Animations**

ACKNOWLEDGMENTS

The editors express their immense gratitude to Bernadette (“Bunny”) Rodak, who laid the foundation for *Rodak's Hematology: Clinical Principles and Applications* with her expert writing, editing, detailed figures, and especially her contribution of almost 300 outstanding digital photomicrographs. Now in its seventh edition, we are honored to continue her work on this exceptional textbook. We sincerely thank George A. Fritsma for his significant contribution to this text as a coeditor in two editions and author of 10 chapters in previous editions, for coauthoring five chapters in the seventh edition, for sharing his immense expertise in hemostasis, and for his constant support and encouragement. We thank Kathryn Doig for her contributions as coeditor for the third edition and author of seven chapters in previous editions and for her tenaciousness, creativity, and care in updating three chapters coauthored in the seventh edition. We thank Larry J. Smith for his expertise and diligence as coeditor of the fifth edition and for authoring a chapter in previous editions. We thank Catherine N. Otto for her expertise and diligence as coeditor of the sixth edition and author of two chapters in previous editions, and authoring three chapters in the seventh edition. The editors also thank the many authors who have made and continue to make significant contributions to this work. All of these outstanding professionals have generously shared their time and expertise to make *Rodak's Hematology: Clinical Principles and Applications* into a worldwide educational resource and premier reference textbook for medical laboratory scientists and technicians as well as pathology and hematology practitioners, residents, and fellows.

We also express our appreciation to Elsevier, especially Sarah Vora, Rachel McMullen, and Kelly Skelton, whose professional support and reminders kept the project on track.

Finally, and with the utmost gratitude, we acknowledge our families, friends, and professional colleagues who have supported and encouraged us through this project.

Elaine M. Keohane
Michelle Montgomery Butina
Kamran M. Mirza
Jeanine M. Walenga

PART I Introduction to Hematology

- 1 An Overview of Clinical Laboratory Hematology, 1**
Elaine M. Keohane
- 2 Patient Safety in Hematology and Hemostasis, 8**
Catherine N. Otto and Karen Golemboski
- 3 Quality Assurance in Hematology and Hemostasis Testing, 18**
Mayukh Kanti Sarkar and George A. Fritsma

PART II Blood Cell Production, Structure, and Function

- 4 Cell Structure and Function, 43**
Elaine M. Keohane
- 5 Hematopoiesis, 59**
Kamran M. Mirza
- 6 Erythrocyte Production and Destruction, 78**
Michelle Montgomery Butina
- 7 Erythrocyte Metabolism and Membrane Structure and Function, 95**
S. Renee Hodgkins
- 8 Hemoglobin Metabolism, 109**
Catherine N. Otto
- 9 Iron Kinetics and Laboratory Assessment, 122**
Kathryn Doig and Yukari Nishizawa-Brennen
- 10 Leukocyte Development, Kinetics, and Functions, 139**
Mark A. Russell and Ameet R. Kini
- 11 Platelet Production, Structure, and Function, 159**
Walter P. Jeske

PART III Laboratory Evaluation of Blood Cells

- 12 Manual, Semiautomated, and Point-of-Care Testing in Hematology, 178**
Karen S. Clark and Teresa G. Hippel
- 13 Automated Blood Cell Analysis, 198**
Elaine M. Keohane
- 14 Examination of the Peripheral Blood Film and Correlation with the Complete Blood Count, 225**
Carolina Vilchez
- 15 Bone Marrow Examination, 244**
Kamran M. Mirza

PART IV Erythrocyte Disorders

- 16 Anemias: Red Blood Cell Morphology and Approach to Diagnosis, 262**
Naveen Manchanda
- 17 Disorders of Iron Kinetics and Heme Metabolism, 275**
Tara Cothran Moon and Kathryn Doig

- 18 Anemias Caused by Defects of DNA Metabolism, 296**
Tara Cothran Moon
- 19 Bone Marrow Failure, 313**
Clara Lo, Bertil Glader, and Kathleen M. Sakamoto
- 20 Introduction to Increased Destruction of Erythrocytes, 330**
Kathryn Doig and Susan A. McQuiston
- 21 Intrinsic Defects Leading to Increased Erythrocyte Destruction, 352**
S. Renee Hodgkins
- 22 Extrinsic Defects Leading to Increased Erythrocyte Destruction—Nonimmune Causes, 379**
Catherine N. Otto
- 23 Extrinsic Defects Leading to Increased Erythrocyte Destruction—Immune Causes, 392**
Ruth Perez
- 24 Hemoglobinopathies (Structural Defects in Hemoglobin), 408**
Tim R. Randolph
- 25 Thalassemias, 440**
S. Renee Hodgkins

PART V Leukocyte Disorders

- 26 Nonmalignant Leukocyte Disorders, 464**
Steven Marionneau
- 27 Introduction to Hematologic Neoplasms, 489**
Constantine E. Kanakis and Kamran M. Mirza
- 28 Flow Cytometric Analysis in Hematologic Disorders, 500**
Magdalena Czader
- 29 Molecular Diagnostics in Hematopathology, 519**
Cynthia L. Jackson and Shashi Mehta
- 30 Cytogenetics, 550**
Gail H. Vance
- 31 Acute Leukemias, 566**
Mark A. Russell and Ameet R. Kini
- 32 Myeloproliferative Neoplasms, 583**
Tim R. Randolph
- 33 Myelodysplastic Neoplasms, 618**
Nicholas C. Brehl
- 34 Mature Lymphoid Neoplasms, 634**
Steven Marionneaux and Peter Maslak

PART VI Hemostasis and Thrombosis

- 35 Normal Hemostasis, 661**
Jeanine M. Walenga and Kristen N. Krum
- 36 Hemorrhagic Disorders and Laboratory Assessment, 686**
Mayukh Kanti Sarkar and George A. Fritsma
- 37 Qualitative Disorders of Platelets and Vasculature, 713**
Walter P. Jeske and Phillip J. DeChristopher

38 Quantitative Disorders of Platelets: Thrombocytopenia and Thrombocytosis, 734

Phillip J. DeChristopher and Walter P. Jeske

39 Thrombotic Disorders and Laboratory Assessment, 761

Mayukh Kanti Sarkar, George A. Fritsma, and Jeanine M. Walenga

40 Antithrombotic Therapies and Laboratory Assessment, 789

Mayukh Kanti Sarkar and George A. Fritsma

41 Laboratory Evaluation of Hemostasis, 811

Mayukh Kanti Sarkar and George A. Fritsma

42 Hemostasis and Coagulation Instrumentation, 841

Debra A. Hoppensteadt

PART VII Hematology and Hemostasis in Selected Populations**43 Hematology and Hemostasis in the Pediatric, Pregnant, Geriatric, and Transgender Populations, 862**

Brandy Gunsolus and Natasha Marie Savage

Hematology/Body Fluids/Hemostasis Reference Intervals, 912**ECHAPTERS (EVOLVE)****E1 Safety in the Hematology Laboratory**

Kathryn E. Golab

E2 Blood Specimen Collection

Stephanie B. Cochrane

E3 Care and Use of the Microscope

Elaine M. Keohane

E4 Body Fluid Analysis in the Hematology Laboratory

Michelle Montgomery Butina

APPENDICES (EVOLVE)

Appendix A: Abbreviations

Appendix B: List of Formulas

Appendix C: Answers

Appendix D: Glossary

An Overview of Clinical Laboratory Hematology

Elaine M. Keohane*

OUTLINE

History

Red Blood Cells

Hemoglobin, Hematocrit, and Red Blood Cell Indices
Reticulocytes

White Blood Cells

Platelets

Complete Blood Count

Blood Film Examination

Endothelial Cells

Coagulation

Advanced Hematology Procedures

Additional Hematology Procedures

Quality Assurance and Quality Control

Safety

The average human possesses 5 liters of blood. Blood transports oxygen from lungs to tissues; clears tissues of carbon dioxide; transports glucose, proteins, and lipids; and moves wastes to the liver and kidneys. The liquid portion is plasma, which, among many components, provides coagulation enzymes that protect vessels from trauma and maintain the circulation.

Plasma transports and nourishes blood cells. There are three categories of blood cells: red blood cells (RBCs), or *erythrocytes*; white blood cells (WBCs), or *leukocytes*; and platelets (PLTs), or *thrombocytes*.¹ Hematology is the study of these blood cells. By expertly staining, counting, analyzing, and recording the appearance, phenotype, and genotype of all three types of cells, the medical laboratory professional is able to predict, detect, and diagnose blood diseases and many systemic diseases that affect blood cells. Physicians rely on hematology laboratory test results to select and monitor therapy for these disorders; consequently, a complete blood count (CBC) is ordered on nearly everyone who visits a provider or is admitted to a hospital.

HISTORY

The first scientists, such as Athanasius Kircher in 1657, described “worms” in the blood, and Anton van Leeuwenhoek in 1674 gave an account of RBCs,² but it was not until the late 1800s that Giulio Bizzozero described platelets as “petite plaques.”³ The development of the Wright stain by James Homer Wright in 1902 opened a new world of visual blood film examination through the

microscope. Although automated analyzers now differentiate and enumerate blood cells, Wright’s Romanowsky-type stain (polychromatic, a mixture of acidic and basic dyes), and refinements thereof, remains the foundation of blood cell identification.⁴

In the present-day hematology laboratory, RBC, WBC, and platelet appearance is analyzed through automation or visually using 500× to 1000× light microscopy examination of cells fixed to a glass microscope slide and stained with *Wright* or *Wright-Giemsa stain* (Chapters 4, 13, 14, and E3). The scientific term for cell appearance is *morphology*, which encompasses cell color, size, shape, cytoplasmic inclusions, and nuclear condensation.

RED BLOOD CELLS

RBCs are anucleate, biconcave, discoid cells filled with a red-dish protein, hemoglobin, which transports oxygen and carbon dioxide (Chapters 8 and 9). RBCs appear salmon pink and measure 7 to 8 μm in diameter with a zone of pallor that occupies one-third of their center (Figure 1.1A), reflecting their biconcavity (Chapters 6 and 7).

Since before 1900, physicians and medical laboratory professionals counted RBCs in measured volumes to detect anemia or polycythemia. *Anemia* means loss of oxygen-carrying capacity and is often reflected in a reduced RBC count or decreased RBC hemoglobin concentration (Chapters 16–25). *Polycythemia* means an increased RBC count reflecting increased circulating RBC mass, a condition that leads to hyperviscosity (Chapter 32).

*The author extends appreciation to George A. Fritsma, whose work in prior editions provided the foundation for this chapter.

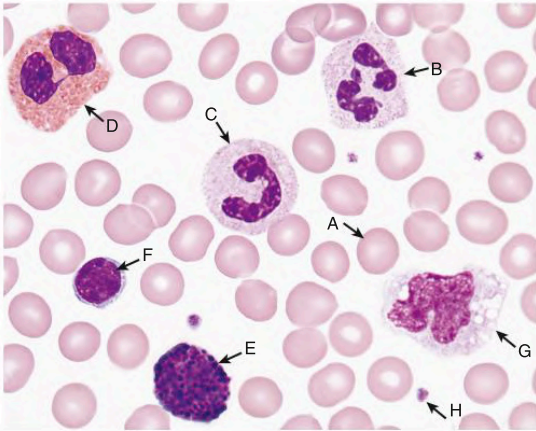


Figure 1.1 Composite of Cells Found in Peripheral Blood of Healthy Individuals. Erythrocyte (red blood cell, RBC) (A); neutrophil (segmented neutrophil, NEUT, SEG, polymorphonuclear neutrophil, PMN) (B); band (band neutrophil, BAND) (C); eosinophil (EO) (D); basophil (BASO) (E); lymphocyte (LYMPH) (F); monocyte (MONO) (G); platelet (PLT) (H). (Wright-Giemsa stain, $\times 1000$.)

Historically, microscopists counted RBCs by carefully pipetting a tiny aliquot of whole blood and mixing it with 0.85% (normal) saline. Normal saline matches the osmolality of blood; consequently, the suspended RBCs retained their intrinsic morphology, neither swelling nor shrinking. A 1:200 dilution was typical for RBC counts, and a glass pipette designed to provide this dilution, the Thoma pipette, was used routinely until the advent of automation.

The diluted blood was transferred to a glass counting chamber called a hemacytometer (Figure 12.1). The microscopist observed and counted RBCs in selected areas of the hemacytometer, applied a mathematical formula based on the dilution and on the area of the hemacytometer counted (Chapter 12), and reported the RBC count in cells per microliter (μL , mCL ; also called *cubic millimeter* [mm^3], milliliter (mL; also called *cubic centimeter* [cc]), or liter (L).

Visual RBC counting was developed before 1900 and, although inaccurate, was the only way to count RBCs until the late 1950s, when automated particle counters became available in the clinical laboratory. The first electronic counter was patented in 1953 by Joseph and Wallace Coulter of Chicago, Illinois,⁵ and today many high-quality automated blood cell analyzers exist using multiple complex technologies (Chapter 13). However, the Coulter principle of direct current electrical impedance is still used to count RBCs in many modern analyzers. Fortunately, the widespread availability of automated cell analysis has replaced visual RBC counting, although visual counting skills remain useful where automated analyzers are unavailable.

Hemoglobin, Hematocrit, and Red Blood Cell Indices

RBCs also are assayed for hemoglobin (HGB) concentration and hematocrit (HCT) (Chapter 12). Hemoglobin measurement

relies on a weak solution of potassium cyanide and potassium ferricyanide (historically known as *Drabkin reagent*). An aliquot of whole blood is mixed with a measured volume of reagent, hemoglobin is converted to stable *cyanmethemoglobin* (hemoglobin-cyanide), and the absorbance or color intensity of the solution is measured in a spectrophotometer at 540 nm wavelength.⁶ The color intensity is compared with that of a known standard and is mathematically converted to hemoglobin concentration. Modifications of the cyanmethemoglobin method are used in most automated applications, although some automated blood cell analyzers replace it with a formulation of the ionic surfactant (detergent) *sodium lauryl sulfate* to reduce environmental cyanide.

Hematocrit is the ratio of the volume of packed RBCs to the volume of whole blood and is manually determined by transferring blood to a plastic tube with a uniform bore, centrifuging, measuring the column of RBCs, and dividing by the total length of the column of RBCs plus plasma.⁷ The normal ratio approaches 50%. Hematocrit is also called *packed cell volume* (PCV), the packed cells referring to RBCs. Often one can see a light-colored layer between the RBCs and plasma. This is the *buffy coat* and contains WBCs and platelets, and it is excluded from the hematocrit determination. The medical laboratory professional may use the three numerical results, RBC count, HGB, and HCT, to compute the RBC indices *mean cell volume* (MCV), *mean cell hemoglobin* (MCH), and *mean cell hemoglobin concentration* (MCHC) (Chapter 12). The MCV, although a volume measurement recorded in femtoliters (fL), reflects RBC diameter on a Wright-stained blood film. The MCHC, expressed in grams per deciliter (g/dL), reflects RBC staining intensity and amount of central pallor. The MCH in picograms (pg) expresses the mass of hemoglobin per cell and parallels the MCHC. A fourth RBC index, *red cell distribution width* (RDW), expresses the degree of *variation* in RBC volume. Extreme RBC volume variability is visible on the Wright-stained blood film as variation in diameter and is called *anisocytosis*. The RDW is based on the standard deviation of RBC volume and is routinely reported by automated blood cell analyzers (Chapter 13). In addition to aiding in diagnosis of anemia, RBC indices provide stable measurements for internal quality control of automated blood cell analyzers (Chapter 3). Sample reference intervals for RBC parameters can be found after the Index at the end of the book; these vary by age and sex (Chapter 43).

Medical laboratory professionals routinely use light microscopy at 500 \times or 1000 \times magnification to visually review RBC morphology, commenting on RBC diameter, color or hemoglobinization, and shape and the presence of cytoplasmic inclusions (Chapters 14 and 16). All these parameters—RBC count, HGB, HCT, indices, and RBC morphology—are employed to detect, diagnose, assess the severity of, and monitor the treatment of anemia, polycythemia, and the numerous systemic conditions that affect RBCs (Chapters 17–25 and Chapter 32). Automated blood cell analyzers are used in nearly all clinical laboratories to generate these data, although visual examination of the Wright-stained blood film is still essential to verify abnormal results.⁸

Reticulocytes

On the Wright-stained blood film, 0.5% to 2.5% of RBCs exceed the 7- to 8- μm average diameter and stain slightly blue-gray. These are *polychromatic (polychromatophilic)* erythrocytes, newly released from the RBC production site: the bone marrow (Chapters 5 and 6). Polychromatic erythrocytes are closely observed because they indicate the ability of the bone marrow to increase RBC production in anemia caused by blood loss or excessive RBC destruction (Chapters 20–24).

Methylene blue dyes, called *nucleic acid stains* or *vital stains*, are used to differentiate and count these young RBCs. Vital (or supravital) stains are dyes absorbed by live cells.⁹ Young RBCs contain ribonucleic acid (RNA) and are called *reticulocytes* when the RNA is visualized using vital stains (Chapter 12). Counting reticulocytes visually by microscopy was (and remains) a tedious and imprecise procedure until the development of automated reticulocyte counting by the TOA Corporation (presently Sysmex) in the 1990s. Now all fully automated blood cell analyzers provide a relative reticulocyte percentage, an *absolute reticulocyte count*, and an especially sensitive measure of RBC production, the *immature reticulocyte fraction* (Chapter 13). However, it is still necessary to confirm automated analyzer counts visually from time to time, so medical laboratory professionals must retain this skill.

WHITE BLOOD CELLS

WBCs, or leukocytes, are a loosely related category of cell types dedicated to protecting their host from infection and injury (Chapters 5 and 10). WBCs are transported in the blood from their source, usually bone marrow or lymphoid tissue, to their tissue or body cavity destination. WBCs are so named because they are nearly colorless in an unstained cell suspension.

WBCs may be counted visually using a microscope and hemacytometer (Chapter 12). The technique is the same as RBC counting, but the typical dilution is 1:20, and the diluent is a dilute acid solution. The acid causes RBCs to *lyse* or rupture; without it, RBCs, which are 500 to 1000 times more numerous than WBCs, would obscure the WBCs. The WBC count reference intervals can be found after the Index at the end of the book. Visual WBC counting has been largely replaced by automated blood cell analyzers, but it is accurate and useful in situations in which no automation is available. Medical laboratory professionals who analyze body fluids such as cerebrospinal fluid or pleural fluid may employ visual WBC counting (Chapter E4).

A decreased WBC count is called *leukopenia*, and an increased WBC count is called *leukocytosis*, but the WBC count alone has modest clinical value. The microscopist must differentiate the categories of WBCs in the blood by using a Wright-stained blood film and light microscopy (Chapters 10 and 14). The types of WBCs found in peripheral blood in healthy individuals are as follows:

- Neutrophils (NEUTs, segmented neutrophils [SEGs], polymorphonuclear neutrophils [PMNs]) (Figure 1.1B). Neutrophils are phagocytic cells whose major purpose is to engulf and destroy microorganisms and foreign material,

either directly or after they have been labeled for destruction by the immune system. The term *segmented* refers to their multilobed nuclei. The cytoplasm of neutrophils contains pink- or lavender-staining granules filled with bactericidal substances. An increase in neutrophils is called *neutrophilia* and often signals bacterial infection. A decrease is called *neutropenia* and has many causes, but it is often caused by certain medications or viral infections.

- Bands (BANDS, band neutrophils) (Figure 1.1C). Bands are slightly less mature neutrophils with a nonsegmented nucleus in a U or S shape. An increase in bands also signals bacterial infection and is customarily called a *left shift*.
- Eosinophils (EOs) (Figure 1.1D). Eosinophils are cells with round, bright orange-red cytoplasmic granules filled with proteins involved in immune system regulation. An elevated eosinophil count is called *eosinophilia* and often signals a response to allergy or parasitic infection.
- Basophils (BASOs) (Figure 1.1E). Basophils are cells with dark purple, irregular cytoplasmic granules that obscure the nucleus. The basophil granules contain histamines and various other proteins. An elevated basophil count is called *basophilia*. Basophilia is rare and often signals a hematologic disease.

The distribution of eosinophils and basophils in blood is so small compared with that of neutrophils that the terms *eosinopenia* and *basopenia* are theoretical and not used. Neutrophils, bands, eosinophils, and basophils are collectively called *granulocytes* because of their prominent cytoplasmic granules, although their functions differ.

- Lymphocytes (LYMPHs) (Figure 1.1F). Lymphocytes comprise a complex system of cells that provide for host immunity. Lymphocytes recognize foreign antigens and mount *humoral* (antibody) and *cell-mediated* immune responses. On the Wright-stained blood film, most lymphocytes are nearly round, are slightly larger than RBCs, and have a round, condensed nucleus and a thin rim of nongranular cytoplasm. An increase in the lymphocyte count is called *lymphocytosis* and often is associated with viral infections. Reactive lymphocytes with characteristic morphology often accompany lymphocytosis (Chapter 26). An abnormally low lymphocyte count is called *lymphopenia* or *lymphocytopenia* and is often associated with drug therapy or immunodeficiency.
- Monocytes (MONOs) (Figure 1.1G). Monocytes are immature *macrophages* passing through the blood from their point of origin, usually the bone marrow, to a targeted tissue location. Macrophages are the most abundant cell type in the body, although monocytes comprise a minor component of peripheral blood WBCs. Macrophages occupy every body cavity; some are motile and some are immobilized. Their tasks are to identify and *phagocytize* (engulf and consume) foreign particles and assist the lymphocytes in mounting an immune response through the assembly and presentation of antigen *epitopes*. On the Wright-stained blood film, monocytes have a slightly larger diameter than other WBCs, blue-gray cytoplasm with fine azure granules, and a nucleus that is usually indented or folded. An increase in the number of

monocytes is called *monocytosis*. Benign monocytosis may be found in certain infections or in inflammation (Chapter 26). Medical laboratory professionals seldom document a decreased monocyte count, so the theoretical term *monocytopenia* is seldom used.

Leukemia is an uncontrolled proliferation of a clone of malignant WBCs. Leukemia may be chronic, for example, chronic myeloid leukemia or chronic lymphocytic leukemia, or acute, for example, acute myeloid leukemia or acute lymphoblastic leukemia (Chapter 27 and Chapters 31–34). Leukemias may involve any of the cell lines and are categorized by their respective immunophenotypes and genetic aberrations (Chapters 28–30). Some leukemias are more common in a specific age group; chronic lymphocytic leukemia is more prevalent in people older than 65 years, whereas acute lymphoblastic leukemia is the most common form of childhood leukemia (Chapters 31 and 34). Medical laboratory scientists participate in characterization of leukemias using Wright-stained bone marrow smears, flow cytometric immunophenotyping, molecular diagnostic technology, cytogenetics, and, occasionally, cytochemical staining (Chapter 15 and Chapters 28–30).

PLATELETS

Platelets, or thrombocytes, are true blood cells that maintain blood vessel integrity by initiating vessel wall repairs (Chapter 11). Platelets rapidly adhere to the surfaces of damaged blood vessels and form aggregates with neighboring platelets to plug the hole in the damaged vessels. Platelets are the major cells that control *hemostasis*, a series of cellular and plasma-based mechanisms that seal wounds, repair vessel walls, and maintain vascular patency (unimpeded blood flow) (Chapter 35). Platelets are only 2 to 4 μm in diameter, round or oval, anucleate, and slightly granular (Figure 1.1H). Their small size makes them appear insignificant, but they are essential to life and are extensively studied for their complex physiology. Uncontrolled platelet and hemostatic activation is responsible for deep vein thrombosis, pulmonary emboli, acute myocardial infarctions (heart attacks), cerebrovascular accidents (strokes), peripheral artery disease, and repeated spontaneous abortions (miscarriages) (Chapter 39).

The microscopist counts platelets employing the same technique used in counting WBCs on a hemacytometer, although a different counting area, diluent, and dilution are usually used (Chapter 12). Owing to their small volume, platelets are hard to distinguish visually in a hemacytometer, and phase microscopy provides for easier identification. Automated blood cell analyzers have largely replaced visual platelet counting and provide greater accuracy (Chapter 13). The reference interval for the platelet count can be found after the Index at the end of the book.

One advantage of automated blood cell analyzers is their ability to generate a mean platelet volume (MPV), which is unavailable through visual methods. The presence of predominantly larger platelets generates an elevated MPV value, which sometimes signals a regenerative bone marrow response to platelet consumption (Chapters 11 and 38).

Elevated platelet counts, called *thrombocytosis*, signal inflammation or trauma but convey modest intrinsic significance. *Essential thrombocythemia* is a rare malignant condition characterized by extremely high platelet counts and uncontrolled platelet production. Essential thrombocythemia is a life-threatening hematologic disorder (Chapters 32 and 38).

A low platelet count, called *thrombocytopenia*, is a common consequence of drug treatment and may be life-threatening. Because the platelet is responsible for normal blood vessel maintenance and repair, thrombocytopenia is usually accompanied by easy bruising and uncontrolled hemorrhage (Chapter 38). Thrombocytopenia accounts for many hemorrhage-related emergency department visits. Accurate platelet counting contributes to patient safety because it provides for the diagnosis of thrombocytopenia in many disorders or therapeutic regimens.

COMPLETE BLOOD COUNT

A CBC is performed on automated blood cell analyzers and includes the RBC, WBC, and platelet measurements indicated in Box 1.1. The medical laboratory professional may collect a blood specimen for the CBC, but a phlebotomist, nurse, physician assistant, physician, or patient care technician may also collect the specimen (Chapters 12, 41, and E2). No matter who collects a blood specimen, the medical laboratory professional is responsible for the integrity of the specimen and ensures that it is submitted in the appropriate anticoagulant and tube and is free of clots and hemolysis (red-tinted plasma indicating RBC damage). The specimen must be of sufficient volume because “short draws” result in incorrect anticoagulant-to-blood ratios. The specimen must be tested or prepared for storage within the appropriate time frame to ensure accurate analysis (Chapter 3) and must be accurately registered in the work list, a process known as specimen *accession*. Accession may be automated, relying on bar code or radiofrequency identification technology, thus reducing instances of identification error.

BOX 1.1 Basic Complete Blood Count Measurements Generated by Automated Blood Cell Analyzers

RBC Parameters	WBC Parameters
RBC count	WBC count
HGB	NEUT count: % and absolute
HCT	LYMPH count: % and absolute
MCV	MONO count: % and absolute
MCH	EO and BASO counts: % and absolute
MCHC	Platelet Parameters
RDW	PLT count
RETIC count	MPV

BASO, Basophil; EO, eosinophil; HCT, hematocrit; HGB, hemoglobin; LYMPH, lymphocyte; MCH, mean cell hemoglobin; MCHC, mean cell hemoglobin concentration; MCV, mean cell volume; MONO, monocyte; MPV, mean platelet volume; NEUT, segmented neutrophil; PLT, platelet; RBC, red blood cell; RDW, red cell distribution width; RETIC, reticulocyte; WBC, white blood cell.

Although all laboratory scientists and technicians are equipped to perform visual RBC, WBC, and platelet counts using dilution pipettes, hemacytometers, and microscopes, most laboratories employ automated blood cell analyzers to generate the CBC. Many blood cell analyzers also provide comments on RBC, WBC, and platelet morphology (Chapter 13). When one of the results from the blood cell analyzer is abnormal, the instrument provides an indication of this, sometimes called a *flag*. In this case, a reflex *blood film examination* is performed (Chapter 14).

The blood film examination (described next) is a specialized, demanding, and fundamental CBC activity. Nevertheless, if all blood cell analyzer results are within reference intervals, the blood film examination is usually omitted from the CBC. However, providers may request a blood film examination on the basis of clinical suspicion even when the analyzer results fall within their respective reference intervals.

BLOOD FILM EXAMINATION

To complete a blood film examination, the microscopist prepares a “wedge-prep” blood film on a glass microscope slide, allows it to dry, and fixes and stains it using Wright or Wright-Giemsa stain (Chapter 14). The microscopist visually performs an estimate of the WBC count (with the 40× or 50× objective at 400× or 500× magnification) and platelet count (with the 100× oil immersion objective at 1000× magnification) for comparison with their respective analyzer counts and investigates discrepancies. Next, the microscopist systematically reviews, identifies, and tabulates 100 (or more) WBCs to determine their percent distribution. This process is referred to as determining the *WBC differential* (“diff”). The WBC differential relies on the microscopist’s skill, visual acuity, and integrity, and it provides extensive diagnostic information. Finally, the microscopist examines the morphology of WBCs, RBCs, and platelets by light microscopy for abnormalities of shape, diameter, color, or inclusions using 1000× magnification. Digital morphology recognition systems such as the CellaVision DM9600 (Chapter 14) automate the WBC, RBC, and platelet morphology assessment and WBC differential processes, but the medical laboratory professional or the hematopathologist is the final arbiter for all cell identification. Results of the CBC, including all automated blood cell analysis and blood film examination parameters and interpretive comments, are provided in paper or digital format for the provider’s review, with abnormal results highlighted.

ENDOTHELIAL CELLS

Because they are structural and do not flow in the bloodstream, endothelial cells, the endodermal cells that form the inner surface of the blood vessel, are seldom studied in the hematology laboratory. Nevertheless, endothelial cells are important in maintaining normal blood flow, in tethering (decelerating) platelets during times of injury, and in enabling WBCs to escape from the vessel to the surrounding tissue when needed (Chapter 35). Increasingly refined laboratory

methods are becoming available to assay and characterize the secretions of these important cells.

COAGULATION

Most hematology laboratories include a blood coagulation-testing department (Chapters 41 and 42). Platelets are a key component of hemostasis, as previously described; plasma coagulation is the second component (Chapter 35). The coagulation system employs a complex sequence of plasma proteins, some enzymes, and some enzyme cofactors to produce clot formation after blood vessel injury. Another six to eight enzymes exert control over the coagulation mechanism, and a third system of enzymes and cofactors digests clots to restore vessel patency, a process called *fibrinolysis*. Bleeding (Chapters 36–38) and clotting (Chapter 39) disorders are numerous and complex, and the coagulation section of the hematology laboratory provides a series of plasma-based and whole blood laboratory assays that assess these plasma proteins and their interactions with hematologic cells.

The medical laboratory professional focuses especially on blood specimen integrity for the coagulation laboratory because minor blood specimen defects, including clots, hemolysis, lipemia, plasma bilirubin, and short draws, render the specimen useless (Chapter 41). High-volume coagulation tests suited to the acute care facility include the platelet count and MPV as described earlier, *prothrombin time* and *partial thromboplastin time* (or activated partial thromboplastin time), *thrombin time* (or thrombin clotting time), *fibrinogen assay*, and *D-dimer assay* (Chapter 41). The prothrombin time and partial thromboplastin time are particularly high-volume assays used in screening profiles. These tests assess each portion of the coagulation pathway for deficiencies and are used to monitor anticoagulant therapy (Chapter 40). In addition to these high-volume screening assays, moderate-volume assays for specific hemostatic parameters, including clot-based assays, chromogenic substrate assays, and immunoassays, are available in specialized or tertiary care facilities. The specialized or tertiary care coagulation laboratory with its interpretive complexities attracts advanced medical laboratory scientists with specialized knowledge and communication skills.

ADVANCED HEMATOLOGY PROCEDURES

Besides performing the CBC, the hematology laboratory provides *bone marrow examinations*, *flow cytometry immunophenotyping*, *cytogenetic analysis*, and *molecular diagnostic assays*. Performing these tests may require advanced preparation or particular dedication by medical laboratory scientists with a desire to specialize.

Medical laboratory scientists assist physicians with bedside *bone marrow* collection, then prepare, stain, and microscopically review bone marrow smears (Chapter 15). Bone marrow *aspirates* and *biopsy specimens* are collected and stained to analyze nucleated cells that are the immature precursors to blood cells (Chapter 5). Cells of the *erythroid* series are precursors to RBCs (Chapter 6); *myeloid* series cells mature to form bands and neutrophils, eosinophils, basophils, and monocytes (Chapter 10); and *megakaryocytes* produce platelets (Chapter 11). Medical

laboratory scientists, clinical pathologists, and hematologists review Wright-stained aspirate smears for morphologic abnormalities, high or low bone marrow cell concentration, and inappropriate cell line distributions. For instance, an increase in the erythroid cell line may indicate bone marrow compensation for excessive RBC destruction or blood loss (Chapter 16 and Chapters 20–24). The biopsy specimen, enhanced by *hematoxylin and eosin* (H&E) staining, may reveal abnormalities in bone marrow architecture indicating leukemia, bone marrow failure, or one of a host of additional hematologic disorders. Results of examination of bone marrow aspirates and biopsy specimens are compared with CBC results generated from the peripheral blood to correlate findings and develop pattern-based diagnoses.

In the bone marrow laboratory, cytochemical stains may occasionally be employed to differentiate abnormal myeloid, erythroid, and lymphoid cells. These stains include *myeloperoxidase*, *Sudan black B*, *nonspecific and specific esterase*, *periodic acid-Schiff*, *tartrate-resistant acid phosphatase*, and *alkaline phosphatase* (Chapters 31 and 32). The cytochemical stains are time-honored tests that in most laboratories have been replaced by flow cytometry immunophenotyping, molecular diagnostic, and cytogenetic techniques (Chapters 28–30). Since 1980, however, *immunostaining* methods have enabled identification of cell lines by detecting lineage-specific antigens on the surface or in the cytoplasm of leukemia and lymphoma cells. An example of immunostaining is a visible dye that is bound to antibodies to CD42b, a membrane protein that is present in the megakaryocytic lineage and may be diagnostic for megakaryoblastic leukemia (Chapter 31).

Flow cytometers may be *quantitative*, such as clinical flow cytometers that have grown from the original Coulter principle, or *qualitative*, including laser-based instruments that have migrated from research applications to the clinical laboratory (Chapters 13 and 28). The former devices are automated clinical blood cell analyzers that generate the quantitative parameters of the CBC through application of electrical impedance and laser or light beam interruption. Qualitative laser-based flow cytometers are mechanically simpler but technically more demanding. Both qualitative and quantitative flow cytometers are employed to analyze cell populations by measuring the effects of individual cells on laser light, such as *forward-angle fluorescent light scatter* and *right-angle fluorescent light scatter*, and by *immunophenotyping* for cell membrane epitopes using monoclonal antibodies labeled with fluorescent dyes. The qualitative flow cytometry laboratory is indispensable to leukemia and lymphoma diagnosis.

Cytogenetics (Chapter 30), a time-honored form of chromosome analysis, examines hematopoietic cells in bone marrow aspirate to identify large numerical or structural abnormalities in chromosomes at the microscopic level of resolution, such as the Philadelphia chromosome, a reciprocal translocation between chromosomes 9 and 22 that is diagnostic in chronic myeloid leukemia, and t(15;17), a translocation between chromosomes 15 and 17 that is diagnostic in acute promyelocytic leukemia. Cytogenomic techniques evaluate whole genome DNA to identify small numerical or structural abnormalities in chromosomes at the submicroscopic level of resolution, such

as gains or losses of minute amounts of DNA. Cytogenetic and cytogenomic analysis remains essential to the diagnosis and treatment of leukemia.

Molecular diagnostic techniques (Chapter 29), the fastest-growing area of laboratory medicine, enhance and even replace some of the advanced hematologic methods. Real-time polymerase chain reaction, microarray analysis, fluorescence in situ hybridization, and next-generation DNA sequencing systems are highly sensitive and specific methods that enable medical laboratory scientists to detect various chromosome abnormalities and gene mutations that confirm specific types of leukemia and lymphoma, establish their therapeutic profile and prognosis, and monitor the effectiveness of treatment.

ADDITIONAL HEMATOLOGY PROCEDURES

Medical laboratory professionals provide several time-honored whole blood methods to support hematologic diagnosis. The *glucose-6-phosphate dehydrogenase assay* phenotypically detects an inherited RBC enzyme deficiency causing episodic hemolytic anemia (Chapter 21). The sickle cell solubility screening assay and its follow-up tests, hemoglobin electrophoresis and high-performance liquid chromatography, are used to detect and diagnose sickle cell anemia and other inherited qualitative hemoglobin abnormalities and thalassemias (Chapters 24 and 25). One of the oldest hematology tests, the *erythrocyte sedimentation rate*, detects inflammation and roughly estimates its intensity (Chapter 12).

Finally, the medical laboratory professional reviews the cell counts, distribution, and morphology in body fluids other than blood (Chapter E4). These include cerebrospinal fluid, synovial (joint) fluid, pericardial fluid, pleural fluid, and peritoneal fluid, in which RBCs and WBCs may be present in disease and in which malignant cells that require specialized detection skills may be present. Analysis of nonblood body fluids is always performed with a rapid turnaround because cells in these environments rapidly lose their integrity. The conditions leading to a need for body fluid analysis are invariably acute.

QUALITY ASSURANCE AND QUALITY CONTROL

Medical laboratory professionals employ particularly complex quality control systems in the hematology laboratory (Chapter 3). Because of the unavailability of weighed standards, the measurement of cells and biological systems defies chemical standardization and requires elaborate calibration, validation, matrix effect examination, linearity, and reference interval determinations. An internal standard methodology known as the *moving average* also supports hematology laboratory applications.¹⁰ Medical laboratory professionals in all disciplines compare methods through clinical efficacy calculations that produce clinical sensitivity, specificity, and positive and negative predictive values for each assay. They must monitor specimen integrity and test ordering patterns and ensure the integrity and delivery of reports, including numerical and narrative statements and reference interval comparisons. As in most branches of laboratory science, the hematology laboratory places an

enormous responsibility for accuracy, integrity, judgment, and timeliness on the medical laboratory professional.

SAFETY

Safety can be discussed in two contexts—laboratory safety and patient safety. *Laboratory safety* requires all medical laboratory professionals to maintain a safe working environment to prevent accidents and mitigate exposure to biological, chemical, electrical, and fire hazards (Chapter E1). Written safety plans, training programs, emergency management plans, and use of appropriate personal protective equipment (PPE) are critical in maintaining a safe laboratory environment.

Patient safety requires all health care professionals to work with each other and their patients and caregivers to improve the delivery of health care and reduce medical errors (Chapter 2). In 2001 the Institute of Medicine (IOM), now the National Academy of Medicine, specified six aims to improve health care delivery to ensure that it is safe, timely, efficient, equitable, patient-centered, and effective.¹¹ Further, in 2003 the IOM specified five core competencies for all health care professionals to achieve those aims: provide patient-centered care, work in interdisciplinary teams, employ evidence-based practice, apply quality improvement, and utilize informatics.¹² Medical laboratory professionals play a vital role in collaborating with other health care providers to improve the delivery of laboratory services and ensure that laboratory tests are appropriately ordered, accurately performed in a timely manner, appropriately interpreted by health care providers, and accurately applied to the individual patient in a clear, timely, equitable, and effective manner.

REFERENCES

1. Smock, K. J. (2019). Examination of the blood and bone marrow. In Greer, J. P., Rodgers, G. M., Glader, B., et al. (Eds.), *Wintrobe's Clinical Hematology*. (14th ed., p. 1–16). Philadelphia: Lippincott Williams and Wilkins.
2. Wintrobe, M. M. (1985). *Hematology, the Blossoming of a Science: A Story of Inspiration and Effort*. Philadelphia: Lea & Febiger.
3. Bizzozero, J. (1882). Über einem neuen formbestandtheil des blutes und dessen rolle bei der thrombose und der blutgerinnung. *Virchows Arch Pathol Anat Physiol Klin Med*, 90, 261–332.
4. Woronzoff-Dashkoff, K. K. (2002). The Wright-Giemsa stain. Secrets revealed. *Clin Lab Med*, 22, 15–23.
5. Coulter, W. H. (1956). High speed automatic blood cell counter and cell size analyzer. National Electronics Conference, Chicago; and (1957) *Proc Natl Electron Conf*, 12, 1034–1042.
6. Klungsöyr, L., & Stöa, K. F. (1954). Spectrophotometric determination of hemoglobin oxygen saturation: the method of Drabkin & Schmidt as modified for its use in clinical routine analysis. *Scand J Clin Lab Invest*, 6, 270–276.
7. Mann, L. S. (1948). A rapid method of filling and cleaning Wintrobe hematocrit tubes. *Am J Clin Pathol*, 18, 916.
8. Barth, D. (2012). Approach to peripheral blood film assessment for pathologists. *Semin Diagn Pathol*, 29, 31–48.
9. Biggs, R. (1948). Error in counting reticulocytes. *Nature*, 162, 457.
10. Gulati, G. L., & Hyun, B. H. (1986). Quality control in hematology. *Clin Lab Med*, 6, 675–688.
11. Institute of Medicine. Committee on Quality of Health Care in America. (2001). *Crossing the Quality Chasm: A New Health System for the 21st Century*. Washington, DC: The National Academies Press.
12. Institute of Medicine. (2003). *Health Professions Education: A Bridge to Quality*. Washington, DC: The National Academies Press.

Patient Safety in Hematology and Hemostasis

Catherine N. Otto and Karen Golemboski

OBJECTIVES

After completion of this chapter, the reader will be able to:

1. Define patient safety.
2. Summarize the content of the National Academy of Medicine reports on health care quality.
3. Define each of the six quality aims for patient safety in health care.
4. Give examples of each of the six quality aims in medical laboratory professional practice in hematology and hemostasis.
5. List the five essential competencies for health care professionals.
6. Give examples of use for each of the five health care professional competencies in medical laboratory practice in hematology and hemostasis.

OUTLINE

Definition of Patient Safety

Definition of Health Care Quality

Total Testing Process in the Clinical Laboratory

Six Aims of Health Care Quality

- Safe Hematology and Hemostasis Testing
- Effective Hematology and Hemostasis Testing
- Efficient Hematology and Hemostasis Testing
- Timely Hematology and Hemostasis Testing
- Patient-Centered Hematology and Hemostasis Testing
- Equitable Hematology and Hemostasis Testing

Essential Competencies for Health Care Professionals

- Interprofessional Teamwork
- Evidence-Based Practice and Patient-Centered Care
- Informatics and Quality Improvement Processes

Applications in the Hematology and Hemostasis Laboratory

- Interprofessional Teamwork in the Hematology and Hemostasis Laboratory
- Evidence-Based Practice in the Hematology and Hemostasis Laboratory
- Patient-Centered Care in the Hematology and Hemostasis Laboratory
- Informatics in the Hematology and Hemostasis Laboratory
- Quality Improvement in the Hematology and Hemostasis Laboratory
- How Can Medical Laboratory Professionals Achieve Competency in These Areas?

CASE STUDY

After studying the material in this chapter, the reader should be able to respond to the following case study. Answers can be found in Appendix C.

Several values were flagged on the complete blood count (CBC) as being below the reference interval from a patient identified as L.M. The CBC results were released to the electronic medical record and to the provider who ordered the CBC. After reviewing the test results, the provider called the clinical laboratory to ask why the CBC report did not include reference intervals for transgender individuals who are transitioning or who have completed their transition.

1. Identify which CBC parameters need separate reference intervals for transgender individuals.
2. Explain how this may impact treatment for this patient.
3. Identify the dimensions of patient safety affected in this situation.
4. Describe solutions (recommendations) to improve dimensions of patient safety.

Patient safety and its importance in providing quality health care and improving patient outcomes came to the forefront in 2000 when the Institute of Medicine (a component of the National Academies of Sciences, Engineering, and Medicine) published *To Err Is Human*, reporting that up to 98,000 people die each year as a result of an adverse event while hospitalized.¹ Since 2000 the Institute of Medicine, now referred to as the National Academy of Medicine (NAM), has published multiple reports in their Quality Chasm Series, defining health care quality and its dimensions, identifying competencies for all health care practitioners (including medical laboratory professionals), and providing recommendations for improving diagnoses.¹⁻³ Although health care delivery systems have adopted quality improvement and other processes to reduce errors in delivery, and health care professional educational programs have incorporated curricula in patient safety competencies,

medical errors still occur every day in every delivery setting in the United States.³ The importance of professionals (medical laboratory professionals) involved in the health care diagnostic process was a key outcome of the 2015 NAM report *Improving Diagnosis in Health Care*.³ This chapter introduces the reader to critical patient safety concepts needed for effective medical laboratory science practice.

DEFINITION OF PATIENT SAFETY

The term *patient safety* is an all-encompassing term that includes all aspects of delivering health care; it is more than just ensuring that a patient does not fall while in the hospital. Patient safety is defined by the NAM as “freedom from accidental injury: avoidance, prevention, and amelioration of adverse outcomes or injuries stemming from the process of care.”²¹ Adverse outcomes that may result from the laboratory testing process include false-positive and false-negative test results; missed and delayed diagnoses; or missed, delayed, or inappropriate treatment. Injuries from the laboratory testing process can include hematomas or nerve damage following venipuncture. From a broader perspective, though, patient safety is related to many more aspects of laboratory practice.

DEFINITION OF HEALTH CARE QUALITY

Following *To Err Is Human*, the subsequent NAM report (*Crossing the Quality Chasm*) detailed the gap between the current US health care system and a system delivering ideal health care, suggesting how health care professionals might move “across the chasm” from a flawed system to a high-quality system. This report defines health care quality as “the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge.”²² Based on this definition, the NAM focuses on both *safety* and *quality* in the outcome of health care for the patient. This may seem intuitive in the 21st century; however, until the early 2000s, evaluation of health care quality focused on meeting accreditation standards such as those from The Joint Commission (for health care organizations) and the College of American Pathologists (for clinical laboratories), which placed a significant focus on the analytical phase of the Total Testing Process in the clinical laboratory (detailed in the following section). Medical laboratory professionals have used quality control and proficiency testing to evaluate analytical quality since the middle of the 20th century. With the changing focus on the patient and the outcome of their care, medical laboratory professionals are now obligated to evaluate and improve the quality of the entire testing process.

TOTAL TESTING PROCESS IN THE CLINICAL LABORATORY

The Total Testing Process in the clinical laboratory is a 3-phase, 11-step process (Figure 2.1). The process begins with the *preanalytical* (also called *preexamination*) phase that includes a clinical question (“Does the patient have this or that condition?”),

followed by identifying the laboratory test to order, and then ordering it.⁴ The next step involves collecting the specimen and transporting it to the medical laboratory.⁴ The *analytical (examination) phase* begins with preparing the specimen for analysis, followed by analysis of the specimen, and then verification of the test results.⁴ The *postanalytical (postexamination) phase* begins with reporting the test results to the provider, who then answers the clinical question and takes action that influences patient care.⁴ Examples of outcomes of clinical laboratory testing include accurate, inaccurate, delayed, or no diagnosis achieved, or accurate, inaccurate, delayed, or no treatment employed. A key element of the Total Testing Process is the importance of *thinking* by the provider (to order the laboratory test and interpret the results within the context of the patient’s symptoms) and the medical laboratory professional (to consult with providers on test selection and test result interpretation), described as the brain-to-brain loop.^{5,6}

SIX AIMS OF HEALTH CARE QUALITY

The second report in the NAM Quality Chasm Collection, *Crossing the Quality Chasm*, identified *six aims or dimensions of health care quality*: safe, effective, efficient, timely, patient-centered, and equitable (Table 2.1).² These six dimensions of health care quality are important because they apply to all aspects of the health care delivery system, and their definitions identify a standard to measure quality. Each of the quality aims can be applied to medical laboratory professional practice in general and to the hematology and hemostasis laboratory specifically, as will be discussed in this chapter. When medical laboratory professionals focus on patient safety and health care quality goals, patients are more likely to avoid adverse outcomes of health care delivery, including errors in diagnosis; delays in treatment; unnecessary testing; and adverse events, such as death, misdiagnosis, mistreatment, and disability. Patient safety and reducing harm to patients requires attention to all six quality aims.

Safe Hematology and Hemostasis Testing

Safe health care is defined as “avoiding harm to patients from the care that is intended to help them.”²² Adverse events and medical errors are serious events that result in harm to patients and care that is unsafe. Laboratory testing services are not immune to errors or adverse events. One outcome of a delay in test results is a delay in diagnosis that leads to delay in treatment, lack of treatment, impairment, or death. Best practices in medical laboratory patient safety ensure that each patient receives the right test for their condition, at the right time, with accurate test results that provide information for the best outcome.

Errors or defects in the other five dimensions of health care affect safe laboratory testing. Patients incur harm if the wrong laboratory test is ordered, if the venipuncture to collect their blood specimen is performed inaccurately, or if the provider does not accurately interpret the test results or makes an inaccurate diagnosis based on the test results. Patients may incur harm if unnecessary laboratory tests are ordered and performed, laboratory test results are not available in a timely manner to

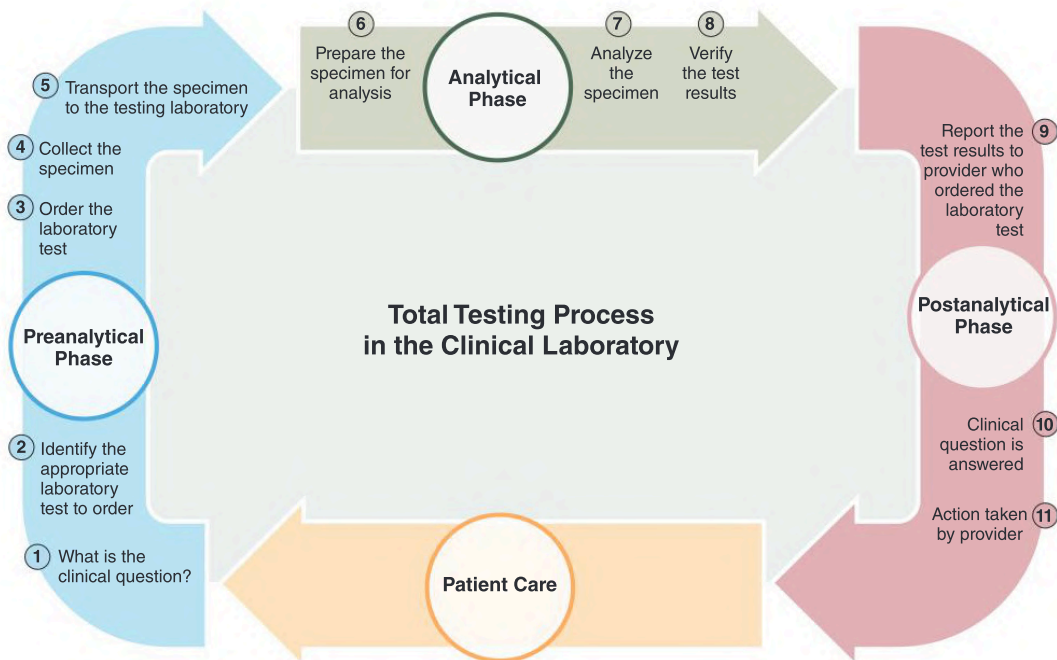


Figure 2.1 Total Testing Process in the Clinical Laboratory. Three phases and 11 steps in the Total Testing Process are depicted. The process begins with the preanalytical phase and flows through the analytical and then postanalytical phases to provide patient care. (Modified from Schumacher, G. E., & Barr, J. T. [1998]. Total testing process applied to therapeutic drug monitoring: impact on patient outcomes and economics. *Clin Chem*, 44, 370–374.)

TABLE 2.1 Quality Aims to Evaluate and Improve Patient Safety in Health Care

Quality Aim	Definition
Safe	"avoiding injuries to patients from the care that is intended to help them."
Effective	"providing services based on scientific knowledge to all who could benefit and refraining from providing services to those not likely to benefit (avoiding underuse and overuse, respectively)."
Efficient	"avoiding waste, including waste of equipment, supplies, ideas, and energy."
Timely	"reducing waits and sometimes harmful delays for both those who receive care and those who give care."
Patient-centered	"providing care that is respectful and responsive to individual patient preferences, needs, and values and ensuring that patient values guide all clinical decisions."
Equitable	"providing care that does not vary in quality because of personal characteristics such as gender, ethnicity, geographic location, and socioeconomic status."

From Institute of Medicine Committee on Quality of Health Care in America. (2001). *Crossing the Quality Chasm: A New Health System for the 21st Century*. Washington, DC, The National Academy Press, pp. 5–6.

diagnose or treat a condition, the patient's input is not considered, or the patient does not have access to clinical laboratory testing.

In the preanalytical phase of testing, specimens for hematology and hemostasis testing must be appropriately collected from an accurately identified patient (Chapter E2). It is standard practice in all aspects of health care delivery to require two patient identifiers (e.g., first and last name and birth date) before any interaction or procedure, yet specimens are still collected from incorrectly identified patients, and specimens that were collected properly are mislabeled. This can lead directly

to patient harm if test results from misidentified specimens are reported using the wrong patient's name.

Defects in specimen integrity (clotted, hemolyzed, incorrect anticoagulant, or insufficient quantity) affect the ability to analyze hematology and hemostasis specimens. Given that hematology and hemostasis tests require anticoagulated whole blood specimens, a clotted specimen cannot be tested, and it must be recollected (Chapters 12 and 41). An unacceptable specimen submitted for analysis is an inefficiency requiring recollection of the specimen at the minimum and no diagnosis or treatment if the specimen is not recollected and analyzed at the worst. Thus

TABLE 2.2 Recommendations From *Choosing Wisely*

Recommendation	Source
"Don't perform repetitive CBC and chemistry testing in the face of clinical and lab stability."	SHM-AHM
"Don't order an erythrocyte sedimentation rate (ESR) to look for inflammation in patients with undiagnosed conditions. Order a C-reactive protein (CRP) to detect acute phase inflammation."	ASCP
"Avoid using hemoglobin to evaluate patients for iron deficiency in susceptible populations. Instead use ferritin."	ASCLS
"Do not order red blood cell folate levels at all. In adults, consider folate supplementation instead of serum folate testing in patients with macrocytic anemia."	ASCP
"Do not perform peripheral blood flow cytometry to screen for hematological malignancy in the settings of mature neutrophilia, basophilia, erythrocytosis, thrombocytosis, isolated anemia, or isolated thrombocytopenia."	ASCP
"Avoid routine prothrombin time (PT) and partial thromboplastin time (PTT, APTT) pre-operative screens on asymptomatic patients, use instead a history-based bleeding assessment test."	ASCLS
"Don't test vitamin K levels unless the patient has an abnormal international normalized ratio (INR) and does not respond to vitamin K therapy."	ASCP
"Don't test or treat for suspected heparin-induced thrombocytopenia (HIT) in patients with a low pre-test probability of HIT."	ASH
"Don't treat patients with immune thrombocytopenic purpura (ITP) in the absence of bleeding or a very low platelet count."	ASH
"Don't order a factor V Leiden (FVL) mutation assay as the initial test to identify a congenital cause for a thrombotic event. First, order a phenotypic activated protein C resistance (APCR) ratio assay."	ASCLS
"Do not test for protein C, protein S, or antithrombin (ATIII) levels during an active clotting event to diagnose a hereditary deficiency because these tests are not analytically accurate during an active clotting event."	ASCP
"Do not order a protein S activity assay for measuring protein S function. Instead order free protein S antigen."	ASCLS

*These tests and their clinical applications are discussed in the chapters of this text.

ASCLS, American Society for Clinical Laboratory Science; ASCP, American Society for Clinical Pathology; ASH, American Society of Hematology; CBC, complete blood count; SHM-AHM, Society of Hospital Medicine-Adult Hospital Medicine.

Data from ABIM Foundation: *Choosing Wisely*. <https://www.choosingwisely.org/>. Accessed October 14, 2022.

it is important to ensure that specimens are recollected for those situations in which the original specimen was inadequate.

Effective Hematology and Hemostasis Testing

Effective health care is defined as "providing services based on scientific knowledge to all who could benefit and refraining from providing services to those not likely to benefit."² This means that medical laboratory professionals focus on providing appropriate laboratory tests and limit the use of laboratory tests that are not beneficial to the patient's condition. Effective laboratory testing requires understanding which laboratory tests are appropriate for specific diseases and their sequential use, communicating that information to providers, and incorporating test ordering guidelines into laboratory information systems. Ensuring that laboratory tests are used effectively requires employing evidence-based laboratory medicine and working with other health care professionals to incorporate and use the best laboratory tests for each disease process.

Identifying appropriate use of laboratory testing is a critical component of providing effective laboratory testing services. An example of a program that lists recommendations for both providers and patients is *Choosing Wisely*, sponsored by the American Board of Internal Medicine (ABIM) Foundation and supported by numerous professional organizations (Table 2.2). *Choosing Wisely* publishes peer-reviewed recommendations for testing supported by evidence.⁷ Two examples related to hematology and hemostasis submitted by the American Society for Clinical Laboratory Science (ASCLS) recommend ordering a free protein S antigen to measure protein S function instead of a protein S assay (Chapter 39) and using ferritin to evaluate

susceptible patients for iron deficiency instead of a hemoglobin level (Chapter 17).⁸

Efficient Hematology and Hemostasis Testing

Efficient laboratory testing is defined as "avoiding waste, including waste of equipment, supplies, ideas and energy."² An efficient laboratory testing process is one that has no defects: the specimen is appropriately collected, it is transported to the medical laboratory in a timely manner, the analysis is accurately performed, and the test results are sent to the provider in a timely manner. There is waste and inefficiency any time there is a problem with specimen integrity (clotted ethylenediaminetetraacetic acid specimen for a CBC or an inadequately filled sodium citrate tube for a prothrombin time) (Chapters 12 and 41). The integrity of each specimen is the responsibility of medical laboratory professionals, regardless of which member of the health care team collects the specimen. Thus the medical laboratory professional is responsible for educating other health care professionals on specimen collection methods and how defects in specimen collection affect patient care.

Beyond analyzing each specimen in an efficient manner, appropriate test utilization is an important goal for medical laboratory professionals. Inappropriate laboratory testing includes overuse, underuse, and misuse. In the hematology laboratory, a common example of overuse is a daily CBC for inpatients with no sign of bleeding or other hemodynamic instability. Overuse is both inefficient and ineffective, as well as unpleasant for the patient. Underuse is equally ineffective; ordering a test that provides diagnostic clarity, for example, allows correct treatment to be started more quickly. Testing misuse might be an order for the wrong test, for example, a factor X assay instead of

anti-factor Xa (Chapters 40 and 41), or the misinterpretation of results from a correctly ordered test, for example, ordering iron studies for a patient with a mean cell volume of 125 fL (Chapters 17 and 18).

Timely Hematology and Hemostasis Testing

Timely laboratory testing is defined as “reducing waits and sometimes harmful delays for both those who receive and those who give care.”² Medical laboratory professionals have been measuring the turnaround time for many laboratory test results since the inception of the profession. Turnaround time is generally considered to be the time elapsed from the test order to the test report, but there is little consistency as to the specifics: Should the measured time start when the test order is placed or when the specimen reaches the laboratory? What is the end of the process—when the result is released or when action is taken with the patient? If only analytical time is tracked, then other phases of the Total Testing Process are not considered. This approach can overlook factors that are important for patients who are waiting in the emergency department or for other health care professionals who need information about the patient. Even though the preanalytical and postanalytical phases of testing involve nonlaboratory personnel, oversight of these phases is still a responsibility of the medical laboratory professional. In the hematology laboratory in particular, results of the CBC are often used with other tests as the basis for decisions about diagnosis, treatment, and hospital admission.

Patient-Centered Hematology and Hemostasis Testing

The definition of patient-centered laboratory testing services is “providing care that is respectful of and responsive to individual preferences, needs, and values and ensuring that patient values guide all clinical decisions.”² Information is a critical component of delivering patient-centered care. Medical laboratory professionals should provide patients with information to prepare for laboratory tests (such as instructions for collecting fasting blood specimens or an explanation of the venipuncture procedure with information for care afterward) and to understand testing (e.g., reasons for genetic testing). Information should be written at an appropriate reading level for patients and available in multiple languages for patients who are not literate in English. Information may be provided as a document distributed to the patient in the phlebotomy waiting area or on the laboratory’s website. Patient-centered service also requires communicating in a manner that meets individual preferences, such as addressing patients using their preferred pronouns and name.

Equitable Hematology and Hemostasis Testing

The definition of equitable laboratory testing services is “providing care that does not vary in quality because of personal characteristics such as gender, ethnicity, geographic location, and socioeconomic status.”² Equitable health care, including laboratory testing, is influenced by social determinants of health. Social determinants of health are “conditions in the places where people live, learn, work, and play that affect a wide range of health and quality of life risks and outcomes.”⁹ Social

determinants of health play a significant role in the differences in individual health status.¹⁰ Examples of social determinants of health include access to health care (e.g., access to health insurance, living in a rural or urban location, availability of transportation), quality of health care (e.g., disparities in the delivery of care, lack of health literacy, language barriers), social and economic factors (e.g., degree of trust in the health care system, cultural beliefs regarding medical care, employment, and education level), physical environment (e.g., air and water quality, community safety, type of housing), and individual behaviors (e.g., use of tobacco, alcohol, or illicit drugs, diet, and exercise).¹¹

Increasing equitable laboratory testing services for hematology and hemostasis testing (in fact, all laboratory testing) requires focusing on improving testing from the patient’s perspective instead of the provider’s habit or convenience. The hours of operation for phlebotomy services are one system perspective to consider for improving equitable access to laboratory testing services. Expanding the hours that phlebotomy services are available to include early morning and evening hours as well as weekends increases access to laboratory testing services to individuals who cannot take time off from work during the day or do not have child care. Medical laboratory professionals can improve the patient experience by providing information about testing in languages other than English to support individuals for whom English is not their first language. If written patient information (e.g., ASCLS Patient Safety Tips¹²) is distributed to patients in English, it is also equitable to provide it in the predominant non-English language of individuals in the community. Equitable testing services are combined with effective testing services when reference intervals are available for parameters that have a sex-based difference (e.g., red blood cell count and hemoglobin level for individuals who are transgender) (Chapter 43). Both laboratory and hospital information systems should allow inclusion of gender identity for patients, not just listing the sex assigned at birth.

ESSENTIAL COMPETENCIES FOR HEALTH CARE PROFESSIONALS

Health Professions Education: A Bridge to Quality, published in 2003 by the Institute of Medicine, provides a blueprint to achieve quality health care.¹³ It identifies the need to prepare future health care professionals with competencies to ensure health care quality. This report identifies *five competencies* considered essential for all health care professionals¹³: practice in interprofessional teams, employ evidence-based practice, provide patient-centered care, use information technology, and apply quality improvement processes. The following sections discuss why these competencies are important for medical laboratory professionals.

Interprofessional Teamwork

Students in different health care professional programs generally learn in separate programs; however, in practice, health care works best when professionals from different disciplines work as a team.¹³ Communication with others is crucial, including providers who need information about test selection, nurses

who are preparing patients for testing, and clerical assistants who are entering test orders. It is important to apply expertise in all aspects of care, and for medical laboratory professionals, that often means where laboratory operations interface with non-laboratorians who order, facilitate, or interpret laboratory tests. Working in interprofessional teams is rooted in the understanding of and respect for the scopes of practice and importance of other health care professionals. Teamwork requires a willingness to share information, to avoid and to resolve conflicts, and to approach situations with an openness to other viewpoints and priorities.¹³

Evidence-Based Practice and Patient-Centered Care

The competencies of evidence-based practice and patient-centered care create a framework on which interprofessional cooperation can be built. First, it is critical to remember that the patient should be at the center of every practice decision. If health care workers focus on the patient and their well-being, different viewpoints become an asset rather than grounds for disagreement. Additionally, when it is agreed that high-quality evidence (such as practice guidelines and peer-reviewed publications) is the basis for practice, each professional can contribute the best evidence from their own scope of practice to create a well-designed approach to patient care. Providing the best evidence to patients in a format they can understand increases shared decision making, which leads to better patient outcomes.¹⁴

Informatics and Quality Improvement Processes

The remaining two competencies are learned skills with significant overlap, which allow professionals to assess and improve systems. Information technology, in addition to facilitating care directly via test ordering and reporting of test results, allows health care professionals to access information and to evaluate data, for example, to locate high-quality evidence and to monitor the state of operations in their own facility.

Health care must be a continuous learning environment: as new evidence becomes available, as practice guidelines are introduced and updated, as benchmarks and outcomes are evaluated, health care professionals should strive to improve systems and processes to achieve high-quality health care. Quality improvement processes such as the Plan-Do-Study-Act (PDSA) method help to structure and monitor interventions for improvement.¹⁵

APPLICATIONS IN THE HEMATOLOGY AND HEMOSTASIS LABORATORY

Interprofessional Teamwork in the Hematology and Hemostasis Laboratory

Teamwork is a skill that is applicable to both the preanalytical and the postanalytical phases of testing. Uncertainty and questions often arise with test selection and specimen collection (preanalytical phase) and then again with test interpretation (postanalytical phase). Decisions on appropriate molecular testing to diagnose leukemias requires teamwork among many health care professionals in various departments such as hematology,

flow cytometry, and cytogenetics (Chapters 28–34). In addition to responding to questions about tests, specimens, and results, medical laboratory professionals should be proactive with educational offerings for other health care professionals on topics that have generated repeated questions from those outside the laboratory. Providers might appreciate information about the effect of pretest probability on test interpretation (Chapter 3), for example, or the application of new parameters reported by the hematology analyzer (Chapter 13). It is important for medical laboratory professionals to maintain an attitude of availability for consultation, recognizing that neither providers nor nurses receive extensive education in these topics.³

Medical laboratory professionals should also be respectful of the expertise available to them from other health care professionals. Nurses may be able to provide insight about a patient's condition that impacts specimen collection, or perhaps providers can consult about unusual results or emerging diseases that relate to hematology testing.

Laboratory expertise that is shared only with other medical laboratory professionals does not always improve patient outcomes. Interpretation of complex laboratory testing may benefit from regularly scheduled, combined efforts from providers and medical laboratory professionals. In some hospitals, diagnostic management teams comprising care providers and medical laboratory professionals (pathologists, laboratory managers, and medical laboratory scientists, including those with a doctorate in clinical laboratory science [DCLS]) work together to evaluate test results from specific patients and provide patient-specific interpretive reports.¹⁶

Evidence-Based Practice in the Hematology and Hemostasis Laboratory

Because it can be difficult to keep up with the pace of new publications in medicine, many professional groups have joined forces to provide widely disseminated guidelines through the *Choosing Wisely* campaign.^{7,8} These recommendations offer a starting point to introduce evidence-based practice into laboratory operations. For example, the *Choosing Wisely* list of the Society of Hospital Medicine-Adult Hospital Medicine (SHM-AHM) includes no repetitive CBC or chemistry testing for patients who are clinically stable (see Table 2.2). A laboratory manager could monitor tests ordered to determine if some providers regularly order repeat testing without obvious evidence of need; if so, an educational initiative may help to reduce unnecessary daily CBC orders. Alternatively, recently reported test results can be displayed within the electronic test ordering system to alert the ordering provider. Appropriate laboratory test utilization can save resources (efficiency) and improve diagnosis (effectiveness), and benefits the patient in terms of fewer specimen collections. A significant percentage of patients in intensive care units and neonatal intensive care units develop anemia during hospitalization, with phlebotomy performed for numerous specimen collections a contributing factor.^{17,18} In addition, the *Choosing Wisely* statements are short and simple enough to provide patient-friendly information, allowing patients to engage in their own care planning through conversations with providers.

Patient-Centered Care in the Hematology and Hemostasis Laboratory

The importance of patient-centered care is emphasized by its inclusion in both the six health care quality aims and the five essential competencies described earlier in “Six Aims of Health Care Quality” and “Essential Competencies for Health Care Professionals,” respectively. The NAM endorses a model of patient-centered care that specifies care and communication that respect patient values and preferences, coordinated care with well-managed transitions, provision of adequate information and education, attention to physical comfort, emotional support, and involvement of family and friends of the patient.¹⁴

Coordinated care includes interprofessional communication, establishment of responsibility and accountability, and anticipating and meeting patients’ needs.¹⁹ Proactively providing information about community transportation options for patients who need to schedule additional laboratory procedures can increase compliance with their treatment plan. Creating a procedure to establish which office will transmit results from emergency department visits to primary care providers will help to ensure continuity of care. Communication with patients by medical laboratory professionals can improve patient compliance with recommended medication-related testing.²⁰ Medical laboratory professionals generally have limited patient interaction and therefore little communication with the patient directly, but attention to communication among professionals can improve care coordination. For example, coordinating results between a hematology laboratory and cytology department regarding body fluid specimens (Chapter E4) increased the detection of malignancies and helped to define the educational interventions required to maintain the improvement.²¹

Medical laboratory professionals can directly affect patient care by helping patients (and those close to them) understand their laboratory test results. Patient portals provide increased access to results, but this is unlikely to help patients engage in their care if the information is not meaningful for nonmedical professionals. In a study piloting a user-centered design for laboratory test results, Zhang and colleagues²² determined that patients found many laboratory reports difficult to read and interpret, with desired information missing or not understandable (such as the implications of abnormal results and next steps). Additionally, providers may find it difficult to extract useful information from reports of complex testing, such as molecular diagnostics.²³ A good starting point would be to track questions received in the laboratory and provide education about the most common inquiries. Providing reports that meet users’ needs will require a joint effort between medical laboratory professionals and providers or patients because only the end users (that is, patients or providers) can determine if the information is usable for them.²⁴

Informatics in the Hematology and Hemostasis Laboratory

The value of informatics in the laboratory, as in other applications of big data, lies in the ability to draw conclusions from large quantities of available data. The process of data analytics may not be required for laboratory practice, but understanding the potential questions

to ask and application of the answers are essential. Data analyses provide a base on which to build each of the other competencies. In a particular facility, questions could include the following:

- What testing patterns indicate a need for clinical decision support systems (e.g., diagnostic algorithms or test bundles)?
- What is the current best evidence for interpretation of a particular analytical procedure?
- How can patients and families access the information they need to participate in shared decision making about their care plan?
- Does the outcome of a particular system meet criteria from benchmark institutions?

Informatics can also move the overall function of the laboratory forward in a more holistic manner. For example, extensive harmonization of laboratory testing and reporting can ensure that patient results for the same analyte from different laboratories are directly comparable.²⁵ Future models suggest a more extensive integration of disciplines, such as radiology and pathology, to improve diagnosis and therapeutic decisions.²⁶ Each of these advances requires laboratory data to be widely available and consistently mined for information.

Quality Improvement in the Hematology and Hemostasis Laboratory

Quality improvement, also known as process improvement, involves monitoring the results of a system or process to determine if the system is functioning optimally. If data show that the results could be improved, a structured plan is developed to sequentially apply changes to the system (interventions), with continued monitoring to identify changes that may result.²⁷ Systems thinking and quality improvement concepts initially proved useful in other industries, such as aviation and manufacturing, and their incorporation into health care has resulted in significant improvement for many patient safety indicators.²⁸

In the hematology and hemostasis laboratory, potential quality improvement projects span all phases of the Total Testing Process. Preanalytical outcomes might include the rate of specimen rejection due to defects in specimen quality (e.g., clots or inadequate blood volume in sodium citrate tubes). Analytical indicators could include failures to recognize an interfering substance (e.g., lipemia causing an erroneously high hemoglobin value). Projects evaluating the postanalytical phase could monitor stat turnaround times or rate of failure to report critical values correctly.²⁷

How Can Medical Laboratory Professionals Achieve Competency in These Areas?

Each of the essential competencies requires intentional preparation and specific learning methods. Few people will enter the medical laboratory profession with an intuitive understanding of quality improvement processes, and simply participating in group projects does not necessarily develop teamwork skills. The education of medical laboratory professionals is always challenging, with an ever-growing body of knowledge and limited time or opportunity for interprofessional activities. New professionals may need to investigate individual opportunities to acquire one or more of these skills, but the effort will pay off in improved patient outcomes.²⁹

SUMMARY

- Patient safety encompasses all aspects of each patient's experience with the health care system.
- It is the responsibility of every health care professional to ensure that patients receive care that is safe, effective, timely, efficient, patient centered, and equitable.
- Improving medical laboratory testing requires that medical laboratory professionals develop skills in each of the five patient safety competencies: practicing in interprofessional

teams, employing evidence-based practice, using information technology, applying quality improvement processes, and providing patient-centered care.

Now that you have completed this chapter, go back and read again the case study at the beginning and respond to the questions presented. Answers can be found in Appendix C.

REVIEW QUESTIONS

Answers can be found in Appendix C.

- Which one of the following is an example of improving patient safety for patients who require a laboratory test as part of their health care?
 - Counting the number of clotted specimens for a CBC received by the laboratory
 - Measuring the amount of time it takes for a CBC to be reported to the provider
 - Ensuring that the correct laboratory test is performed for the patient's condition
 - Wearing a laboratory coat and gloves while analyzing specimens
- What is the focus of the National Academy of Medicine's definition of health care quality?
 - Meeting College of American Pathologists accreditation requirements
 - Improving patients' health outcomes
 - Meeting The Joint Commission accreditation requirements
 - Improving laboratory proficiency testing outcomes
- Which one of the following examples of collected data is needed for a medical laboratory professional to improve the efficiency of the preanalytical phase of the Total Testing Process in the clinical laboratory?
 - The number of underfilled sodium citrate tubes for prothrombin time procedures
 - The number of times the quality control specimens are outside ± 2 SD
 - The number of times the proficiency testing does not meet requirements
 - The number of times a prothrombin time procedure needs to be repeated
- Which one of the following actions can lead to harm for a patient who needs laboratory testing?
 - Asking the patient their name and birth date before performing venipuncture for a CBC
 - Reviewing the results of the quality control specimens before analyzing the patient's specimen
 - Sending an abnormally low platelet count result to a provider without completing the required confirmation checks
 - Daily maintenance on the coagulation analyzer before analyzing quality control specimens
- Which one of the following is an example of improving the effectiveness of hematology laboratory testing?
 - Following the guidelines promoted by *Choosing Wisely* for inpatients
 - Counting the number of clotted CBC specimens received in the laboratory
 - Measuring the amount of time it takes for a CBC to be completed after it is collected
 - Performing quality control on the hematology analyzer before analyzing patient specimens
- Which one of the following statements accurately characterizes the subject of *Crossing the Quality Chasm*?
 - Certain competencies are essential for all health care professionals.
 - Good health care can be described using six different dimensions of care.
 - Laboratory records should include quality control and proficiency testing results.
 - Many Americans experience harm as a result of health care procedures.
- Which one of the following is an example of interprofessional teamwork?
 - An interpreter was hired by the laboratory director to translate patient venipuncture preparation instructions into Vietnamese to accommodate a large immigrant population.
 - Medical laboratory scientists in the hematology laboratory discuss an unusual abnormal cell found on a slide.
 - The charge nurse on one floor asks the medical laboratory scientist in hematology to create an educational presentation about anticoagulants and phlebotomy.
 - The *Choosing Wisely* campaign recommends a C-reactive protein level to detect inflammation instead of the erythrocyte sedimentation rate.
- Which one of the following illustrates evidence-based practice?
 - Good health care can be described using six different dimensions of care.
 - Many Americans experience harm as a result of health care procedures.
 - Medical laboratory scientists in the hematology laboratory discuss an unusual abnormal cell found on a slide.
 - The *Choosing Wisely* campaign recommends a C-reactive protein level to detect inflammation instead of the erythrocyte sedimentation rate.

- Etiology (*Continued*)
 inadequate intake, 276
 increased need, 276
 iron overload, 287
 acquired, 287
 hereditary, 287
 megaloblastic anemia, 297–300, 297b
 defect in megaloblastic anemia caused by
 deficiency in folate and vitamin B₁₂,
 298–300, 299f
 other causes, 300
 physiologic roles of vitamin B₁₂ and folate,
 297–298, 298f
 sickle cell anemia, 414–416
 thrombosis, 762
 Etranacogene dezaparovec (Hemgenix, Behring),
 705
 Euchromatin, 46–47
 Evacuated tubes, 881.e13, 881.e14f
 Evidence-based practice, 13
 in hematology and hemostasis laboratory, 13
 Exercise-induced hemoglobinuria, 384
 Exercise-induced thrombocytosis, 753
 Exhausted platelets, 726
 Exocytosis, 49
 Exposure controls and personal protection, 881.e7
 External quality assessment, 33
 Extracellular ferritin, 131
 Extracellular matrix (ECM), 52, 61–62
 Extracorporeal membrane oxygenation (ECMO),
 751, 795
 Extramedullary hematopoiesis, in primary
 myelofibrosis, 605
 Extravascular cords, 62, 63f
 Extravascular hemolysis, 91, 338–339, 338f
 Extrinsic hemolytic conditions, 332
 Extrinsic tenase, 670
 Eyepieces, microscope, 881.e27
 Eyewear, 881.e4
- F**
- Facilitated diffusion, plasma membrane, 48–49
 Factor V, 670
 deficiency, 706, 706f
 depleted plasma, 769–770
 Leiden mutation, 762, 769–770
 assay, 770
 Factor Va, 670
 Factor VII deficiency, 706, 706f
 Factor VIII, 671
 in arterial thrombosis predictors, 774
 assay
 procedure for, 829
 reference curve for, 829, 829f
 structure and function of, 701
 Factor X deficiency, 706, 706f
 Factor XI, 671–672
 deficiency, 705, 706f
 Factor XIII, 672–673
 assay, 831
 deficiency, 706–707, 706f
 Factor XIII inhibitors, 693
 Fainting (syncope), 881.e18
 Familial pseudohyperkalemia, 362
 Fanconi anemia, 318–319, 737
 Fat cells, 55
 Favism, 370
 Feasibility, assay, 36
 Fechtner syndrome, 737
 Fedratinib, 598
 Ferritin, 124, 131, 133–134
 absorption, 124, 125f
 Ferrokines, impaired, 281–283
 Ferroportin, 281–282
 Ferrozine, 132
 Fetal hemoglobin, drugs to increase, 424
 Fetus. *See also* Neonates
 fetal thrombocytopenia, 738t
 hemolytic disease of, 401–403, 402t
 marrow megakaryocytes, 738
 thalassemias with increased levels of
 hemoglobin, 451
 Fibrin
 degradation, 681, 681f
 formation, 672–673, 673f
 Fibrinogen, 666
 activity, in arterial thrombosis predictors,
 773–774, 773f
 in elderly adults, 874
 structure, 672–673, 672f
 Fibrinogen assay, 5, 827–828
 calibration curve, 828, 828f
 limitations of, 828
 procedure for, 827–828
 quality control for, 828
 reagent for, 827
 results and clinical utility of, 828
 test protocol for, 828
 Fibrinogen equivalent units (FEUs), 774–775
 Fibrinolysis, 678–681, 679f, 679t
 control of, 679f, 679t, 680–681
 disseminated intravascular coagulation and,
 383
 in elderly adults, 874
 plasmin, 679
 plasminogen, 679
 activation, 680
 Fibrinolysis assays, 831–833
 D-dimer immunoassay, 831–832
 fibrin degradation product immunoassay,
 831–832
 plasminogen, 832
 chromogenic substrate, 832, 832f
 plasminogen activator inhibitor-1, 833
 principle of, 833, 833f
 tissue plasminogen activator assay, 832–833
 principle of, 833, 833f
 specimen collection for, 833
 Fibrinolytic drugs, 790
 Fibrinolytic inhibitors, deficiency of, 707
 Fibrinolytic therapy, 804
 Fibroblasts, 55
 Fibronectin, 90
 Field diaphragm, 881.e28
 50x oil immersion objective examination of blood
 films, 231
 Films, peripheral blood, 226–235
 drying of, 229
 examination of, 231–235
 10x objective, 231
 40x high-dry objective, 231, 232b
 50x oil immersion objective, 231, 232b
 100x oil immersion objective, 231–232
 for anemia, 267t
 automated microscopic, 235
 macroscopic, 231
 for malaria, 385, 385f
 microscopic, 231–235
 optimal assessment area, 232, 233f
 specimen collection for, 226–227, 226f
 staining of, 229–230
 automated, 228–229
 features of proper, 230, 231b
 manual technique, 229, 230f
 quick, 230
 types of, 227–229, 228f
 wedge, 227–228, 228f
 Fire drills, 881.e6
 Firefighting measures, 881.e7
 Fire hazards, 881.e6, 881.e6t
 Fire response plan, 881.e6
 First-aid measures, 881.e7
 Fish tapeworm, 303
 Fitusiran (Sanofi), 704–705
 Five-part differential, 202
 Flaggging, 219
 in automated assay performance, 849, 849b
 Flat field lenses, 881.e28
 Flippases, 100
 Floppases, 100
 Flow cytometers, 202
 Flow cytometry, 501f, 502
 analysis of, 503–505
 data analysis, 505, 505f–506f
 gating in, 503–505
 in hematologic disorders, 500–518
 lymphoid neoplasms, 510–513
 myeloid neoplasms, 506–510, 506f–507f
 cell populations identified by, 505–506
 erythroid lineage, 506
 granulocytic lineage, 506
 lymphoid lineage, 506
 megakaryocytic lineage, 506
 monocytic lineage, 506
 cell sorting and, 515
 diagram of, 503, 504f
 hematological antigens used in, 504t
 hematologic malignancies, immunophenotyping
 of, 513–516, 515f
 immunophenotyping, 5–6
 lineage-associated markers in, 503t
 multicolor or multiparameter, 502
 in platelet function testing, 857
 principle and instrumentation of, 502–503
 specimen processing in, 502
 FLT3, 72
 Fluorescein-labeled proerolysin variant (FLAER),
 367
 Fluorescence flow cytometry, for WBC count,
 WBC differential, NRBCs, and reticulocyte
 analyses, 207–210, 209f
 Fluorescence, in flow cytometry, 503, 504f
 Fluorescence in situ hybridization (FISH),
 554–556, 556f–557f
 Fluorescence resonance energy transfer (FRET),
 533
 Fluorescence technology, 199
 Fluorescent dyes, 203
 Fluorescently labeled fragments, 537, 540f
 Fluorescent microscope, 881.e31
 Fluorescent platelet count (PLT-F), 209–210
 Fluorescent spot test, 372
 Fluorescent staining, 202–203
 Foam cells, 473
 Focus controls, microscope, 881.e28
 Folate, 297–298, 298f
 assays for, 305–306, 307f
 defect in megaloblastic anemia caused by,
 298–300, 299f
 deficiency
 causes of, 301, 301b, 306b
 laboratory tests used to, 308t
 systemic manifestations of, 300–301
 Folate deficiency, 366
 Folded cells, 267t
 Folic acid deficiency, in elderly adults, 873
 Follicular lymphoma, 648, 648f
 Fondaparinux, 791t, 798–799, 799f
 Food-cobalamin malabsorption, 303
 Foramina, 62–63
 40x high-dry objective examination of blood films,
 231, 232b
 Forward scatter (FSC), 207–209
 4Ts scoring system, for heparin-induced
 thrombocytopenia, 779, 779t
 FOXP3⁺, 316
 Fragmentation hemolysis, 91
 Free cholesterol, 99
 FREEDOM trial, 598
 Free eosin, 229

- Free methylene blue, 229
 Free protein S (PS) deficiency, 765t
 French-American-British (FAB) classification, 491–492, 623
 Front-end load capability, 203
 Fructose-bisphosphate aldolase, 96, 97f
 Full-term infant, platelet count reference intervals for, 867t
 Full-term neonate, 863–864
 hemoglobin for, reference interval, 865
 Full-term neonates, 863–864
 Functional iron deficiency (FID), 134, 134f, 220–221
 Fungal organisms, 481–482, 482f
- ## G
- G1 checkpoint, 53
 G1 (gap 1) stage, cell cycle, 52
 G2 (gap 2) stage, cell cycle, 52
 G6PD deficiency, 368–373
 Gain-of-function mutation, 493
 Gardos channel, 362
 Gastric analysis, 306
 Gastric bypass surgery, 266
 Gating, 503–505
 Gaucher cells, 471
 Gaucher disease, 48, 470–473, 472t
 Gaussian distribution, 30, 31f
 Gelatinase granules, 141
 Gender-affirming hormone therapy (GAHT), 874–875
 Gene amplification, 493
 Gene expression studies, 592
 Gene function, 627
 Genes, 522–523
 Gene therapy, 425–427, 449–450
 Genetic abnormalities, myelodysplastic neoplasms with, 623–624
 with biallelic *TP53* inactivation, 624
 with low blasts and isolated 5q deletion, 623–624
 with low blasts and *SF3B1* mutation, 624
 Genetics
 acquired aplastic anemia and, 315
 acute lymphoblastic leukemia and, 570
 acute myeloid leukemia and, 571–573, 572f
 central dogma in, 521–523
 congenital dyserythropoietic anemia and, 323–324
 defects in, causing thalassemia, 443, 444f
 Diamond-Blackfan anemia and, 322–323
 dyskeratosis congenita and, 319–320
 Fanconi anemia, 319
 globin, 409–410
 of globin synthesis, 442, 442f
 hemoglobin, 410–411, 410t
 molecular, in chronic myelogenous leukemia, 585–586, 585f
 mutations
 cis, 432
 point, 522–523
 Shwachman-Bodian-Diamond syndrome, 320–321
 sickle cell anemia and, 412–413, 413f
 Genetic testing, for hemostatic disorders, 834, 834t
 Genome-editing technologies, 425, 427
 Geometric mean, 21
 Gerbich antigens, 360
 Geriatric hematology and hemostasis
 anemia and, 871–873
 ineffective erythropoiesis, 873
 of inflammation, 872–873
 iron deficiency anemia, 873
 nutritional deficiencies, 873
 unexplained anemia of aging, 873
 hematopoiesis, 871
 Geriatric hematology and hemostasis (*Continued*)
 hemostasis in, 874
 neoplasia in, 873, 874t
 parameters of, 871
 monocytes and macrophages, 871
 platelets, 871
 red blood cells, 871, 872t
 white blood cells, 871
 Geriatric hematology and hemostasis, 870–874
 Gestational age, birth weight and, 863–864
 Gestational hematology and hemostasis, 868–870
 anemia and, 868–869
 acute blood loss, 869
 hemoglobinopathies, 869
 iron deficiency anemia, 868
 megaloblastic anemia, 869
 parasitic infections, 869
 hemostasis, 869–870
 thrombocytopenia and bleeding disorders, 870, 870t
 thrombophilia and thrombosis, 869–870
 Gestation, hematopoiesis and, 863
 Giant cell (temporal) arteritis, 190
 Giant platelets, 221
 Giant platelet syndromes, inherited, 717, 718t
 Girdle syndrome, sickle cell disease and, 418
 Givinostat, 598–599, 604
 Glanzmann thrombasthenia, 714–716
 laboratory features of, 715
 treatment of, 715–716
 Global coagulation assays, 833–834
 TEG and ROTEM, 833–834
 thrombin generation assays as, 834
 Global hemostasis assessment, 853–855, 854f, 855t
 Globin. *See also* Hemoglobin
 biosynthesis, 114
 chain synthesis, 268
 genetic structure, 409–410
 regulation, 114–115
 structure, 110–111, 110t, 111f
 synthesis of, genetics of, 442, 442f
 Globin transcription factor-1 (GATA-1), 160, 160b
 Gloves, 881.e3, 881.e5f, 881.e12
 Glucose-6-phosphate dehydrogenase (G6PD), 97f, 98, 368–373, 368f, 369t
 acute hemolytic anemia, 370, 370b
 assay, 6
 chronic hereditary nonspherocytic hemolytic anemia, 371
 clinical manifestations, 370–371
 laboratory findings, 371–373
 hemolytic anemia, general tests for, 371
 tests for, 371–373, 372f
 neonatal hyperbilirubinemia, 370–371
 pathophysiology, 370
 treatment, 373
 Glut1, 361–362
 Glutathione reductase, 98
 Glycation, 112
 Glyceraldehyde-3-phosphate dehydrogenase, 96, 97f
 Glycine, 112–113
 Glycocalyx, 45, 165
 Glycolipids, 100–101
 Glycolysis, anaerobic, 96–98, 96b, 97f, 98t
 diversion pathways, 98–99
 hexose monophosphate, 97f, 98, 98t
 methemoglobin reductase, 97f, 98–99
 Rapoport-Luebering, 97f, 99
 first phase, 96, 98t
 second phase, 96, 98t
 third phase, 96–98, 98t
 Glycoprotein C (GPC), 360
 Glycoproteins, 165
 Glycosylation, 101
 Glycosylphosphatidylinositol (GPI), 364f
 Golgi apparatus, 45f, 46t, 47, 254
 GPI-anchored proteins, 364–365
 GPI anchor, paroxysmal nocturnal hemoglobinuria and, 364
 GP IIb/IIIa (α_{IIb}/β_3) receptor inhibitors, 723–724
 G-protein coupled receptors, 52
 G-proteins, 171, 172f
 inositol triphosphate-diaclyglycerol activation pathway and, 173
 α -Granule deficiency, 720, 720f
 Granules, 229
 basophils, 148–149, 149b
 eosinophils, 146, 147b
 neutrophil, 139–140, 142b
 platelet, 165f, 166, 166t
 promyelocyte or myelocyte devoid of, 621, 622f
 α -Granules, 717
 α -Granule deficiency, 720, 720f
 Granulocyte-monocyte progenitor (GMP), 140–141
 Granulocytes, 139–149, 578
 basophils, 3, 139–140, 147–149
 development, 148
 functions, 148–149
 granules, 148–149, 149b
 immature, 148
 kinetics, 148
 mature, 148, 148f
 eosinophils, 3, 139–140, 146–147
 development, 146
 functions, 146–147
 granules, 146, 147b
 kinetics, 146
 mature, 146, 147f
 metamyelocytes, 146
 myelocytes, 146
 mast cells, 149, 149f
 neutrophils, 3, 139–146
 development, 140–143, 141f
 functions, 144–146
 granules, 141, 142b
 kinetics, 143–144
 metamyelocytes, 141, 141f, 144f
 myeloblasts, 141, 141f
 myelocytes, 141, 142f–143f
 promyelocytes, 141, 141f, 143f
 segmented, 141–143, 145f
 Granulocytic lineage, 506
 Granulomas, 246
 Granzyme B, 148–149
 Gray platelet syndrome, 720, 720f
 Growth factors
 hematopoietic, 70–72, 71f
 receptors, 56, 492
 Guanine, 523–524
 Guanosine diphosphate (GDP), 52
 Guanosine triphosphate (GTP), 52
- ## H
- Hairy cell leukemia (HCL), 321t, 645–646, 645f
 Hand-foot syndrome, 423
 Hand hygiene, 881.e2, 881.e3f
 Handling and storage, 881.e7
 Hand washing, 881.e12
 Haptocorin, 301–303
 Haptoglobin, 128, 335–337, 337f, 344–345
 hemopexin-methalbumin system, 336f, 337
 Harlem-C-Georgetown, 429
 Hazard(s) identification, 881.e7
 HCT. *See* Hematocrit
 Health care, 13
 Health care delivery systems, 8–9
 Health care professionals, essential competencies for, 12–13
 evidence-based practice and patient-centered care, 13

- Health care professionals, essential competencies for (*Continued*)
informatics and quality improvement processes, 13
interprofessional teamwork, 12–13
- Health care quality
definition of, 9
six aims of, 9–12, 10t
effective hematology and hemostasis testing, 11, 11t
efficient hematology and hemostasis testing, 11–12
equitable hematology and hemostasis testing, 12
patient-centered hematology and hemostasis testing, 12
safe hematology and hemostasis testing, 9–11
timely hematology and hemostasis testing, 12
- Health Professions Education: A Bridge to Quality*, 12
- Healthy, definition of, 263
- Heavy chain disease, 656–657
- Heinz bodies, 268t, 370, 434
- HELLP syndrome, 383, 870
- Helmet cell, 267t
- Hemacytometers, 2, 180, 180f
procedure for, 181b, 182f
- Hemangioma-thrombocytopenia syndrome, 727
- Hematocrit (HCT), 2
elevated, sodium citrate volume adjustment for, 813–814, 814f
pediatric, 865
point-of-care testing, 194, 194f–195f
reticulocyte production index and, 189
rule of three, 186
- Hematogone, 152, 152f
- Hematologic malignancies
cellular processes perturbed in, 492, 492b
immunophenotyping of, 513–516, 515f
therapy for, general categories of, 494–497, 494b
- Hematologic neoplasia, in elderly adults, 873, 874t
chronic lymphocytic leukemia, 873
myelodysplastic neoplasms, 873
myeloproliferative neoplasms, 873
- Hematology
evidence-based practice in, 13
informatics in, 13
interprofessional teamwork in, 12–13
patient-centered care in, 13
quality improvement in, 13
- Hematology laboratory, safety in, 881.e1–881.e10
occupational hazards, 881.e6
biohazards in blood and body fluids, 881.e8
chemical hazards, 881.e6
electrical hazards, 881.e8
fire hazards, 881.e6, 881.e6t
radioactive hazards, 881.e8
standard precautions, 881.e2
hepatitis B virus vaccination, 881.e5
housekeeping, 881.e5
laundry, 881.e5
Occupational Safety and Health Administration Standard, 881.e2
regulated medical waste management, 881.e6
training and documentation, 881.e6
- Hematoma, 881.e18, 881.e18f
- Hematopoiesis, 59–77
adult tissue, 60–68
bone marrow, 60–64, 62f–63f
liver, 64, 64f
lymph nodes, 66, 67f
spleen, 64–66, 65f–66f
thymus, 66–68, 67f–68f
aging and, 871
- Hematopoiesis (*Continued*)
development, 59–60, 61f
hepatic phase, 60
medullary phase, 60
mesoblastic phase, 60
hormone therapy and, 875
ineffective, 299, 321t
lineage-specific, 72–73
erythropoiesis, 72
leukopoiesis, 72
megakaryocytopoiesis, 72–73
of neonate, 863
prenatal, 863
in primary myelofibrosis, 605
sex hormone effects on, 875
sites of, by age, 61f
stem cells and cytokines, 68–72
cytokines and growth factors, 70–72, 71f
stem cell cycle kinetics, 70, 70f
stem cell phenotypic and functional characterization, 70
stem cell theory, 68–70, 69f, 69t
therapeutic applications, 73, 73t–74t
- Hematopoietically active bone marrow, 61
- Hematopoietic inductive microenvironment, 69–70
- Hematopoietic microenvironment, 55–56, 63–64
- Hematopoietic stem and progenitor cells (HSPCs), 425
- Hematopoietic stem cells (HSCs), 59, 68–69, 450
for aplastic anemias, 319–320
for chronic myelogenous leukemia, 589
for sickle cell disease, 423–424
- Hematopoietic stem cell transplantation (HSCT), 448–450
for leukocyte neoplasms, 496–497, 497f
- Heme. *See also* Hemoglobin
biosynthesis, 112–114, 113f
with bound iron, 128
metabolism disorders, 275–295
regulation, 114
structure, 110, 110f
- Heme absorption, 124, 125f
- Heme carrier protein 1 (HCP1), 124, 337
- Heme, catabolism, 333, 333f
- Heme regulatory gene-1 (HRG-1), 124
- Hemochromatosis, 287t
protein, 127t, 287
- Hemoconcentration, 881.e18
- HemoCue, 184b, 185f
- Hemoglobin, 2
Bart hydrops fetalis syndrome, 454
biosynthesis, 112–114
assembly, 113f, 114
globin, 114
heme, 112–114, 113f
ontogeny, 114, 115f, 115t
- C, 428–429, 429f
crystal, 267t, 269f
- C-Harlem, 429, 432
concentration, point-of-care testing, 194
content of reticulocytes, 132t, 134
- C-thalassemia, 455
- D, 430
degradation, 333, 334b
determination, 183–184
principle, 183–184
sources of error and comments, 184b
- development, 410
dyshemoglobins, 118–119
carboxyhemoglobin, 119
methemoglobin, 118–119
sulfhemoglobin, 119
- E, 429–430, 430f
- E-thalassemia, 455
fragmentation hemolysis and salvage of, 335–338, 340b
- Hemoglobin (*Continued*)
function, 116–118
carbon dioxide transport, 117, 118f
nitric oxide transport, 118
oxygen transport, 116–117, 116f–117f
- G, 430
genetic mutations, 410–411, 410t
compound heterozygosity with hemoglobin S and, 430–432, 431f
glycation, 112, 345
- H, 268t
disease, 453–454
with increased and decreased oxygen affinity, 434–435
- induction agents, 449
- M, 432–434
mean cell, 2
measurement, 119
metabolism, 109–121
- O-Arab, 430
pediatric, 865
physiologic fragmentation hemolysis and salvage of, 335–338, 340b
production regulation, 114–116
reference interval for, 865
rule of three, 186
- S, 412–428
compound heterozygosity with, 430–432, 431f
concomitant CIS mutations with, 432
Korle Bu, 432
- S-Antilles, 432, 433t
- SC, 431
crystal, 267t, 269f
- SD, 432
SD-Punjab, 432
SG-Philadelphia, 432
SO-Arab, 432
solubility test, 420–421, 421f
- S-Oman, 432, 433t
- S-thalassemia, 454–455
structure, 110–112, 112f
complete molecule, 111–112, 111f–112f
globin, 110–111, 110t, 111f
heme, 110, 110f
unstable variants, 434
variants, 411, 412b–413b
assessment of normal and, 456–457, 456f–457f
geographic distribution of inherited, 414f
structural, thalassemia associated with, 454–455, 455t
unstable, 434
zygosity and, 411
- Hemoglobin determination
Abbott, 210
Beckman Coulter, 205
errors in, 216–218
Siemens Healthineers, 213
spectrophotometry for, 203
Sysmex, 207
- Hemoglobin distribution width (HDW), 213
- Hemoglobinemia, 335, 340b
- Hemoglobinopathies, 408–439, 409f
defined, 409
genetic mutations and, 410–411, 410t
global burden of, 435
hemoglobin C, 428–429, 429f
hemoglobin C-Harlem, 429
hemoglobin D and hemoglobin G, 430
hemoglobin development and, 410
hemoglobin E, 429–430, 430f
hemoglobin M, 432–434
hemoglobin O-Arab, 430
hemoglobin SC and hemoglobin SG-Philadelphia, 432
hemoglobin S, concomitant cis mutations with, 432, 433t

- Hemoglobinopathies (*Continued*)
 hemoglobin S-Korle Bu, 432
 hemoglobins with increased and decreased oxygen affinity, 434–435
 hemoglobin S- β -thalassemia, 431
 nomenclature, 411–412
 pathophysiology, 411
 during pregnancy, 869
 sickle cell disease, 66, 412–427
 clinical features, 416–419, 416b
 course and prognosis, 427
 etiology and pathophysiology, 414–416
 geographic distribution of inherited hemoglobin variants and, 414–416, 414f
 history of, 412–413
 incidence with malaria, 419–420
 inheritance pattern, 413, 413f
 irreversible, 415
 laboratory diagnosis, 420–422, 420f–421f
 malaria and, 419–420
 prevalence, 413–414
 reversible, 415
 trait, 427–428
 treatment, 422–427
 SO-Arab and SD-Punjab, 432
 structure of globin genes and, 409–410
 zygosity and, 411
- Hemoglobinuria, 340, 366
 exercise-induced, 384
- Hemogram. *See* Complete blood count
- Hemojuvelin, 127t
- Hemolysis, 331, 333–338, 366, 747, 881.e19
 acute, 331–332, 341
 bilirubin metabolism and, 333–335, 333f
 blood loss and, 264–265
 chronic, 331–332, 341
 classification of hemolytic disorders, 331–333, 331t
 clinical features, 340–341
 clinical signs and symptoms, 341
 acute hemolysis, 341
 chronic hemolysis, 341
 differential diagnosis, 346–347, 347f, 348t
 extrinsic, 332
 fragmentation, 91, 332
 macrophage-mediated hemolysis vs., 339t
 pathologic, 339–340, 341f–344f
 plasma hemoglobin salvage, 335–338, 336f, 340b
 inherited, 332
 intravascular, 91
 intrinsic, 332
 laboratory findings, 346
 tests of accelerated red blood cell destruction, 342–345
 tests of increased erythropoiesis, 345–346, 346t
 laboratory tests to determine specific processes, 346, 346t
 macrophage-mediated, 91
 nonimmune drug-induced, 404
 pathologic macrophage-mediated, 338–339, 338f
 plasma hemoglobin salvage and fragmentation, 335–338, 340b
 site and mechanism of, 332–333
 in specimen quality set points, 849
- Hemolysis area (HA), 458–459
- Hemolytic anemias, 220, 287, 301, 331, 331t
 alloimmune, 396–401
 hemolytic disease of the fetus and newborn, 401–403, 402t
 hemolytic transfusion reaction, 401
 autoimmune, 396–401
 characteristics of, 398t
 cold agglutinin disease, 399–400, 400f
- Hemolytic anemias (*Continued*)
 mixed-type, 401
 paroxysmal cold hemoglobinuria, 331–332, 400–401
 warm, 397–399
 clinical features, 340–341
 differential diagnosis, 346–347, 347f
 general tests for, 371
 immune, 392–407, 393f–395f
 drug-induced, 403–404, 403f
 laboratory findings in, 396, 397f
 major mechanisms of, 396f
 overview of, 393–396, 394b
 pathophysiology, 393–396
 laboratory findings, 342, 346t
 macroangiopathic, 383–384
 exercise-induced hemoglobinuria, 384
 traumatic cardiac hemolytic anemia, 383, 384f
 malaria and, 332
 microangiopathic, 380–383, 381b
 disseminated intravascular coagulation, 383
 HELLP syndrome, 383
 hemolytic uremic syndrome, 382–383
 thrombotic thrombocytopenic purpura, 381–382, 382f
 nonimmune causes, 379–391, 380f, 380b
 babesiosis and, 386–387
 clinical findings, 387
 geographic distribution, 387
 laboratory findings and diagnosis, 387, 387f
 bartonellosis, 387–388
 clostridial sepsis, 387
 drugs and chemicals, 388
 extensive burns, 388, 388f
 infectious agents, 384–388
 malaria, 384–385
 clinical and laboratory findings, 385
 hemolytic anemia caused by, 384–388
 microscopic examination, 385, 385f
 pathogenesis, 384–385
 Plasmodium falciparum and, 385, 386f
 Plasmodium knowlesi and, 385, 386f
 Plasmodium malariae and, 385, 386f
 Plasmodium ovale and, 385, 386f
 Plasmodium vivax and, 385, 385f
 prevalence, 384
 red blood cell injury, 388, 388f
 venoms, 388
 nonimmune causes, malaria, 332
 pathophysiology of, 364–365
- Hemolytic crises, 358–359
- Hemolytic disease of the fetus and newborn (HDFN), 401–403, 402t
- Hemolytic jaundice, 340
- Hemolytic transfusion reaction (HTR), 401
- Hemolytic uremic syndrome (HUS), 382–383, 749–750
 atypical, 750
 differentiation, 749t
- Hemopexin, 128, 336f, 337
- Hemophagocytic lymphohistiocytosis, 467
- Hemophilia
 A, 701–705
 clinical manifestations, 702
 contemporary therapy, 704
 genetics, 701–702
 and inhibitors, 704–705
 laboratory diagnosis, 702–703, 702t
 traditional therapy, 703–704
 B, 705
 C, 705
- Hemorrhage, 686
 acquired vs. congenital, 688, 688b
 anemia and, 263, 277
 bleeding time test, 33–34
- Hemorrhage (*Continued*)
 chronic renal failure and, 691–692
 deep tissue bleeding, 735
 laboratory assessment and, 686–712
 localized vs. generalized, 687
 mucocutaneous vs. anatomic, 687–688, 687t
 nephrotic syndrome, 691–692
 from platelet abnormalities, 735
 reactive thrombocytosis associated with, 752
 reversal of warfarin overdose based on, 794t
 signs, hemostatic defect, 687b
 symptoms, 686–688, 735
 and thrombocytopenia, 735
 vitamin K deficiency and, 692
- Hemorrhagic disease of the newborn, vitamin K deficiency, 692
- Hemorrhagic thrombocythaemia, 599
- Hemosiderin, 340, 345f
- Hemostasis, 4, 661–685
 clot-based screening tests for coagulation disorders, 821–827
 coagulation factor assays for, 827–831
 cofactors in, 670–671
 disorders, genetic testing for, 834, 834t
 fibrinolysis assays, 831–833
 global coagulation assays for, 833–834
 hormone therapy and, 875
 instrumentation, 841–861, 850b
 laboratory evaluation of, 811–840
 laboratory tests, and liver disease, 691t
 overview of, 662
 platelet activation markers, 821
 primary, 662, 662t
 primary standards, 22–23
 secondary, 662, 662t
 vascular intima in, 662–665. *See also* Vascular intima
 viscoelastometry for, 833–834
- Hemostasis laboratory
 evidence-based practice in, 13
 informatics in, 13
 interprofessional teamwork in, 12–13
 patient-centered care in, 13
 quality improvement in, 13
- Hemostasis specimen collection, 812–815
 anticoagulants for, 813–814
 citrate theophylline adenosine dipyridamole, 814
 EDTA, 813
 sodium citrate as, 813
 blood
 clotted, 815
 materials for, 813–814
 collection tubes for, 813
 needle selection in, 813, 813t
 procedure for, 814–815
 with butterfly set, 814
 with syringe, 815
 venipuncture and, 814–815
 short draw in, 814
 using capillary puncture, 815
 from vascular access devices, 815
 errors in, 814t
 heparinized, 813
 management of, 815–817
 preparation, 816–817
 transport and storage, 815–816
 patient management during, 812
 platelet function tests for, 817–821
 transport and storage of, 816t
- Hemostasis testing
 effective hematology and, 11, 11t
 efficient hematology and, 11–12
 equitable hematology and, 12
 patient-centered hematology and, 12
 safe hematology and, 9–11
 timely hematology and, 12

- Hemostatic system, cell-based physiologic coagulation, 674–676, 675f
- Henoch-Schönlein purpura, 728
- Heparin, 881.e13
- Heparin action, 795
- Heparin cofactor II (HC II), 677
- Heparin-induced thrombocytopenia (HIT), 778–781
- inactivated, 821
- clinical scoring for, 778–779, 779t
- confirmatory platelet activation assays for, 780, 780f
- enzyme immunoassays for, 780, 780f
- pathophysiology of, 778, 779f
- platelet counts for, 778–779, 779t
- rapid turnaround assays for, 780–781
- therapy for, 781
- Heparin resistance, 771
- Hepatic disease, 764t
- Hepatic function test, 266
- Hepatic phase, of hematopoiesis, 60
- Hepatitis B virus (HBV), 881.e12
- vaccination, 881.e5
- Hepcidin, 125–127, 126f, 127t, 281–282
- Hepcidin-ferroportin axis, 125
- Hepcidin production
- erythrocyte iron sensing and, 127–128, 129f–130f
- liver iron sensing and, 126–127, 126f, 127t
- Hephaestin, 126
- Hereditary elliptocytosis (HE), 104, 359–361
- clinical and laboratory findings, 360–361, 360f–361f
- pathophysiology, 360
- treatment, 361
- Hereditary hemochromatosis (HH), 287, 287t
- Hereditary hemorrhagic telangiectasia, 727
- Hereditary hydrocytosis, 354–355, 361–362
- clinical and laboratory findings, 362, 362f
- pathophysiology, 361–362
- Hereditary iron overload, 287
- Hereditary nonspherocytic hemolytic anemia, 98
- Hereditary ovalocytosis, 361
- clinical and laboratory findings, 361
- pathophysiology, 361
- Hereditary pyropoikilocytosis (HPP), 354–355
- Hereditary red blood cell membrane abnormalities, 354–363, 355b
- Hereditary sideroblastic anemias, 284–286, 286f
- Hereditary spherocytosis (HS), 104, 354t, 355–359
- additional tests, 357–358, 358f
- clinical and laboratory findings, 355–357, 359, 359t
- complications, 358–359
- differential diagnosis, 359, 359t
- pathophysiology, 355, 356f
- treatment, 359, 359f
- Hereditary xerocytosis (HX), 105, 354–355, 362
- clinical and laboratory findings, 362
- pathophysiology, 362
- Hermansky-Pudlak syndrome, 718–719
- Hetastarch, 724
- Heterochromatin, 46–47
- Heterozygosity, compound, 430–432, 431f
- Hexokinase, glucose-6-phosphate isomerase, 96, 97f
- Hexose monophosphate pathway, 97f, 98, 98t
- High hyperdiploidy, 557
- High-molecular-weight kininogen (HMWK), 670
- High-performance liquid chromatography (HPLC), 421–422, 422f
- thalassemia and, 457, 457f
- High-throughput sequencing (HTS), 834, 858
- Histiocytes, 881.e47, 881.e47f
- Histologic sections, bone marrow aspiration, 251
- History, of laboratory hematology, 1–7
- HIT. *See* Heparin-induced thrombocytopenia
- HIT Expert Probability (HEP) score, 779
- HLA-DR, 70, 505
- Hodgkin lymphoma, 246, 653–655, 654f
- Holotranscobalamin assay, 306
- Homocysteine, assays for, 305, 307f
- Homocysteinemia, 764
- Homology directed repair (HDR), 426
- HOPE trial, 425
- Hormone replacement therapy (HRT), 875
- Hormones, 875
- of megakaryocytopoiesis, 163, 163t
- Hormone therapy
- and hematopoiesis, 875
- and hemostasis, 875
- Housekeeping, 881.e5
- monocyte/macrophage functions, 151
- Howell-Jolly bodies, 268t, 269f
- H pattern, antecubital fossa, 881.e16, 881.e16f
- Human granulocytic anaplasmosis (HGA), 481
- Human immunodeficiency virus (HIV), 622–623, 738
- acquired aplastic anemia and, 315
- flow cytometry and, 514
- Pneumocystis jiroveci* and, 881.e47, 881.e47f
- Human monocytic ehrlichiosis (HME), 481
- Human plasma-derived fibrinogen concentrates, 689
- Humoral response, 3
- 100x oil immersion objective examination of blood films, 231–232
- HUS. *See* Hemolytic uremic syndrome
- Hyaline thrombi, 750
- Hybridization probes, 533
- Hydrodynamic focusing, 200, 503
- Hydrophobic ligands, 49–50
- Hydroxycarbamide therapy, 425
- Hydroxyethyl starch, 724
- Hydroxymethylbilane, 113–114
- Hyperaggregable platelets, 727
- Hypercoagulability, 762
- Hypercoagulable state, molecular techniques for, 858t
- Hyperdiploid cells, 557
- Hyperfibrinogenemia, 765t
- Hyperparathyroidism, 246
- Hyperproliferation, 596
- Hypersegmentation, neutrophil, 304, 475, 475f
- Hypersplenism, 66
- Hypertonic cryohemolysis test, 358
- Hypochromic microcytes, 620
- Hypodiploid cell, 557, 558f
- Hypofibrinogenemia, 706f, 796
- Hypoplasia, bone marrow, 322t
- Hypoplastic MDS (h-MDS), 624
- Hypovolemia, 418–419
- Hypoxia, 87, 87b
- methemoglobinemia and, 118
- I**
- Ibrutinib (Imbruvica), 724–725
- Icterus, in specimen quality set points, 849
- Identification, 881.e7
- chromosome, 553, 554f
- Idiopathic thrombocytosis, 599
- Immature basophils, 148, 148f
- Immature granulocytes, Pelger Huet neutrophils and, 474–475
- Immature platelet fraction (IPF), 240
- Immature reticulocyte fraction (IRF), 3, 220
- anemia diagnosis and, 265
- Immature T cells, 153
- Immersion oil, 881.e30
- Immune hemolytic anemia, 392–407, 393f–395f
- drug-induced, 403–404, 403f
- laboratory findings in, 396, 397f
- major mechanisms of, 396t
- overview of, 393–396, 394b
- pathophysiology, 393–396
- Immune system
- acquired aplastic anemia and, 316
- basophils and, 148
- in elderly adults, 871
- eosinophils and, 144
- mast cells, 149
- monocyte/macrophage function and, 151
- neutrophils and, 144
- Immune thrombocytopenia, during pregnancy, 870
- Immune thrombocytopenic purpura, 740
- acute, 740
- chronic vs., 740, 740t
- diagnosis of, 740
- hemorrhage risk, 740
- incidence of, 740
- treatment of, 740
- chronic, 740–741, 741f
- acute vs., 740, 740t
- incidence of, 740
- peripheral blood abnormalities in, 741
- platelet destruction in, 741
- risk factors for, 741
- treatment of, 741
- drug-induced immune-mediated thrombocytopenia, 741–744, 742b, 743f
- Immune tolerance induction (ITI), 693
- Immunoassay technology, 846
- Immunologic assays, 846
- Immunologic endpoint detection, 845–846
- Immunophenotyping, in acute lymphoblastic leukemia, 569–570, 569t
- Immunosuppressive therapy, 628
- Impaired fibrinolysis, 833
- Impedance technology, 200–201
- limitations of, 216
- Imprints, core biopsy, 250
- Improving Diagnosis in Health Care*, 8–9
- Inclusions, erythrocytes, 268t
- Incubated osmotic fragility test, 357
- Independent expert laboratories, 23
- Indices, red blood cell, 2
- complete blood count with, 265
- mean cell hemoglobin, 2
- mean cell hemoglobin concentration, 2
- mean cell volume, 2
- Indirect antiglobulin test (IAT), 396
- Indirect chromogenic assay, 845
- Indirect reference interval determination, 30
- Indirect transmission, 881.e12
- Ineffective erythropoiesis, 264, 444, 873
- folic acid deficiency, 873
- insufficient and, 264
- vitamin B₁₂ deficiency, 873
- Ineffective hematopoiesis, 299, 321t
- Ineffective thrombopoiesis, 735
- Infection, 370
- infection control, responsibility of phlebotomist in, 881.e12
- Infections
- associated with thrombocytopenia, 739
- babesiosis and, 386–387
- clinical findings, 387
- geographic distribution, 387
- laboratory findings and diagnosis, 387, 387f
- bartonellosis, 387–388
- clostridial sepsis, 387
- Epstein-Barr virus, 315
- hemolytic anemia caused by, 384–388
- malaria, 332
- clinical and laboratory findings, 385
- hemolytic anemia caused by, 384–388
- microscopic examination, 385, 385f
- pathogenesis, 384–385
- Plasmodium falciparum* and, 385, 386f
- Plasmodium knowlesi* and, 385, 386f
- Plasmodium malariae* and, 385, 386f

- Infections (*Continued*)
Plasmodium ovale and, 385, 386f
Plasmodium vivax and, 385, 385f prevalence, 384
 neonatal hematologic response to, 867
 sickle cell disease and, 418
- Infectious disease load, pathogen detection and, 542
 Infectious mononucleosis, 484
 Infectious wastes, 881.e12
- Inflammation, 597
 anemia of, 281–284
 etiology, 281–283
 laboratory diagnosis of, 283–284, 283f
 treatment of, 284
 chronic, thrombotic risk components of, 764t
 and disease, reactive thrombocytosis associated with, 753
- Inflammation, platelets and, 173
- Informatics, 13
 in hematology and hemostasis laboratory, 14
- Information technology, 13
- Inherited aplastic anemia, 318–321
 dyskeratosis congenita, 319–320
 Fanconi anemia, 318–319
 Shwachman-Bodian-Diamond syndrome, 320–321
- Inherited FXIII deficiency, 706
- Inherited giant platelet syndromes, 717, 718t
- Inherited hemolytic conditions, 332
- Inherited platelet disorders, 714, 716t
- Inherited thrombocytopenia, 735–737
 associated with chromosomal abnormalities, 735–737
 Fanconi anemia, 737
 list of, 736t
 May-Hegglin anomaly, 737, 737f
 neonatal thrombocytopenia and, 738, 738t
 TAR syndrome, 737
- Innate immunity, 151
- Inositol triphosphate-diaclyglycerol activation pathway, 173
- Insertion, chromosome, 558, 558f
- Institute of Medicine (IOM), 8–9
- Insufficient erythropoiesis, 264
- Integrins, 52, 144
- Intercept, 25
- Interferon therapy, thrombocytopenia by, 739
- Interferon- α , 589
- Interleukins (ILs), 71
- Intermediate angle scatter (IAS) scatter, 210
- Intermediate filaments, 46t, 48
- Internal quality control, 31–33
- Internal tandem duplication, 493
- International Classification of Diseases-Tenth Revision (ICD-10) system, 834
- International Consensus Classification (ICC), 623, 625t
- International Council for Standardization in Haematology (ICSH), 216
- International Normalized Ratio, 823
- International Prognostic Scoring System (IPSS), 627
- International sensitivity index (ISI), 793
- International Society for Laboratory Hematology (ISLH), 203
- Interphase, 53
- Interprofessional teamwork, 12–13
 in hematology and hemostasis laboratory, 13
- Interpupillary control, microscope, 881.e27
- Interstitial deletion, 558, 558f
- Intracellular acidosis, 263–264
- Intracellular calcium pyrophosphate crystals, 881.e45f
- Intracellular iron
 regulation, 131
 trafficking, 131
- Intravascular hemolysis, 91, 332, 339–340, 341f–344f
- Intravenous direct thrombin inhibitors, 801–802, 801f
- Intravenous (IV) fluids, 417
- Intravenous therapy, 881.e19
- Intrinsic accessory pathway proteins. *See* Contact factors
- Intrinsic factor, lack of, 303
- Intrinsic hemolytic conditions, 332
- Intrinsic tenase, 670
- Ionic iron absorption, 125–126, 125f
- Ionized calcium (Ca^{2+}), 668
- Iron, 122–138
 chemistry, 123
 compartments, 123, 123t
 deficiency, 134, 134f, 279. *See also* Iron deficiency anemia
 dietary, 131
 kinetics, 124–131
 cellular, 129–131
 disorders, 275–295
 recycling, body iron and salvage, 128–129
 systemic body, 124–128, 124f
 laboratory assessment of body, 132–134, 132t
 ferritin, 133–134
 hemoglobin content of reticulocytes, 134
 percent transferrin saturation, 132–133
 Prussian blue staining, 133
 serum iron, 132
 soluble transferrin receptor, 134
 soluble transferrin receptor/log ferritin, 134
 Thomas plot, 134, 134f
 total iron-binding capacity, 132
 zinc protoporphyrin, 134
- Iron deficiency anemia, 276–281
 in elderly adults, 873
 epidemiology of, 279
 etiology of, 276–277
 chronic blood loss, 277
 impaired absorption, 276–277
 inadequate intake, 276
 increased need, 276
 laboratory diagnosis of, 279–281
 specialized tests of, 280–281, 281f
 pathogenesis of, 277–278, 277f
 stage 1, 278
 stage 2, 277f, 278
 stage 3, 277f, 278
 treatment and its effects, 281
 pediatric, 865–866
 in pregnancy, 868
 reactive thrombocytosis associated with, 753
 thalassemia minor and, 459
- Iron overload, 286–289
 differential diagnosis of, 280t, 289
 etiology of, 287
 laboratory diagnosis of, 288–289
 directed testing, 288
 directed testing for treatment, monitoring, and genetic counseling, 288–289
 routine testing, 288
 phenotype and epidemiology of, 288
 sickle cell disease and, 423
 treatment of, 289
- Iron-sulfur clusters, 123, 123t
- Irreversible sickle cells, 415
- Ischemia, 762
- iSED (Alcor Scientific), 191
- Isochromosomes, 558, 558f
- Iso citrate dehydrogenase 1 (*IDH1*), 596–597
- Iso citrate dehydrogenase 2 (*IDH2*), 596–597
- Isoelectric focusing (IEF), 422
- Isolation, nucleic acid, 527–529
- Iso volumetric sphering, 200
- I-STAT instrument, 194, 194f
- J**
- JAK2 inhibitors, 450, 598
- JAK2 V617F mutation, 594, 598–599, 875
- Jakitinib, 598
- Janus kinase 2 (JAK2), 52
- Jaundice, 370–371
 hemolytic, 340
 prehepatic, 340
- Joint Commission, 38
- Juvenile myelomonocytic leukemia (JMML), 609–610
 clinical presentation of, 609
 diagnosis of, 609
 peripheral blood and bone marrow, 609
 prognosis of, 609–610
- K**
- Karyogram, 554
- Karyotype, 554
- Kasabach-Merritt syndrome, 727
- Keratocyte, 267t
- Kidneys
 chronic renal failure and hemorrhage, 691–692
 disease, chronic, 324–325
 renal peritubular interstitial cells, 72
- Kinetics
 basophils, 148
 eosinophils, 146
 iron, 124–131
 cellular, 129–131
 recycling, body iron and salvage, 128–129
 systemic body, 124–128, 124f
 monocyte/macrophage, 150–151, 151f
 neutrophils, 143–144
- KIT ligand, 72, 163
- Kleihauer-Betke acid elution slide test, 458
- Koaguloviskosimeter, 842
- Koehler illumination, 881.e29
- Kringles, 679
- KRT232 inhibitor, 598–599
- Kupffer cells, 64, 282
- L**
- Laboratory diagnosis, 288–289. *See also* Assays; Clinical and laboratory findings; Differential diagnosis
 anemia of chronic inflammation, 283, 283f
 babesiosis, 387, 387f
 chronic eosinophilic leukemia, 609
 chronic myelogenous leukemia, 587–588
 chronic neutrophilic leukemia, 607–608
 directed testing for diagnosis, 288
 directed testing for treatment, monitoring, and genetic counseling, 288–289
 essential thrombocythemia, 599
 hemoglobin E, 430, 430f
 hemoglobin SC, 431
 iron deficiency anemia, 279–281
 diagnosis of iron deficiency in, 279–280, 280t
 screening for, 278f, 279
 specialized tests, 280–281, 281f
 iron overload, 288–289
 directed testing, 288
 directed testing for treatment, monitoring, and genetic counseling, 288–289
 routine testing, 288
 mastocytosis, 611–612
 megaloblastic anemia, 303–306
 screening tests, 303–305
 specific diagnostic tests, 305–306, 305f
 molecular methods, 527, 528b
 of polycythemia vera, 601–602, 602b
 routine testing, 288
 sickle cell disease, 420–422, 420f–421f
 of thalassemias, 455–459, 456t
 unstable hemoglobin variants, 434
 β -thalassemia minor, 452

- Laboratory hematology
 additional procedures, 6
 advanced procedures, 5–6
 blood film examination in, 5
 body iron status, 132–134, 132t
 coagulation in, 5
 complete blood count in, 4–5, 4b
 endothelial cells in, 5
 history of, 1–7
 platelets in, 4
 quality assurance and quality control, 6–7
 red blood cells in, 1–3, 2f
 white blood cells in, 3–4
- Laboratory Medicine Quality Improvement, 38
- Laboratory safety, 7
- Laboratory staff competence, 36–38
- Laboratory testing services, 9
- Lactate dehydrogenase, 96–98, 266, 345
 levels, 304–305, 305b
- Lagging strand, DNA replication, 527
- Laminar flow, 200
- Langerhans cells, 246
- Large granular lymphocytes (LGLs), 646
- L-arginine, 424
- Latent iron deficiency, 134, 134f
- Late-term neonates, 863–864
- Laundry, 881.e5
- Leading strand, DNA replication, 527
- Lead poisoning, 286
- Lecithin cholesterol acyltransferase, 99–100
- Lee-White whole-blood coagulation time test, 821
- Left shift, band neutrophils, 3, 237, 238b
- Lenalidomide, 628
- Lentiviral vectors, 425
- Leukemias, 4, 321, 321t, 490, 642–646
 acute. *See* Acute leukemias
 B lymphoblastic, 511, 512f
 chronic. *See* Chronic leukemias; Chronic lymphocytic leukemia; Chronic myelogenous leukemia
 chronic lymphocytic leukemia, 642–644, 643f, 643b, 644t
 cytogenetics, 559–561, 559b
 defined, 567
 flow cytometric analysis of, 506–510
 hairy cell leukemia, 645–646, 645f
 large granular lymphocytes, 646
 large granular lymphocytic, 646
 minimal residual disease in, 535, 537f
 monoclonal B-cell lymphocytosis, 644
 small lymphocytic lymphoma, 642–644
 spleen in, 66
 thrombotic risk components of, 764t
 T lymphoblastic, 511, 513f
 T-prolymphocytic leukemia, 644–645, 645f
- Leukemic stem cells, 492
- Leukemic transformation, 607
- Leukemogenesis, 492
- Leukemoid reaction, 476, 477t
- LeukoChek, 183f
- Leukocyte adhesion disorder type I, 469
- Leukocyte adhesion disorder type II, 469
- Leukocyte adhesion disorder type III, 469
- Leukocyte neoplasms, 489–499
 classification schemes of, 490f, 491–492
 general characteristics of, 490–491
 incidence, prevalence, and etiology of, 491
 molecular pathogenesis of, 492–494
 DNA repair genes, 494
 epigenetic mechanisms, 492–493, 492t
 hematologic malignancies, cellular processes perturbed in, 492, 492b
 oncogenes, 493, 494t
 tumor suppressor genes, 493–494, 494t
 therapy for, 494–497, 494b
 chemotherapy, 494–495
 hematopoietic stem cell transplantation, 496–497, 497f
- Leukocyte neoplasms (*Continued*)
 radiation, 495
 supportive, 495
 targeted, 495–496
- Leukocyte number and function, congenital
 defects of, 465–470
 22q11.2 deletion syndrome, 466
 Bruton tyrosine kinase deficiency, 466–467
 Chédiak-Higashi syndrome, 467
 phagocyte number and/or function, congenital
 defects of, 467–470
 severe combined immune deficiency, 465–466
 Wiskott-Aldrich syndrome, 466
- Leukocytes, 3
 adhesion disorders, 468–469
 counts, 3, 232b
 peripheral blood film examination, 232–234, 233f
 relative vs. absolute, 237t
 summarizing, 236–237, 236t
 white blood cell differential, 232–234, 233f, 304
 development of, 139–158
 granulocytes, 140–149
 basophils, 3, 139–140, 147–149
 eosinophils, 3, 139–140
 mast cells, 149, 149f
 neutrophils, 3, 139–146
 lymphocytes, 3
 T, 64–65, 67–68
 mononuclear cells, 140
 lymphocytes, 151–154
 monocytes, 149–151
 morphologic abnormalities of, without associated immunodeficiency, 474–476
 Alder-Reilly anomaly, 475
 May-Hegglin anomaly, 475–476, 475f
 neutrophil hypersegmentation, 475, 475f
 Pelger-Huët anomaly, 474
 pseudo- or acquired Pelger-Huët anomaly, 474–475
 in neonates
 eosinophils and basophils, 866
 lymphocytes, 866–867, 867f
 quantitative abnormalities of, 476–479, 476b, 477t
 basophils, 478
 eosinophils, 478
 lymphocytes, 479
 monocytes, 478–479
 neutrophils, 476–478
 storage artifacts in, 479
- Leukocytosis, 3
 Leukoerythroblastic picture, 476
 Leukoerythroblastic reaction (LER), 476
 Leukoerythroblastosis, 476
- Leukopenia, 3
 Leukopoiesis, 72
 Levels of laboratory assay approval, 28, 29t
 Levey-Jennings chart, 31, 32f
 L-glutamine, 424
 Licensure, laboratory staff, 38
 Lifecodes PF4 IgG (Immucor GTI) kit, in enzyme immunoassays, 780
- Ligands, 49–50, 165
- Ligase, 527
- Light absorbance end-point detection, 846, 846f
- Light scatter
 for RBC and platelet analyses, 213, 215f
 signals, 210–212
 for WBC count, WBC differential, NRBCs and reticulocyte analysis, 213–216, 215f
- Light transmission aggregation (LTA) detection, 855
- Light transmittance platelet aggregometry, 780
 platelet-rich plasma for, 816
- Lineage-specific hematopoiesis, 72–73
 erythropoiesis, 72
 leukopoiesis, 72
 megakaryocytopoiesis, 72–73
- Linearity, 26–28, 28f
- Linear regressions, 25, 27f
- Lipemia, in specimen quality set points, 849
- Lipids, RBC membrane, 100, 100f
- Lipoprotein (a), in arterial thrombosis predictors, 773
- Liver, 64, 64f
 biopsy, Prussian blue staining and, 132t, 133
 pathophysiology, 64
- Liver disease
 coagulopathy, 690–691
 disseminated intravascular coagulation, 693
 hemostasis laboratory tests, 691t
 platelet dysfunction in, 725–726
- Liver iron sensing and hepcidin production, 126–127, 126f, 127c
- Liver sensing
 of circulating iron, 126f, 127, 128f
 of stored iron, 126f, 127
- LMWH. *See* Low-molecular-weight heparin
- Location
 basophilic normoblast, 83, 83f
 erythrocyte, 86, 87f
 orthochromic normoblast, 84, 84f
 polychromatic erythrocyte, 85, 85f–86f
 polychromatic normoblast, 84, 84f
 pronormoblast, 82
- Long-term testosterone therapy, 875
- Loss-of-function mutations, 493
- Lot-to-lot comparisons, 29, 30t
- Low-angle light scatter (LALS), 206
- Lower limit of detection, 28
- Lower median-angle light scatter (LMALS), 206
- Low molecular weight heparin (LMWH), 791t, 797–798
 action, 797, 797f
 laboratory assessment of, 797–798, 798f
 therapy, 797
- Lumbar puncture, 881.e36, 881.e37f
- Luminescence detector, 855
- Lupus anticoagulants, 825–826
 profile, 766–769, 767f
 clot-based, 768
- Lupus erythematosus cells, 881.e42, 881.e43f, 881.e44
- Luspatercept, 598, 628
- Lymphatic capillaries, 66
- Lymph nodes, 66, 67f
 pathophysiology, 66
- Lymphoblastic leukemia/lymphoma, flow
 cytometric analysis of, 510–513
- Lymphoblasts, 490f, 491, 567, 881.e40f
- Lymphocytes, 3, 151–154, 483–484, 881.e38, 881.e38f
 B, 151–152
 bone marrow aspiration examination, 257, 257f
 development, 152–153, 152f–153f
 natural killer cells, 151
 pediatric, 866–867, 867f
 quantitative abnormalities of, 479
 lymphocytosis, 479
 lymphopenia, 479
 reactive lymphocytes, 483–484
 T, 64–65, 67–68, 151
- Lymphocytopenia, 3
- Lymphocytosis, 3, 479
- Lymphoid lineage, 506
- Lymphomas, 490
 Hodgkin, 246
- Lymphopenia, 479
- Lysosomal storage disorders (LSDs), 470–474
- Lysosome membrane, 48
- Lysosomes, 46t, 48, 165f, 166

M

- Macroangiopathic hemolytic anemia, 383–384
 exercise-induced hemoglobinuria, 384
 traumatic cardiac hemolytic anemia, 383, 384f

- Macrocytes
 associated disease states, 267t
 oval, 267t
- Macrocytic anemias, 268–270
 algorithm for preliminary investigation of, 309f
 certain drugs, 297b
 nonmegaloblastic, 306–308
- Macrophage colony-stimulating factor (M-CSF), 149
- Macrophages, 3–4, 61–62
 in elderly adults, 871
 functions, 151
 kinetics, 150–151, 151f
 mediated hemolysis, 91
 -mediated hemolysis, 333–335, 335f
 fragmentation hemolysis vs., 338–339, 339t
 pathologic, 338–339, 338f
 in serous fluids, 881.e39
- Macropinocytosis, 124
- Major basic protein (MBP), 147
- Major molecular response (MMR), 590
- Malabsorption, 303
- Malaria, 332
 clinical and laboratory findings, 385
 hemolytic anemia caused by, 384–388
 microscopic examination, 385, 385f
 pathogenesis, 384–385
 Plasmodium falciparum and, 385, 386f
 Plasmodium knowlesi and, 385, 386f
 Plasmodium malariae and, 385, 386f
 Plasmodium ovale and, 385, 386f
 Plasmodium vivax and, 385, 385f
 prevalence, 384
- Malignant cells, in cerebrospinal fluid, 881.e39, 881.e42
- Malignant lymphoma cell clusters, 256
- Mantle cell lymphoma, 648–649, 649f
- Manual cell counts, 180–183
 body fluid, 183
 calculations for, 180–183
 disposable blood cell count dilution systems, 183, 183f
 equipments for, 180, 180f
 with most common dilutions, 183t
 platelet, 182
 principle, 180
 red blood cell, 183
 reticulocyte, 187–190
 white blood cell, 181
- Manual wedge technique, 227–228, 228f
- Marginal zone lymphoma, 650–651, 651f
- Marginated neutrophil pool (MNP), 144
- Massive hemorrhage, 688–689
- Massive transfusion protocols (MTPs), 688–689
- Massive transfusion, trauma-induced
 coagulopathy, 688–689
- Mast cells, 149, 149f
 growth factor, 163
- Mastectomy, 881.e19
- Mastocytosis, 611–612
 clinical presentation of, 611
 diagnosis of, 611–612
 incidence of, 611
 pathogenetic mechanism, 612
 prognosis of, 612
- Matriptide-2, 127t
- Matrix-assisted laser desorption/ionization-time of flight (MALDI-TOF) mass spectrometry, 544
- Maturation, RBC
 criteria used in identification of erythroid precursors in, 80–81, 81f, 81b
 process, 79
 sequence, 81–86, 82f, 82t
 terminology, 79t
- Mature basophils, 148, 148f
- Mature eosinophils, 146
- Mature lymphoid neoplasms, 510–513, 634–660, 635b
 approach to diagnosis of, 637
 Catovsky-Matutes scoring for, 643b
 chromosome and gene abnormalities in, 636t
 classification schemas based on cell differentiation, 635–637
 clinical behavior of, 637b
 clinical signs and symptoms of, 637
 common immunophenotypes for, 640t
 diagnostic procedure for, 637–641
 anatomic pathology testing, 641
 clinical laboratory testing, 637–641, 640f
 imaging studies, 641
 prognostic assessment, 642
 staging system, 641–642, 642t, 644t
 genetic abnormalities, 635, 636f
 Hodgkin lymphoma, 653–655, 654f
 immunologic diversity, 635
 leukemias and, 642–646
 monoclonal B-cell lymphocytosis (MBL), 644
 non-Hodgkin lymphoma and, 646–653, 646b
 T-prolymphocytic leukemia, 644–645, 645f
 treatment of, 646
 WHO classification of, 638b–639b
- Mature red blood cells, 62
- May-Hegglin anomaly (MHA), 475–476, 475f, 737, 737f
- MCH. *See* Mean cell hemoglobin
- MCHC. *See* Mean cell hemoglobin concentration
- McLeod syndrome (MLS), 363
- MCV. *See* Mean cell volume
- MD Anderson Prognostic Scoring System (MDAPSS), 627
- MDS. *See* Myelodysplastic syndromes
- MDS/MPN with *SF3B1* mutation and thrombocytosis (MDS/MPN-*SF3B1-T*), 627
- Mean cell hemoglobin (MCH), 2, 187, 237, 865
 anemia diagnosis and, 265
 megaloblastic anemia and, 304
- Mean cell hemoglobin concentration (MCHC), 2, 187, 237, 865
 anemia diagnosis and, 265
 megaloblastic anemia and, 304
- Mean cell volume (MCV), 2, 187, 237, 238t, 356–357, 865
 anemia diagnosis and, 265
 exercise-induced hemoglobinuria and, 384
 hemolysis diagnosis and, 346
 megaloblastic anemia and, 304
- Mean, computation of, 20–21
- Mean fluorescence intensity (MFI), 358
- Mean peroxidase activity index (MPXI), 215
- Mean platelet volume (MPV), 163, 221
- Mechanical clot endpoint detection, 843, 844f, 846f
- Median-angle light scatter (MALS), 206
- Median, determination of, 21
- Medical errors, 9
- Medical laboratory professionals, 12–14
- Medullary phase of hematopoiesis, 60
- Megakaryoblasts, 161f, 162
 acute megakaryoblastic leukemia, 575, 577f
- Megakaryocytes, 60, 62, 63f, 160, 161f
 bone marrow aspirate examination, 252–253, 252f, 256
 differentiation and progenitors, 160, 161f
- Megakaryocytic hypoplasia, 735
- Megakaryocytic lineage, 506
- Megakaryocytopoiesis, 72–73, 160–163
 endomitosis, 160, 160b
 hormones and cytokines of, 163, 163t
 megakaryocyte differentiation and progenitors, 160, 161f
 megakaryocyte membrane receptors and markers, 162, 163t
 terminal megakaryocyte differentiation, 160–162, 161f, 162t
 thrombocytopoiesis, 161f–162f, 162
- Megaloblastic anemia, 268–270, 296b, 297
 caused by defects of DNA metabolism, 296–312
 differential diagnosis, 321t
 in elderly adults, 873
 etiology of, 297–300, 297b
 defect in megaloblastic anemia caused by deficiency in folate and vitamin B₁₂, 298–300, 299f
 other causes of, 300
 physiologic roles of vitamin B₁₂ and folate, 297–298, 298f
 laboratory diagnosis of, 303–306
 screening tests, 303–305
 specific diagnostic tests, 305–306
 in pregnancy, 869
 systemic manifestations of folate and vitamin B₁₂ deficiency, 301–303
 treatment of, 308
 vitamin deficiencies, causes of, 301–303
- Megaloblastic crisis, 358–359
- Megaloblastosis, causes of, 300
- Membrane, 99–105
 deformability, 99, 104, 353–368
 lipids, 99–101, 100f
 osmotic balance and permeability, 104–105
 proteins, 45, 101–104, 102f, 103t
 cytoskeletal, 102f, 103–104, 104t, 105f
 transmembrane, 45, 101–103, 102f, 103t
 structure and function, 95–108, 353–354
- Membrane abnormalities, 353–368
 abetalipoproteinemia, 363
 acquired, 363–368
 acquired red blood cell, 363–368
 acquired stomatocytosis, 363
 chorea acanthocytosis, 363
 cryohydrocytosis, 362
 familial pseudohyperkalemia, 362
 hereditary elliptocytosis, 359–361
 clinical and laboratory findings, 360–361, 360f–361f
 pathophysiology, 360
 treatment, 361
 hereditary hydrocytosis, 354–355, 361–362
 clinical and laboratory findings, 362, 362f
 pathophysiology, 361–362
 hereditary ovalocytosis, 361
 clinical and laboratory findings, 361
 pathophysiology, 361
 hereditary red blood cell, 354–363, 355b
 hereditary spherocytosis, 355–359
 additional tests, 357–358, 358f
 clinical and laboratory findings, 355–357, 359, 359t
 complications, 358–359
 differential diagnosis, 359, 359t
 pathophysiology, 355, 356f
 treatment, 359, 359f
 hereditary with acanthocytes, 362–363
 hereditary xerocytosis, 354–355, 362
 clinical and laboratory findings, 362
 pathophysiology, 362
- McLeod syndrome, 363
- neuroacanthocytosis, 363
- paroxysmal cold hemoglobinuria, 331–332
- paroxysmal nocturnal hemoglobinuria, 364–368
 acquired aplastic anemia and, 315
 differential diagnosis, 321t
- Rh deficiency syndrome, 362
- spur cell anemia, 363
 structure and function and, 353–354
- Membrane inhibitor of reactive lysis (MIRL), 103
- Membrane proteins, 358
- Membrane structure and function, 99–105
- Mesenchymal cells, 61–62
- Mesoblastic phase of hematopoiesis, 60
- Mesothelial cells, in cerebrospinal fluid, 881.e42

- Metabolism, erythrocytes, 95–108
 energy production through anaerobic glycolysis, 96–98, 96b, 97f, 98t
 erythrocyte membrane, 99–105
 deformability, 99, 104
 lipids, 99–101, 100f
 osmotic balance and permeability, 104–105
 proteins, 101–104, 102f, 103t
 cytoskeletal, 102f, 103–104, 104t, 105f
 transmembrane, 101–103, 102f, 103t
 structure and function, 95–108
 erythrocyte membrane structure and function, 99–105
 glycolysis diversion pathways, 98–99
 hexose monophosphate, 97f, 98, 98t
 methemoglobin reductase, 97f, 98–99
 Rapoport-Luebering, 97f, 99
- Metamyelocytes
 eosinophils, 146
 neutrophils, 141, 141f, 144f
- Metaphase, 53
 analysis, 554
 checkpoint, 53
 chromosomes, 553
- Metastatic tumors, 246
- Methanol-free stain, 230
- Methemoglobin, 118–119
 reductase pathway, 97f, 98–99
- Methemoglobinemia, 118–119
- Methylcobalamin, 297
- Methylene blue, 242
- Methylmalonic acid, 305–306, 306b, 307f
- Microangiopathic hemolytic anemia (MAHA), 380–383, 381b, 747, 748f, 776–777
 disseminated intravascular coagulation, 383
 HELLP syndrome, 383
 hemolytic uremic syndrome, 382–383
 thrombotic thrombocytopenic purpura, 381–382, 382f
- Micro Chromatic Detection for Haematology (MCDh), 230
- Microcyte, 267t
- Microcytic anemias, 268
- Microfilaments, 46t, 48, 165–166, 165f
- Microhematocrit, 184–186
 maximum packing time for, 185b
 principle, 184–186
 procedure, 185f, 185b
 sources of error and comments, 185b
- Microscope(s), 881.e26
 basic troubleshooting, 881.e30
 care of, 881.e30
 component parts and their functions, 881.e27, 881.e27f
 compound, 881.e26, 881.e27, 881.e27f
 darkfield microscopy, 881.e31
 examination of peripheral blood films, 231–235
 fluorescent microscope, 881.e31
 immersion oil and types, 881.e30
 operating procedure with Koehler illumination, 881.e29
 phase-contrast microscope, 881.e30
 polarized light microscope, 881.e31
 principles of, 881.e26
- Microscopy, of malaria, 385, 385f
- Microsomal triglyceride transfer protein (MTP) gene, 363
- Microstrokes, 419
- Microtubules, 46t, 48, 165–166, 165f
 circumferential, 165–166
- Miller disc, 188f, 188b
- Minimal residual disease in leukemia, 535, 537f
- Mitochondria, 46t, 47–48, 47f
- Mitogen-activated protein kinase (MAPK) stress response, 424
- Mitosis, 53
- Mixed phenotype acute leukemias (MPALs), 577
- Mixed-type autoimmune hemolytic anemia, 401
- Mode, determination of, 21
- Model 700 aggregometer, 856
- Modified Westergren erythrocyte sedimentation rate, 190, 191f
- Moist chamber, 181b
- Molecular alterations, myelodysplastic neoplasms, 627
- Molecular coagulation testing, 857–858, 858t
- Molecular diagnostics, in hematopathology, 519–549, 520f–521f, 520b–522b
 amplification of nucleic acids by polymerase chain reaction, 529–532, 530f
 for amplifying DNA, 529, 530f
 reverse transcription for amplifying RNA, 530–532, 531f
 chromosomal microarrays, 542, 543f
 current developments in, 542–545
 detection of amplified DNA, 532–533
 capillary gel electrophoresis, 532, 532f
 DNA sequencing, 536–538, 540f
 restriction endonuclease methods, 533
 diagnosis assays, 5
 next-generation sequencing, 538–542, 541f
 nucleic acid isolation, 527–529
 pathogen detection and infectious disease load, 522b, 542
 real-time polymerase chain reaction, 533–536, 533f
 digital polymerase chain reaction, 535, 538f
 minimal residual disease in leukemia, 535, 537f
 multiplex ligation-dependent probe amplification, 535, 539f
 mutation enrichment strategies, 535–536
 qualitative, 534–535, 534f
 quantitative, 535, 536f
 structure and function of DNA in, 521–527
 central dogma in genetics and, 521–523, 522f
 DNA at molecular level and, 523–524, 523f–525f
 DNA replication and the cell cycle, 525–527, 526f
 transcription and translation in, 524–525
 testing overview, 527, 528b
- Momelotinib, 598
- MOMENTUM clinical trial, 598
- Monochromatic light, 202
- Monoclonal B-cell lymphocytosis (MBL), 644
- Monoclonal gammopathy of undetermined significance (MGUS), 655
- Monocyte distribution width (MDW), 206
- Monocytes, 3–4, 149–151, 881.e38, 881.e38f
 acute monocytic leukemia, 574–575, 576f
 development, 149–150
 in elderly adults, 871
 functions, 151
 green-blue inclusions in, 482, 482f
 intracellular organisms in, 481–482
 kinetics, 150–151, 151f
 pediatric, 867
 quantitative abnormalities of, 478–479
 monocytopenia, 479
 monocytosis, 478, 478b
 secondary changes in, 479–482
- Monocytic lineage, 506
- Monocytopenia, 479
- Monocytosis, 3–4, 478, 478b
- Mononuclear cells, 140, 149–154
 lymphocytes, 3, 151–154
 monocytes, 3–4, 149–151
- Mononucleosis, infectious, 484
- Monophyletic theory, 68
- Monosodium urate crystals, 881.e45, 881.e45f
- Morphology, 1
 of acute lymphoblastic leukemia, 568, 569f
 chronic lymphocytic leukemia, 643, 643f
 classification of anemia based on mean cell volume, 268–271
 hereditary elliptocytosis, 360, 360f
 red blood cell, 234
- Motility, defects of, 467
- Moving average of red blood cell indices, 32–33
- M pattern, antecubital fossa, 881.e16, 881.e16f
- MPL gene mutation, 737
- MPNs. *See* Myeloproliferative neoplasms
- mRNA processing errors, 443
- M (mitosis) stage, cell cycle, 53
- Mucocutaneous hemorrhage, 687
- Mucopolysaccharidoses, 470
- Multianalyte polarized scatter separation (MAPSS), for
 WBC count, WBC differential, NRBC, platelet, and reticulocyte analysis, 210–213, 211f–212f
- Multiple myeloma, 246, 655–656, 656f, 725
- Multiplex ligation-dependent probe amplification (MLPA), 535, 539f
- Mycoplasma pneumoniae*, 399
- Mycosis fungoides* (MF), 651–652, 652f
- Myeloblasts, 141, 142f, 567
 acute monoclonal leukemias, 574–575, 576f
- Myelocytes, 141, 141f
 eosinophils, 146
 neutrophils, 141, 143f
- Myelodysplasia, acute myeloid leukemia with, 573
- Myelodysplastic/myeloproliferative neoplasms, 618–633, 873. *See also* Myeloproliferative neoplasms
 abnormal cellular function, 623
 childhood myelodysplastic neoplasms, 626
 with increased blasts, 626
 with low blasts, 626
 chronic myelomonocytic leukemia, 626
 classification of, 623, 626b
 French-American-British classification, 623
 International Consensus Classification, 623, 625t
 World Health Organization classification, 623, 624b
 cytogenetics, 627
 with defining genetic abnormalities, 623–624
 with biallelic *TP53* inactivation, 624
 with low blasts and isolated 5q deletion, 623–624
 with low blasts and *SF3B1* mutation, 624
 epigenetics, 627
 etiology, 619–620
 future directions, 628
 MDS/MPN, not otherwise specified, 627
 molecular alterations, 627
 morphologically defined, 624–626
 with increased blasts, 626
 with low blasts, 624
 myelodysplastic neoplasm, hypoplastic, 624
 myelodysplastic/myeloproliferative neoplasms, 626–627
 chronic myelomonocytic leukemia, 626
 classification of, 626b
 MDS/MPN, not otherwise specified, 627
 with neutrophilia, 626–627
 with *SF3B1* mutation and thrombocytosis, 627
 with neutrophilia, 626–627
 peripheral blood and bone marrow,
 morphologic abnormalities in, 620–622
 dyserythropoiesis, 620, 620f
 dysmegakaryopoiesis, 622, 622f–623f
 dysmyelopoiesis, 620–622, 621f–622f, 621b
 prognosis, 627–628
 treatment, 628
- Myelodysplastic/myeloproliferative neoplasm with neutrophilia (MDS/MPN-N), 626–627

- Myelodysplastic neoplasm with biallelic *TP53* inactivation (MDS-biTP53), 624
- Myelodysplastic neoplasm with increased blasts (MDS-IB), 626
- Myelodysplastic neoplasm with low blasts (MDS-LB), 624
- Myelodysplastic neoplasm with low blasts and isolated 5q deletion (MDS-5q), 623–624
- Myelodysplastic syndromes (MDS), 300, 321f, 508–510, 511f, 619
- Myelofibrosis, 598, 604–605
with myeloid metaplasia, 604
primary, 604–607
collagen in, 604–605
hematopoiesis and extramedullary hematopoiesis in, 605
incidence and clinical presentation of, 605
pathogenetic mechanism of, 605
peripheral blood and bone marrow in, 605, 606f, 606t
treatment and prognosis of, 605–607
- Myeloid cells, 62, 63f, 621f
nuclear ring in, 620, 622f
- Myeloid-erythroid (ME) layer, concentrate smears, 250
- Myeloid/lymphoid neoplasms, 610–611
- Myeloid neoplasm post cytotoxic therapy (MN-pCT), 619–620
- Myeloid neoplasms with germline predisposition, 620
- Myeloid sarcoma, 576, 588
- Myeloperoxidase (MPO)
deficiency, 470
stains and interpretations, 577–578, 578f
- Myelophthisic anemia, 324, 324f
- Myeloproliferative neoplasm-not otherwise specified, 610
diagnosis, 610
prognosis, 610
- Myeloproliferative neoplasms (MPNs), 583–617, 725, 763–764, 764t, 873
categories, 584
chronic eosinophilic leukemia, 608–609
chronic myelogenous leukemia (CML), 584–592
cytogenetics of Philadelphia chromosome and, 584–585
incidence of, 584
laboratory findings of, 587–588
molecular genetics in, 585–586, 585f
pathogenetic mechanism of, 586, 586f
peripheral blood and bone marrow, 587, 587f–588f, 588t
progression of, 588–589
treatment of, 589–592, 589f, 591f
chronic neutrophilic leukemia, 607–608
in elderly adults, 873
essential thrombocythemia, 4, 599–601, 753–754
clinical presentation of, 599
diagnosis of, 599
incidence of, 599
pathogenetic mechanism of, 599
peripheral blood and bone marrow, 599–600, 600f, 600t
treatment and prognosis of, 600–601
flow cytometric analysis of, 508–510
juvenile myelomonocytic leukemia, 609–610
clinical presentation of, 609
diagnosis of, 609
peripheral blood and bone marrow, 609
prognosis of, 609–610
mastocytosis, 611–612
not otherwise specified, 610
diagnosis, 610
prognosis, 610
polycythemia vera, 601–604
- Myeloproliferative neoplasms (MPNs) (*Continued*)
clinical presentation of, 602–603
diagnosis of, 601–602, 602b
incidence of, 601
pathogenetic mechanism of, 594f–595f, 601
peripheral blood and bone marrow, 602, 603f, 603t
treatment and prognosis of, 603–604
primary myelofibrosis, 604–607
collagen in, 604–605
hematopoiesis and extramedullary hematopoiesis in, 605
incidence and clinical presentation of, 605
pathogenetic mechanism of, 605
peripheral blood and bone marrow in, 605, 606f, 606t
treatment and prognosis of, 605–607
thrombocytosis associated with, 753–754
MYH9 gene, mutations in, 737
- N**
- NAM. *See* National Academy of Medicine
- α -naphthyl acetate, 578–579
- α -naphthyl butyrate esterase reaction, 579, 579f
- National Academy of Medicine (NAM), 8–9, 14
- Natural killer (NK) cells, 151
development, 153
functions, 154
Navitoclax, 598
- Near-haploid cells, 557
- Near-patient viscoelastometry (VET), 797
- Neck, microscope, 881.e27
- Necrosis, 54, 55f, 55t, 762
- Needle
bone marrow aspiration and biopsy, 247, 247f
selection of, for hemostasis blood specimen collection, 813, 813t
venipuncture, 881.e13, 881.e15f
- Needle holders, venipuncture, 881.e13, 881.e15f
- Neimann-Pick disease, 48
- Neisseria meningitidis*, 367–368
- Neogenin (NEO), 126f, 127t
- Neonatal alloimmune neutropenia, 477
- Neonatal alloimmune thrombocytopenia, 744
- Neonatal autoimmune thrombocytopenia, 744–745
- Neonatal hyperbilirubinemia, 370–371
- Neonatal purpura fulminans, 772
- Neonatal thrombocytopenia, 738
causes of, 738
and fetal thrombocytopenia, classification of, 738t
Neonates. *See also* Children; Pediatric hematology and hemostasis
anemia in, 864
full-term
hemoglobin for, reference interval, 865
platelet count reference intervals for, 867t
gestational age and birth weight in, 863–864
hematologic response to infection, 867
hemolytic disease of fetus and, 401–403, 402t
hemostasis, 867–868
bleeding and thrombosis, 868
hemostatic components, 868
specimen collection and management, 867
mean monocyte count of, 867
neonatal thrombocytopenia, 738
causes of, 738
and fetal thrombocytopenia, classification of, 738t
platelet values in, 867, 867t–868t
polycythemia in, 864
postterm, 863–864
preterm, 863–864
hemoglobin values in, 865
platelet count reference intervals for, 867t
red blood cell values in, 864–865
- Neonates (*Continued*)
anemia, 865–866
distribution width, 865
erythrocyte morphology, 864–865, 864f
hematocrit, 865
hemoglobin, 865
indices, 865
mean cell hemoglobin, 865
mean cell hemoglobin concentration, 865
mean cell volume, 865
reticulocyte count, 865, 865f
sickle cell disease screening in, 422
specimen collection for, 864
white blood cell values in, 866–867
eosinophils and basophils, 866
lymphocytes, 866–867, 867f
- Neoplasms. *See also* Cancer
acute myeloid, flow cytometric analysis of, 506–510
chronic myelogenous leukemia, 584–592
cytogenetics, 560–561, 560f
flow cytometric analysis of, 506–510
incidence of, 584
laboratory findings of, 587–588
molecular genetics in, 585–586, 585f
pathogenetic mechanism of, 586, 586f
peripheral blood and bone marrow, 587, 587f–588f, 588t
Philadelphia chromosome and, 584–585
progression of, 588–589
treatment of, 589–592, 589f, 591f
chronic neutrophilic leukemia, 607–608
essential thrombocythemia, 4, 599–601
clinical presentation of, 599
diagnosis of, 599
incidence of, 599
pathogenetic mechanism of, 599
peripheral blood and bone marrow, 599–600, 600f, 600t
treatment and prognosis of, 600–601
leukocyte, 489–499
classification schemes of, 490f, 491–492
general characteristics of, 490–491
incidence, prevalence, and etiology of, 491
molecular pathogenesis of, 492–494
DNA repair genes, 494
epigenetic mechanisms, 492–493, 492t
hematologic malignancies, cellular processes perturbed in, 492, 492b
oncogenes, 493, 494t
tumor suppressor genes, 493–494, 494t
therapy for, 494–497, 494b
chemotherapy, 494–495
hematopoietic stem cell transplantation, 496–497, 497f
radiation, 495
supportive, 495
targeted, 495–496
mature lymphoid, 634–660, 635b
approach to diagnosis of, 637
Catovsky-Mattes scoring for, 643b
classification schemas based on cell differentiation, 635–637
clinical behavior of, 637b
clinical signs and symptoms of, 637
common immunophenotypes for, 640t
diagnostic procedure for, 637–641
anatomic pathology testing, 641
clinical laboratory testing, 637–641, 640f
imaging studies, 641
prognostic evaluation, 642
staging system, 641–642, 642t, 644t
genetic abnormalities, 635, 636t
Hodgkin lymphoma, 653–655, 654f
immunologic diversity, 635
leukemias and, 642–646

- Neoplasms (*Continued*)
 monoclonal B-cell lymphocytosis (MBL), 644
 non-Hodgkin lymphoma, 646–653, 646b
 T-prolymphocytic leukemia, 644–645, 645f
 treatment of, 646
 WHO classification of, 638b–639b
 myelodysplastic/myeloproliferative. *See also*
 Myeloproliferative neoplasms
 myelodysplastic syndromes, 321t
 myeloid/lymphoid neoplasms, 610–611
 myeloproliferative, 583–617, 763–764, 764t
 chronic eosinophilic leukemia, 608–609
 chronic myelogenous leukemia (CML), 584–592
 cytogenetics of Philadelphia chromosome and, 584–585
 incidence of, 584
 laboratory findings of, 587–588
 molecular genetics in, 585–586, 585f
 pathogenic mechanism of, 586, 586f
 peripheral blood and bone marrow, 587, 587f–588f, 588t
 progression of, 588–589
 treatment of, 589–592, 589f, 591f
 chronic neutrophilic leukemia, 607–608
 essential thrombocythemia, 4, 599–601
 clinical presentation of, 599
 diagnosis of, 599
 incidence of, 599
 pathogenic mechanism of, 599
 peripheral blood and bone marrow, 599–600, 600f, 600t
 treatment and prognosis of, 600–601
 flow cytometric analysis of, 508–510
 mastocytosis, 611–612
 not otherwise specified, 610
 polycythemia vera, 601–604
 clinical presentation of, 602–603
 diagnosis of, 601–602, 602b
 incidence of, 601
 pathogenic mechanism of, 594f–595f, 601
 peripheral blood and bone marrow, 602, 603f, 603t
 treatment and prognosis of, 603–604
 primary myelofibrosis, 604–607
 collagen in, 604–605
 hematopoiesis and extramedullary hematopoiesis in, 605
 incidence and clinical presentation of, 605
 pathogenic mechanism of, 605
 peripheral blood and bone marrow in, 605, 606f, 606t
 treatment and prognosis of, 605–607
 secondary, myeloid, 576
 Nephelometric endpoint detection, 845–846, 845f, 846t
 Nephelometry, 845–846
 Nephrotic syndrome, hemorrhage and, 691–692
 Nerve damage, 881.e19
 Neuroanthocytosis, 363
 Neutropenias, 3, 467–468, 476–478, 866
 acquired, 477
 autoimmune, 478
 congenital, 467–468, 468t
 cyclic, 468
 drug-induced, 477
 neonatal alloimmune, 477
 Neutrophil extracellular traps (NETs), 146
 Neutrophilia, 3, 468–469, 476, 476b, 866
 Neutrophils, 3, 139–146, 145f, 881.e38, 881.e38f
 development, 140–143, 141f
 with Döhle Bodies, 480f
 functions, 144–146
 granules, 141, 142b
 green-blue inclusions in, 482, 482f
 Neutrophils (*Continued*)
 hypersegmentation of, 304, 475, 475f
 intracellular organisms in, 481–482
 bacteria and fungal organisms, 481–482, 482f
 kinetics, 143–144
 metamyelocytes, 141, 144f, 256, 257f
 myeloblasts, 141
 myelocytes, 141, 143f, 256, 257f
 promyelocytes, 141
 pyknosis and apoptosis in, 481
 apoptotic nuclei, 481, 481f
 neutropenia, 476–478
 neutrophilia, 476
 quantitative abnormalities in, 475, 475f
 quantitative abnormalities of, 476–478
 leukemoid reaction, 476
 leukoerythroblastic reaction, 476
 neutropenia, 476–478
 neutrophilia, 476
 secondary changes in, 479–482
 segmented, 141–143, 145f, 256, 257f
 Neutrophil, vacuolation, 480–481
 autophagic vacuolation, 480–481
 toxic vacuoles, 480
 Next-generation sequencing (NGS), 538–542, 541f
 Niemann-Pick disease (NP), 470, 473–474, 473f
 acute neuronopathic form, 473
 nonneuronopathic form, 473
 NP type C, 473–474
 Nijmegen-Bethesda assay, for anti-factor VIII inhibitor, 830–831
 Nijmegen-Bethesda units (NBUs), 693
 Nitric oxide (NO), 365
 transport, 118
 Nitrofurantoin, 724
 Nodal marginal zone lymphoma, 651
 Nomenclature
 cytogenetic, 556–557, 557f
 hemoglobinopathies, 411–412
 procoagulants, 666–668, 667f, 667t
 transmembrane proteins, 101
 Nonclonal or secondary acquired SAs, 286
 Non-Hodgkin lymphoma, 646–653, 646b
 adult T-cell leukemia/lymphoma, 646–647, 647f
 anaplastic large cell lymphoma, 652, 652f
 Burkitt's lymphoma, 647–648, 648f
 diffuse large B cell lymphoma, 649–650, 650f
 follicular lymphoma, 648, 648f
 mantle cell lymphoma, 648–649, 649f
 marginal zone lymphoma, 650–651, 651f
 mycosis fungoides (MF)/Sézary syndrome, 651–652, 652f
 nodal marginal zone lymphoma, 651
 peripheral T cell lymphoma, not otherwise specified (PTCL,NOS), 653, 653f
 Nonhomologous end joining (NHEJ), 426
 Nonimmune causes of hemolytic anemia, 379–391, 380f, 380b
 babesiosis and, 386–387
 clinical findings, 387
 geographic distribution, 387
 laboratory findings and diagnosis, 387, 387f
 bartonellosis, 387–388
 clostridial sepsis, 387
 drugs and chemicals, 388
 extensive burns, 388f
 infectious agents, 384–388
 malaria, 332, 384–385
 clinical and laboratory findings, 385
 hemolytic anemia caused by, 384–388
 microscopic examination, 385, 385f
 pathogenesis, 384–385
Plasmodium falciparum and, 385, 386f
Plasmodium knowlesi and, 385, 386f
Plasmodium malariae and, 385, 386f
Plasmodium ovale and, 385, 386f
 Nonimmune causes of hemolytic anemia (*Continued*)
Plasmodium vivax and, 385, 385f
 prevalence, 384
 venoms, 388
 Nonimmune drug-induced hemolysis, 404
 Nonimmune drug-induced thrombocytopenia, 751
 Nonmalignant leukocyte disorders, 464–488
 infectious mononucleosis, 484
 leukocyte number and function, congenital defects of, 465–470
 22q11.2 deletion syndrome, 466
 Bruton tyrosine kinase deficiency, 466–467
 Chédiak-Higashi syndrome, 467
 phagocyte number and function, congenital defects of, 467–470
 severe combined immune deficiency, 465–466
 Wiskott-Aldrich syndrome, 466
 primary immunodeficiency diseases, 465–470
 quantitative abnormalities of leukocytes, 476–479
 secondary morphologic changes, 479–484
 eosinophils and basophils, 482–483
 leukocytes, storage artifacts in, 479
 lymphocytes, 483–484
 neutrophils and monocytes, secondary changes in, 479–482
 Nonmegaloblastic anemias, 270
 Non-transfusion-dependent thalassemia (NTDT), 446, 450
 Normocytic anemia, 270
 NRBCs. *See* Nucleated red blood cells
 Nuclear-cytoplasmic asynchrony, 299–300
 Nuclear envelope, 47
 Nuclear transcription factors, 492
 Nucleated cells, 62
 Nucleated red blood cells (NRBCs), 205f
 automated blood cell analysis, clinical utility of, 221
 blood cell analyzers, 204t
 cytochemistry and light scatter for, 213–216, 215f
 fluorescence flow cytometry for, 207–210, 209f
 MAPSS for, 210–213, 211f–212f
 volume, conductivity, scatter technology, 206–207, 206f–207f
 Nucleic acid
 amplification of, by polymerase chain reaction, 529–532, 530f
 isolation, 527–529
 sequencing, 536–542
 stains, 3
 Nucleolar organizer regions, 554
 Nucleoli, 47
 Nucleolus, cell, 46t
 Nucleoside, 523
 Nucleosome, 553
 Nucleotide strands, 523, 523f
 Nucleus, cell, 44, 46–47, 46t
 basophilic normoblast, 83, 83f
 chromatin, 46–47
 erythrocyte, 86, 87f
 nuclear envelope, 47
 nucleoli, 47
 orthochromic normoblast, 84, 84f
 polychromatic erythrocyte, 85, 85f–86f
 polychromatic normoblast, 83, 84f
 pronormoblast, 81, 83f
 to-cytoplasm ratio, 81b
 Null hypothesis, 19–20
 Numerical aperture (NA), 881.e28
 Numeric chromosome abnormalities, 557, 558f
 Nutritional deficiencies, in elderly adults, 873
- O**
 Obesity, 881.e19
 Obizur (Takeda), 693

- Objective lenses, microscope, 881.e28, 881.e28f
- Occupational hazards, 881.e6
 biohazards in blood and body fluids, 881.e8
 chemical hazards, 881.e6
 electrical hazards, 881.e8
 fire hazards, 881.e6, 881.e6f
 radioactive hazards, 881.e8
- Occupational Safety and Health Administration (OSHA), 881.e2, 881.e12
 applicable safety practices required by, 881.e2
- Odds ratios effects on diagnostic efficacy, 34–36
- Okazaki fragments, 527
- Oligoblastic leukemia, 619
- Oncogenes, 493, 494f
- 100x oil immersion objective examination of
 blood films, 231–232
- Ontogeny, hemoglobin, 114, 115f, 115t
- Opacity, 206
- Open reagent systems, in coagulation
 instrumentation, 848
- Optical genome mapping (OGM), 544, 544f
- Optical light scatter, 201f, 202
- Optical tube, microscope, 881.e27
- Organic anion transporter (OAT) proteins, 333f, 334
- Orthochromic normoblast, 84–85, 84f
- Orthogonal light (90°) scatter, 202
- Osmoscan, 358
- Osmosis, 48–49
- Osmotic balance, of erythrocyte membrane,
 104–105
- Osmotic fragility, 357
- Osteoblasts, 55, 61–62, 254, 254f
- Osteoclasts, 55, 61–62, 254
- Outer coverings, 881.e2
- Oval macrocytes, 267t, 620f
- Ovalocytes, 269f
- Overhydrated hereditary stomatocytosis (OHS),
 361–362
 clinical and laboratory findings, 362, 362f
 pathophysiology, 361–362
- Overhydrated stomatocytosis, 105
- Overlap neoplasm, 508–510
- Overload, iron, 286–289
 etiology of, 287
 laboratory diagnosis of, 288–289
 sickle cell disease and, 423
 treatment of, 289
- Oxalate bind calcium, 881.e13
- Oxidant stress, 368
- Oxidation, 370
- Oxidative stress, 370
- Oxygen affinity, hemoglobins with increased and
 decreased, 434–435
- Oxygen transport, 116–117, 116f–117f
 dyshemoglobins and, 118–119
 sulfhemoglobin and, 119
- P**
- P2Y₁₂ (ADP) receptor inhibitors, 723
- Packed cell volume (PCV), 2, 184
- Pacritinib, 598
- Pancytopenia, 315–317, 317f, 317t
 differential diagnosis, 321, 321t–322t
- PAP-8E, 855–856, 856f
- Pappenheimer bodies, 268t
- PAR-1 antagonists, 724
- Paracrine signaling, 49
- Parasites
 babesiosis and, 386–387
 clinical findings, 387
 geographic distribution, 387
 laboratory findings and diagnosis, 387, 387f
 infections, during pregnancy, 869
 malaria and, 332, 385
 clinical and laboratory findings, 385
 hemolytic anemia caused by, 384–388
- Parasites (*Continued*)
 pathogenesis, 384–385
Plasmodium falciparum and, 385, 386f
Plasmodium knowlesi and, 385, 386f
Plasmodium malariae and, 385, 386f
Plasmodium ovale and, 385, 386f
Plasmodium vivax and, 385, 385f
 prevalence, 384
 sickle cell disease and, 419–420
 stool analysis for, 306
- Parcentric, 881.e30
- Parenteral antiplatelet therapeutic drugs, 803
- Parfocal, 881.e28
- Paroxysmal cold hemoglobinuria (PCH),
 400–401
- Paroxysmal nocturnal hemoglobinuria (PNH),
 331–332, 364–368, 763–764
 acquired aplastic anemia and, 315
 classification, 365–366, 366f
 clinical manifestations, 365, 365t
 differential diagnosis, 321
 flow cytometry and, 514–515, 515f
 hemolytic anemia, pathophysiology of, 364–365
 laboratory findings in, 366–367, 366f, 367f
 thrombotic risk component of, 764t
 treatment, 367–368
- Parsaclisib, 598
- Partial thromboplastin time (PTT), 5, 30, 824–825
 as diagnostic assay, 825
 mixing studies for, 825–826
 detection of, factor deficiencies and, 826
 lupus anticoagulants, 826
 specific factor inhibitors, 826
 monitoring heparin therapy with, 825
 principles for, 824, 824f
 procedure for, 825
 quality control for, 825
 reference interval for, 825
 single-factor assays using, 828–830
 for unfractionated heparin
 clinical practice of, 796
 limitations of, 796–797
 therapeutic range, 795–796, 796f
- Partial voteout, 206
- Particle smears of bone marrow aspirate, 250
- Passive transport, plasma membrane, 48–49
- Pathogen detection and infectious disease load,
 522b, 542
- Pathogenetic mechanism, in chronic neutrophilic
 leukemia, 608
- Pathologic fragmentation hemolysis, 339–340,
 341f–344f
- Pathologic macrophage-mediated hemolysis,
 338–339, 338f
- Pathophysiology
 acquired aplastic anemia, 315–316
 anemias, 271, 272b
 bone marrow failure, 314
 chronic myelogenous leukemia, 586, 586f
 dehydrated hereditary stomatocytosis, 362
 dyskeratosis congenita, 319–320
 essential thrombocythemia, 599
 Fanconi anemia, 319
 hemoglobin C, 428, 429f
 hemoglobin E, 429
 hemoglobinopathies, 411
 hemolytic anemia, 364–365
 hereditary elliptocytosis, 360
 hereditary hydrocytosis, 361–362
 hereditary ovalocytosis, 361
 hereditary spherocytosis, 355, 356f
 hereditary xerocytosis, 362
 immune hemolysis, 393–396, 394f–395f
 iron deficiency anemia, 277–278, 277f
 liver, 64
 lymph node, 66
 malaria, 384–385
- Pathophysiology (*Continued*)
 overhydrated hereditary stomatocytosis,
 361–362
 polycythemia vera, 594f–595f, 601
 primary myelofibrosis, 605
 pyruvate kinase deficiency, 373
 Shwachman-Bodian-Diamond syndrome,
 320–321
 sickle cell anemia, 414–416
 Southeast Asian ovalocytosis, 361
 spleen, 65f, 66
 stage 1, 278
 stage 2, 277f, 278
 stage 3, 277f, 278
 thalassemia, 444–445, 445f
 thymus, 68
- Patient-centered care, 13
 in hematology and hemostasis laboratory, 14
- Patient-centered hematology, and hemostasis
 testing, 12
- Patient-centered laboratory testing services, 12
- Patient safety, 7
 definition of, 9
 in hematology and hemostasis testing, 8–17
- PCH. *See* Paroxysmal cold hemoglobinuria
- Pearson correlation coefficient, 24–25
- Pearson marrow-pancreas syndrome (PMPS), 285
- Pediatric hematology and hemostasis, 863–868
 developmental stages in, 863
 gestational age and birth weight in, 863–864
 hematopoiesis in, 863
 neonatal hemostasis, 867–868
 bleeding and thrombosis, 868
 hemostatic components, 868
 specimen collection and management, 867
 platelet values in the neonate, 867, 867t
 red blood cell values in the neonate, 864–865
 anemia, 865–866
 distribution width, 865
 erythrocyte morphology, 864–865, 864f
 hematocrit, 865
 hemoglobin, 865
 indices, 865
 mean cell hemoglobin, 865
 mean cell hemoglobin concentration, 865
 mean cell volume, 865
 reticulocyte count, 865, 865f
 specimen collection for the neonate, 864
 white blood cell values in, 866–867
 eosinophils and basophils, 866
 lymphocytes, 866–867, 867f
 monocytes, 867
- Pediatric phlebotomy, 881.e18
- Pelabresib, 598
- Pelger-Huët anomaly (PHA), 474
 challenges associated with, 474
 pseudo- or acquired, 467
- Pelger Huet neutrophils
 and immature granulocytes, 474–475
 pseudo- and true Pelger-Huët neutrophils, 475
- Penicillin, 418
- Pentasaccharide, 795
- Pentose phosphate shunt, 97f, 98, 98t
- Peptide epitopes, 102
- Percent transferrin saturation, 132–133, 133f
- Periarteriolar lymphatic sheath, 64–65
- Periosteal arteries, 62–63
- PerIPHERAL blood
 and bone marrow, morphologic abnormalities
 in, 620–622
 dyserythropoiesis, 620, 620f
 dysmegakaryopoiesis, 622, 622f–623f
 dysmyelopoiesis, 620–622, 621f–622f, 621b
 chronic eosinophilic leukemia and, 608–609
 chronic myelogenous leukemia and, 587,
 587f–588f, 588t
 chronic neutrophilic leukemia and, 607

- Peripheral blood (*Continued*)
 essential thrombocythemia and, 599–600, 600f, 600t
 polycythemia vera and, 602, 603f, 603t
 primary myelofibrosis and, 605, 606f, 606t
- Peripheral blood films, 225–243, 360–361
 for anemia, 267t
 examination of, 231–235
 10x objective, 231
 40x high-dry objective, 231, 232b
 50x oil immersion objective, 231, 232b
 100x oil immersion objective, 231–232
 automated microscopic, 235
 macroscopic, 231
 for malaria, 385, 385f
 microscopic, 231–235
 optimal assessment area, 232, 233f
 performance of white blood cell differential, 232–234, 233f
 platelet estimate, 234–235
 red blood cell morphology, 234
 film preparation, 227–229, 228f
 automated slide making and staining, 228–229
 drying of films, 229
 manual wedge technique, 227–228, 228f
 specimen collection for, 226–227, 226f
 staining of, 228–229
 automated, 228–229
 features of proper, 230, 231b
 manual, 229, 230f
 quick, 230
 Wright (Wright-Giemsa), 229–230
 thalassemia diagnosis and, 455
- Peripheral eosinophilia, in chronic eosinophilic leukemia, 608
- Peripheral proteins, 103
- Peripheral T cell lymphoma, not otherwise specified (PTCL,NOS), 653, 653f
- Periprocedural management, of anticoagulants, 802–803
- Permeability, of erythrocyte membrane, 104–105
- Pernicious anemia, 268–270, 303, 307f
- Peroxidase, 202–203
- Peroxidase (PEROX) channel, 214, 215f
- PERSIST-1 clinical trial, 598
- Personal protective equipment (PPE), 7, 881.e2
- Petechiae, 687, 735, 735f, 881.e19
- PFA-100 Platelet Function Analyzer, 856, 857f
- PFA-100 system, for antiplatelet drugs, 804
- Phagocyte number, congenital defects of, 467–470
- Phagocytes, congenital defects of, 467–470
- Phagocytize, 3–4
- Phagocytosis, 49, 145, 145b
- Phagosomes, 48
- Phase-contrast microscope, 881.e30
- Phenotype and epidemiology, 288
- Phenotypic assays, 372
- Phenotypic mosaicism, 365
- Philadelphia chromosomes, 511, 559–561, 584–585
- Phlebotomist, responsibility in infection control, 881.e12
- Phlebotomy. *See also* Specimen collection
 iron overload treatment, 289
 legal issues in, 881.e23
 for polycythemia vera treatment, 603–604
 trays, 881.e4
- Phosphatidylcholine, 100
- Phosphatidylethanolamine, 100
- Phosphatidylinositol, 103
 glycan anchor biosynthesis, 103
- Phosphatidylinositol *N*-acetylglucosaminyltransferase subunit A, 364–365
- Phosphatidylserine, 99, 666
- 6-phosphofructokinase, 96
- Phosphoglycerate mutase, 96–98
- Phospholipase C, 173
- Phospholipids, 99, 164–165
- Phosphopyruvate hydratase, 96–98
- Photo-optical clot endpoint detection, 844, 844f, 846t
- Physical and chemical properties, 881.e7
- Physiological adaptations in anemia, 263–264
- Physiologic anemia
 of infancy, 864
 of pregnancy, 868
- Physiologic fragmentation hemolysis, 332, 335–338
 macrophage-mediated hemolysis vs., 339t
 pathologic, 339–340, 341f–344f
 plasma hemoglobin salvage and, 335–338, 336f, 340b
- Physiologic hemolysis, 331, 333–338
 acute, 331–332
 bilirubin metabolism and, 333–335, 333f
 chronic, 331–332
 classification of hemolytic disorders, 331–333, 331t
 clinical features, 340–341
 differential diagnosis, 346–347, 347f, 348t
 fragmentation, 332
 macrophage-mediated hemolysis vs., 339t
 pathologic, 339–340, 341f–344f
 plasma hemoglobin salvage, 335–338, 336f, 340b
 inherited, 332
 laboratory findings, 346
 tests of accelerated red blood cell destruction, 342–345
 tests of increased erythropoiesis, 345–346, 346t
 laboratory tests to determine specific processes, 346, 346t
 pathologic macrophage-mediated, 338–339, 338f
 plasma hemoglobin salvage and fragmentation, 335–338, 340b
- Physiologic roles, of vitamin B₁₂ and folate, 297–298, 298f
- Pica, 263
- Piecemeal degranulation, 146–147
- PIGA* gene, 364–365
- PIGA* mutant, 365
- Pinocytosis, 49
- Placenta-dependent oxygenation, 864
- Plan achromatic lens, 881.e28
- Plan apochromatic lens, 881.e28
- Plan-Do-Study-Act (PDSA) method, 13
- Plasma
 cells, 152, 258, 258f
 in disseminated intravascular coagulation, 778
 membrane, 44–45, 46t
 receptors for adhesion, 166–168, 167f, 168t
 transport. *See* Plasma membrane transport
 platelet-poor plasma specimens, 816–817
 platelet-rich
 light-transmittance platelet aggregometry, 817–818, 817f–819f
 plasma specimens, 816
 procoagulants. *See* Procoagulants
 trauma-induced coagulopathy, 689
- Plasma cell lymphocyte, 152, 153f
- Plasma cell neoplasms, 655–657
 diagnostic criteria for, 656b
 heavy chain disease, 656–657
 monoclonal gammopathy of undetermined significance, 655
 multiple myeloma, 655–656, 656f
 plasmacytoma, 656
 Waldenström macroglobulinemia, 656–657
- Plasma cells, 152
- Plasmacytoid lymphocytes, 152, 153f
- Plasmacytoma, 656
- Plasma hemoglobin, 342–344
- Plasma kallikrein-kinin system, 671
- Plasma membrane transport, 48–49, 48b
 active transport, 49
 facilitated diffusion, 48–49
 passive transport, 48–49
 phagocytosis, 49
 pinocytosis, 49
 receptor mediated endocytosis, 49
 simple diffusion, 48–49
 vesicular transport, 49
- Plasmin, 679
- Plasminogen, 679, 832
 chromogenic substrate, 832, 832f
- Plasminogen activation, 680
- Plasminogen activator inhibitor-1 (PAI-1), 680, 833, 833f
 principle of, 833
- Plasminogen activator inhibitor-2 (PAI-2), 680
- Plasminogen activator inhibitory type-1 (PAI-1), 874
- Plasmodium falciparum*, 369, 385, 386f
- Plasmodium knowlesi*, 385, 386f
- Plasmodium malariae*, 385, 386f
- Plasmodium ovale*, 385, 386f
- Plasmodium vivax*, 385, 385f
- Platelet aggregometers, 855–856, 856f, 856t
- Platelet aggregometry, 817–821, 817f–818f
 agonists, 818t, 819–821
 platelet lumiaggregometry, 818–819, 820f, 820t
 platelet-rich plasma specimens, 816
 using platelet-rich plasma, 817–818, 817f–819f
 whole-blood specimens for, 816, 818, 819f
- Platelet analysis
 Abbott, 210
 automated blood cell analysis, clinical utility of, 221
 Beckman Coulter, 205–206
 light scatter for, 213, 215f
 MAPSS for, 210–213, 211f–212f
- Platelet clumping, 219, 227f
- Platelet destruction
 immune mechanisms of, 740–745
 drug-induced immune-mediated thrombocytopenia, 741–744, 742b, 743f
 immune thrombocytopenic purpura, 740
 acute, 740
 chronic, 740, 741f
 increased, 735, 739–751
 by immunologic responses, 739–740
 nonimmune mechanisms of, 745–751
 hemolytic disease of newborn, 746
 hypertensive disorders, 746
 idiopathic thrombocytopenic purpura (ITP), 740
 incidental thrombocytopenia of pregnancy, 746
 preeclampsia, 746
 thrombotic thrombocytopenic purpura, 746–749
- Platelet distribution, DC detection system for, 207, 208f
- Platelet distribution width (PDW), 240
- Platelet factor 4 (PF4), 778, 796
 drug-induced thrombocytopenia and, 742
- Platelet Function Analyzer (PFA-100), 856, 857f
- Platelet function testing, 855–857
 flow cytometry, 857
 for hemostasis, 817–821
 bleeding time test, 817
 heparin-induced thrombocytopenia assays in, 821
 platelet aggregometry as, 817–821
 von Willebrand factor activity assays in, 821
- platelet aggregometers, 855–856, 856f, 856t
 platelet function analyzers, 856–857

- Platelet granulation, abnormal, 622, 622f
 Platelet production, impaired or decreased, 735–739
 acquired (drug-induced) hypoplasia, 738–739
 autosomal dominant thrombocytopenia, 737
 categories, 739–740
 congenital amegakaryocytic thrombocytopenia, 737
 ineffective thrombopoiesis, 735
 inherited thrombocytopenia/congenital hypoplasia, 735–737
 associated with chromosomal abnormalities, 735–737
 Fanconi anemia, 737
 list of, 736f
 May-Hegglin anomaly, 737, 737f
 neonatal thrombocytopenia and, 737f, 738
 TAR syndrome, 737
 neonatal thrombocytopenia, 738, 738t
 X-linked thrombocytopenia, 737–738
 Platelets, 163–164, 665–666, 666f
 abnormalities
 bleeding disorders from, 735
 distribution or dilution of, 751
 activation, 169–171
 adhesion, 169, 170f
 aggregation, 169–170, 171f
 eicosanoid synthesis, 171–172, 173f
 G-proteins, 171, 172f
 inositol triphosphate-diaclyglycerol pathway, 173
 markers, 821
 microparticles, 171
 pathways, 171–173
 secretion, 171, 172t
 concentrate, trauma-induced coagulopathy, 689
 consumption or sequestration, and neonatal thrombocytopenia, 738
 counts, 182, 227
 clinical bleeding and, 735
 for heparin-induced thrombocytopenia, 778–779, 779t
 point-of-care testing, 194–195
 procedure, 182b
 reference range for, 735
 summarizing, 240–241, 240f, 241b
 in elderly adults, 871
 estimate, 234b
 HELLP syndrome, 383
 impedance histograms for, 200, 201f
 and inflammation, 173
 megakaryocytopoiesis, 160–163
 endomitosis, 160, 160b
 hormones and cytokines of, 163, 163t
 megakaryocyte differentiation and progenitors, 160, 161f
 megakaryocyte membrane receptors and markers, 162, 163t
 terminal megakaryocyte differentiation, 160–162, 161f, 162t
 thrombocytopoiesis, 161f–162f, 162
 in neonate, 867, 867t–868t
 proteome, 174
 reticulated, 164, 164f
 satellitosis, 226
 shedding, 161f–162f, 162
 stress, 164, 164f
 ultrastructure, 164–169
 additional membrane receptors, 168–169
 cytoskeleton, 165–166, 165f
 dense tubular system, 165, 165f
 plasma membrane receptors for adhesion, 166–168, 167f, 168t
 platelet granules, 165f, 166, 166t
 resting plasma membrane, 164–165, 164f
 seven-transmembrane repeat receptors, 168, 169t
 surface-connected canalicular system, 165, 165f
 “Platelet satellitosis”, 182b
 Platelet secretion disorders, 717–721
 dense granule deficiency, 717–720, 718b, 719f
 thromboxane pathway disorders, 720–721
 PlateletWorks platelet function assay, 804, 857
 Pluripotent hematopoietic stem cell, 68
 Pneumatic tube system, 881.e4
 Pneumococcal disease, and SCD, 423
 Pneumocystis jirovecii, 881.e47, 881.e47f
 PNH. *See* Paroxysmal nocturnal hemoglobinuria
 Poikilocytosis, 267t
 Point mutations, 493, 522–523
 Point-of-care (POC) testing, 192–195
 cell and platelet counts, 195
 coagulation, 851–853, 852t
 hematocrit, 194, 194f–195f
 hemoglobin concentration, 194
 Poisoning, lead, 286
 Polarized light microscope, 881.e31
 PolyA tail, 531–532
 Polychromatic erythrocytes, 3, 85–86, 85f–86f
 Polychromatic normoblast, 83–84, 84f
 Polycythemia, 1–2, 864
 Polycythemia vera (PV), 601–604, 875
 clinical presentation of, 602–603
 diagnosis of, 601–602, 602b
 incidence of, 601
 pathogenetic mechanism of, 594f–595f, 601
 peripheral blood and bone marrow, 602, 603f, 603t
 treatment and prognosis of, 603–604
 Polymerase chain reaction (PCR), 529–532, 530f
 digital, 535, 538f
 pathogen detection and infectious disease load, 522b, 542
 real-time, 533–536, 533f
 digital polymerase chain reaction, 535, 538f
 minimal residual disease in leukemia, 535, 537f
 multiplex ligation-dependent probe amplification, 535, 539f
 mutation enrichment strategies, 535–536
 qualitative, 534–535, 534f
 quantitative, 535, 536f
 reverse transcription, 530–532, 531f
 single-sided, 537
 thalassemia diagnosis by, 457–458
 Polymorphonuclear cells (PMNs), 139–140, 145f
 Poly(RC) binding proteins (PCBP), 125, 131
 Population incidence effects on diagnostic efficacy, 34–36
 Porphobilinogen, 113–114
 Porphyrias, 64, 284, 284f
 Postanalytical phase, in Total Testing Process, 9
 Postanalytical quality assurance, 20t, 38
 Posterior superior iliac crest, 246, 246f
 Postpartum hemorrhage, 701
 Postpolycythemic myeloid metaplasia, 603
 Postsplenectomy thrombocytosis, 752f
 Postterm neonates, 863–864
 Posttransfusion purpura (PTP), 745
 Prasugrel, 723, 791t
 for oral antiplatelet therapeutic drugs, 803
 platelet aggregometry and, 820
 Preanalytical phase, in Total Testing Process, 9
 Preanalytical quality assurance, 19t, 38
 Precision, 25–26
 in coagulation instrumentation, 848
 Prediction interval, 21
 Predominance of fetal hemoglobin (Hb F), 864
 Preeclampsia, in pregnancy, 870
 Prefibrotic myelofibrosis, diagnostic criteria for, 604
 Pregnancy. *See also* Gestational hematology and hemostasis
 anemia and, 868–869
 acute blood loss, 869
 hemoglobinopathies, 869
 iron deficiency anemia, 868
 megaloblastic anemia, 869
 parasitic infections, 869
 thrombocytopenia during, 870, 870t
 hemolytic disease of newborn, 746
 idiopathic thrombocytopenic purpura (ITP), 740
 incidental thrombocytopenia of pregnancy, 746
 preeclampsia, 745b, 746
 thrombotic thrombocytopenic purpura, 746–749
 Prehepatic jaundice, 340
 Preleukemia, 619
 Premature infant. *See* Preterm infant
 Prematurity, anemia of, 864
 Prenatal hematopoiesis, 863
 Pre-T cells, 153
 Preterm infant, platelet count reference intervals for, 867t
 Preterm neonate, hemoglobin values in, 865
 Primaquine, 388
 Primary active transport, plasma membrane, 49
 Primary fibrinolysis, 679, 776
 Primary (azurophilic) granules, 141
 Primary hemostasis, 687
 Primary immunodeficiency diseases, 465–470
 congenital defects of phagocytes as, 467–470
 lysosomal storage diseases, 470–474
 morphologic abnormalities of leukocytes without associated immunodeficiency, 474–476
 Primary myelofibrosis (PMF), 604–607
 collagen in, 604–605
 hematopoiesis and extramedullary hematopoiesis in, 605
 incidence and clinical presentation of, 605
 pathogenetic mechanism of, 605
 peripheral blood and bone marrow in, 605, 606f, 606t
 treatment and prognosis of, 605–607
 Primary standards, 22–23
 Primary structure, hemoglobin, 111–112
 Primary thrombocythemia. *See* Essential thrombocythemia
 Primary thrombocytosis, 599
 Primary tube sampling, in coagulation instrumentation, 848
 Proapoptotic Bak proteins, 162
 Procoagulant cofactors, in hemostasis, 670, 670t
 Procoagulants
 classification and function of, 668–673, 668f, 668b
 nomenclature of, 666–668, 667f, 667t
 Proficiency systems, laboratory staff, 36
 Promegakaryocyte, 161f, 162
 Prometaphase, 53
 M (mitosis) stage, 53
 Promonocytes, 149, 574–575, 576f
 Promoters, 524–525
 Promyelocytes, 141, 141f, 143f
 Pronormoblast, 81–82, 83f
 Prophase, 53
 Proportional systematic error, 25
 Prostacyclin, 168
 Prostaglandin pathway, drugs inhibiting, 722–723
 Protamine sulfate, for LMWH-associated bleeding, 797
 Pro-T cells, 153
 Proteinase K, 528

- Proteins
4.1, 101, 102f
4.2, 101
body iron and
 bone morphogenic, 127t
 hemochromatosis, 127t
 hemojuvelin, 127t
- C
 activity, 764
 assays, 772, 772f
 control pathway, 771–773
 deficiency, 765f, 771–772
 inhibitor, 678
 regulatory system, 676, 677f
 central dogma in genetics and, 521–523
 cytokine, 71
 induced by vitamin K antagonists (PIVKA),
 669, 690, 792
 mutations that alter membrane transport, 355b
 organic anion transporter, 333f, 334
 RBC membrane, 45, 101–104, 102f, 103t
 cytoskeletal, 102f, 103–104, 104t, 105f
 transmembrane, 101–103, 102f, 103t
S, 676–677
 activity, 764
 assays, 772–773, 772f, 773t
 deficiency, 771–772
- Proteoglycans, 165
Proteome, platelets, 174
Prothrombin complex concentrate (PCC), 799
Prothrombin deficiency, 706t
Prothrombin fragment, 670
Prothrombin G20210A, 764, 765t, 770
Prothrombin time, 5, 822–824
 as diagnostic assay, 823
 international normalized ratio (PT/INR)
 in warfarin therapy, 793, 794f
 limitations of, 823–824, 823t
 minimal effectiveness of, as screening tool, 823
 principle for, 822
 procedure for, 822
 quality control for, 822–823
 reference interval, 823
 reporting of, 823
Protooncogene, overexpression of, 493
Prussian blue staining, 133, 255, 255f
Pseudo-Chédiak-Higashi granules, 467
Pseudodiploid cells, 557
Pseudo-Gaucher cells, 471–473
Pseudogout, 881.e45
Pseudoleukocytosis, 226
Pseudo- or acquired Pelger-Huët anomaly
 (PPHA), 474–475
PTT. *See* Partial thromboplastin time
Pulmonary embolism, 774–775
Pulmonary hypertension (PHT), 418
Pulse signals, 210
Pure erythroid leukemia, 575
Pure red cell aplasia (PRCA), 321–323
Purine, 523–524, 524f
Purpura, 687, 735, 735f
Purpura fulminans, 750–751, 775
Pyknosis, neutrophils, 481
 apoptotic nuclei, 481, 481f
 pyknotic nuclei, 481
Pyknotic nuclei, 481
Pyrimidine 5'-nucleotidase type 1 (P5'NT-1)
 deficiency, 374
Pyrimidines, 523–524, 524f
Pyroptosis, 620
Pyrosequencing, 537
Pyruvate kinase, 96–98, 97f
 deficiency, 373–374
 clinical manifestations, 373
 laboratory findings, 373–374, 374f
 pathophysiology, 373
 treatment, 374
- Q
Qualitative platelet disorders, 714–721, 714b, 715f,
 716t
 inherited giant platelet syndromes, 717, 718t
 platelet adhesion, 716–717
 platelet aggregation, 714–716
 platelet dysfunction, 721–727, 722f, 722t
 cardiopulmonary bypass surgery, 726
 drug-induced defects, 722–725
 hereditary afibrinogenemia, 726
 hyperaggregable platelets, 727
 liver disease, 725–726
 medical conditions, 726
 multiple myeloma and Waldenström
 macroglobulinemia, 725
 myeloproliferative neoplasms, 725
 uremia, 726
 platelet secretion, 717–721
 dense granule deficiency, 717–720, 718b, 719f
 thromboxane pathway disorders, 720–721
 receptors and signaling pathways, disorders
 of, 721
Qualitative real-time polymerase chain reaction,
 534–535, 534f
Quality assessment, external, 33
Quality assurance, 6–7
 agencies addressing, 38
 assay feasibility and, 36
 assessing diagnostic efficacy in, 33–36, 34f, 35t
 components of, 19, 19t, 19b
 external quality assessment, 33
 in hematology and hemostasis testing, 18–42
 laboratory staff competence and, 36–38
 lot-to-lot comparisons, 29, 30t
 postanalytical, 20t, 38
 preanalytical, 19t, 38
 receiver operating characteristic curve, 36, 37f
 reference interval
 direct, 30
 indirect, 30
 statistical significance and expressions of
 central tendency and dispersion, 19–21
 coefficient of variation, 21
 mean in, 20–21
 median in, 21
 mode in, 21
 standard deviation in, 21, 22f
 statistical significance, 19–20, 20t
 variance in, 21
 therapeutic target range, 30
 validation, 21–28
 accuracy, 22–23
 analytical measurement range, 26–28
 analytical sensitivity, 28
 analytical specificity, 28
 documentation and reliability, 28
 levels of laboratory assay approval and, 28,
 29t
 linearity, 26–28, 28f
 lower limit of detection, 28
 precision, 25–26
 statistical tests, 23–25
Quality Chasm Series, 8–9
Quality control, 6–7, 19
 controls, 31–32, 32f, 32t
 delta checks, 33
 for fibrinogen assay, 828
 internal, 31–33
 moving average of red blood cell indices, 32–33
 for partial thromboplastin time, 825
 for prothrombin time, 822–823
 for single-factor assays, using the PTT, 830
 for thrombin clotting time, 827
Quality improvement, 13
 in hematology and hemostasis laboratory, 14
Quality specimen, requirements for, 881.e22
- Quantitative real-time polymerase chain reaction,
 535, 536f
Quantra coagulometer, 834
Quaternary structure, hemoglobin, 112
Quebec platelet disorder, 720
Quick stains, 230
- R
Radiation therapy, for leukocyte neoplasms, 495
Radioactive hazards, 881.e8
Radiofrequency conductivity, 201–202,
 201f–202f
Random access testing, in coagulation
 instrumentation, 848
Rapid turnaround assays, for heparin-induced
 thrombocytopenia, 780–781
Rapoport-Luebering pathway, 97f, 99
RBC hemoglobin content histogram (RBC HC),
 213
RBM8A gene, 737
Reactive lymphocytes, 153, 483–484
Reactive monocytes, 482, 482f
Reactive thrombocytosis, 752–753, 752f
 associated with hemorrhage or surgery, 752
 associated with inflammation and disease, 753
 associated with iron deficiency anemia, 753
READACRIT centrifuge, 185b, 187f
Reagent handling, in coagulation instrumentation,
 848–849
Reagent tracking, in coagulation instrumentation,
 848–849
Real-time polymerase chain reaction, 533–536,
 533f
 digital polymerase chain reaction, 535, 538f
 minimal residual disease in leukemia, 535,
 537f
 multiplex ligation-dependent probe
 amplification, 535, 539f
 mutation enrichment strategies, 535–536
 qualitative, 534–535, 534f
 quantitative, 535, 536f
Rebound thrombocytosis, 753
Receiver operating characteristic curve (ROC),
 36, 37f
Receptor-mediated endocytosis, 49, 129
Receptors, 49–50
Recombinant activated coagulation factor VII
 (rFVIIa), 689
Recombinant interleukin-11, 738–739
Recombinant TPA analogue (rTPA), 804
Recycling, body iron and salvage, 128–129
Red blood cells. *See* Erythrocytes
 Abbott, 210
 agglutination, effects of, 218–219
 Beckman Coulter, 205–206
 DC detection system for, 207, 208f
 impedance histograms for, 200, 201f
 light scatter for, 213, 215f
 membrane, structure and function, 99–105
 oscilloscope display and histogram, 199–200,
 200f
 survival, 345
Red cell distribution width (RDW), 2, 219–220,
 220f, 265
 anemia diagnosis and, 265–266
 morphologic classification and, 271
 in red blood cell indices, 865
Reference intervals, 29–31, 31f, 236
 for globin synthesis, 442, 442t
Reference limit, 34
Reference methods, 23
Reflex testing, in automatic ordering/performing
 test, 849
Refractive index, 881.e30
Refractory anemia, 619
Regulated medical waste management, 881.e6

- Regulation
of body iron
erythrocyte iron sensing and hepcidin production, 127–128, 129f–130f
liver iron sensing and hepcidin production, 126–127, 126f, 127f
liver sensing of circulating iron, 126f, 127, 128f
liver sensing of stored iron, 126f, 127
cellular iron, 129, 130f
hemoglobin production, 114–116
systemic body iron, 126–128, 126f, 127f, 281–282
erythrocyte iron sensing and hepcidin production, 127–128, 129f–130f
liver iron sensing and hepcidin production, 126–127, 126f, 127f
liver sensing of circulating iron, 126f, 127, 128f
liver sensing of stored iron, 126f, 127
- Regulatory information, 881.e7
- Reilly bodies, 475
- Relaxed state, hemoglobin, 116, 117f
- Reliability and documentation, 28
- Renal insufficiency, 750
- Renal iron salvage, 337–338
- Renal peritubular interstitial cells, 72
- Rendu-Osler-Weber syndrome, 727
- Replication, DNA, 525–527, 526f
- Reptilase time, 827
- Respiratory burst, defects of, 469–470, 469t
- Resting plasma membrane, 164–165, 164f
- Restriction endonuclease methods, 533
- Retic scatter absorption cytogram, 215–216
- Reticular adventitial cells, 55, 61–62
- Reticulated platelets, 164, 164f
- Reticulocyte analysis
automated blood cell analysis, clinical utility of, 220–221
cytochemistry and light scatter for, 213–216, 215f
fluorescence flow cytometry for, 207–210, 209f
MAPSS for, 210–213, 211f–212f
volume, conductivity, scatter technology, 206–207, 206f–207f
- Reticulocytes, 3
blood cell analyzers, 204t
control, 189
count, 187–190, 239
absolute, 3, 189
automated, 190
corrected, 189
equation reference interval, 189
errors in, 219
hemolysis and, 346
Miller disc for, 188f, 188b
in paroxysmal nocturnal hemoglobinuria, 366
pathophysiologic classification of, 271, 272b
pediatric, 865, 865f
principle of, 187–188, 188f
procedure, 188b
sources of error and comments, 188f, 188b, 191f
erythropoietin (EPO) and early release of, 88
hemoglobin content of, 132t, 134, 220–221
hemolysis and, 346
production index, 189, 265
shift, 88, 189
- Reticulocytosis, 346–347, 373, 400
- Retraction, 61
- Retroviruses, 781
- Reverse transcription polymerase chain reaction, 530–532, 531f
- Reversible sickle cells, 415
- Revised International Prognostic Scoring System (IPSS-R), 627
- Revolving nosepiece, microscope, 881.e28
- rFVIIa. *See* Recombinant activated coagulation factor VII
- Rhabdomyolysis, 117
- Rh-associated glycoprotein (RhAG), 361–362
- Rh deficiency syndrome, 362
- Rh system, 102–103
- Ribonucleic acid (RNA), 3
central dogma in genetics and, 521–523, 522f
fluorescence in situ hybridization, 554–555
isolated from clinical specimens, 528–529
in mitochondria, 48
necrosis and, 54
nucleoli and, 47
reverse transcription polymerase chain reaction for amplifying, 530–532, 531f
ribosomes and, 47
transcription and translation, 524–525
- Ribosomes, 46t, 47
- Ring chromosomes, 558, 558f
- Ring sideroblasts, 284
- Risk factors, thrombosis, 763–765
- Ristocetin cofactor, 697–699
- Ristocetin induced platelet agglutination (RIPA) assay, 699
- Rivaroxaban, 800, 800t
- Robertsonian translocation, 559, 559f
- Ropoginterferon α -2b, 598–599
- Rosenthal syndrome, 705
- Rotated light scatter (RLSn), 206
- Rotational thromboelastometry (ROTEM), 833–834, 854, 854f
- Rough endoplasmic reticulum (RER), 46t, 47
- Routine cleaning, 881.e5
- Routine venipuncture, vein selection for, 881.e16
- Rule of three, 186
- Ruptured eosinophils, 482
- Rusfertide, 598–599
- Russell viper venom test, 827
- Ruxolitinib, 598
- S**
- Safe health care, 9
- Safe hematology and hemostasis testing, 9–11
- Safety, 7
laboratory safety, 7
patient safety, 7
personal protective equipment (PPE), 7
- Safety Data Sheets (SDS), 881.e7
- Safety shields, 881.e4f
- Sanger DNA sequencing, 536–538, 540f, 858
- Sarcoma, myeloid, 576
- SARS-CoV-2 (COVID-19), 742–743
- Satellitosis, 219
- Saturation, transferrin, 132, 132t, 279–280
- Scatter signals, 202
- Schistocytes, 267t, 269f
- Schistosoma haematobium*, 279
- Schizocyte, 267t
- Scopio Labs X100, 235
- Scott syndrome, 721
- Scramblases, 100
- Screening tests, 34. *See also* Laboratory diagnosis
- Sea-blue histiocytes, 473
- Sebastian syndrome, 737
- Secondary active transport, plasma membrane, 49
- Secondary hemostasis, 687
- Secondary myeloid neoplasms, 576
- Secondary structure, hemoglobin, 111–112
- Secondary thrombocytopenia, 745
- Secretory granule, 146
- Secretory vesicle, 146
- Sedimentation rate, erythrocytes, 6, 190–192
automated, 191–192
disposable kits, 191, 193t
factors affecting, 192t
- Sedimentation rate, erythrocytes (*Continued*)
modified Westergren, 190, 191f
reference interval, 190b
sources of error and comments, 190b
Wintrobe, 190–191
- Segmented neutrophils, 256, 257f, 474
- Seizures, 881.e19
- Selectins, 144
- Selective serotonin reuptake inhibitors, 423
- Senescence, 91
- Senile purpura, 728
- Separator gel, 881.e13
- Sepsis, clostridial, 387
- Sequencing, DNA, 536–538, 540f
- Serine proteases, 668, 668t
- Serotonin release assay (SRA), for heparin-induced thrombocytopenia, 780, 781f
- Serous fluid, 881.e40, 881.e41f, 881.e44f
differential cell counts of, 881.e41, 881.e42f, 881.e43f, 881.e44f
gross examination of, 881.e41
transudates vs. exudates, 881.e40, 881.e41t
- Serum bilirubin, 334b
- Serum ferritin, 283
level, 132t, 133
- Serum gastrin, 306
- Serum haptoglobin, 266
- Serum iron, 132, 132t
- Seven-transmembrane repeat receptors, 168, 169t
- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV2), 781, 830
- Severe combined immune deficiency (SCID), 465–466
- Sex hormone effects, on hematopoiesis, 875
- Sézary syndrome, 651–652, 652f
- SF3B1* mutation, 624
- Shear force, 169
- Shift, 220
- Shift reticulocytes, 88, 189
- Shift to the left, 479–480
- Shigella*, 382
- Shock, 418–419
- Shortened red blood cell life span, 283
- Shwachman-Bodian-Diamond syndrome (SBDS), 316, 320–321
- Shwachman-Diamond syndrome (SDS), 468
- Sickle cells, 66, 267t, 269f
disease, 412–427
clinical features, 416–419, 416b
course and prognosis, 427
dysfunctional endothelial nitric oxide synthase, 415–416
etiology and pathophysiology, 414–416
gene therapy, 425–427
geographic distribution of inherited hemoglobin variants and, 414f
history of, 412–413
incidence with malaria, 419–420
infection prevention, 423
inheritance pattern, 413, 413f
intracellular hydration, 415
irreversible, 415
laboratory diagnosis, 420–422, 420f–421f
mutation, 414
newer drug options, 424–425
pain care, 423
polymerization and sickling, 414–415
prevalence, 413–414
rapid detection and genotyping of, 422
reversible, 415
stem cell transplant, 423–424
transfusions, 423
treatment, 422–427
hemoglobin SC disease and, 431
malaria and, 419–420
trait, 427–428

- Side fluorescent light (SFL), 207–209
- Sideroblastic anemias (SAs), 276, 284–286, 285f, 285b
 acquired sideroblastic anemias, 286
 in elderly adults, 873
 hereditary sideroblastic anemias, 284–286
 lead poisoning and, 286
 porphyrias, 284, 285t
- Sideropenia, 280
- Siderophages, 881.e39
- Side scatter (SSC), 202, 207–209
- Siemens ADVIA 2120i, 204t
- Siemens Healthineers, 213–216, 214f
 cytochemistry and light scatter, for WBC count, WBC differential, NRBCs and reticulocyte analysis, 213–216, 215f
 hemoglobin determination, 213
 RBC and platelet analyses, light scatter for, 213, 215f
- Siemens PFA-100 Platelet Function Analyzer, 856, 857f
- Signaling receptors, 101
- Signal transduction, 101
 pathways, 50, 586, 586f
 proteins, 492
- Signet ring cells, 881.e42, 881.e42f
- Silent carriers, 355–356
- Silent carrier state
 of α -thalassemia, 452
 of β -thalassemia, 446–447
- Simple diffusion, plasma membrane, 48–49
- Simple microscope, 881.e27
- Single-factor assays, using the PTT, 828–831, 829t
 expected results and clinical utility of, 829–830
 limitations of, 830
 principle of, 828–829
 quality control for, 830
- Single-molecule real-time sequencing (SMRT), 544
- Single nucleotide polymorphism array (SNP-A), 542
- Single-sided PCR, 537
- Sister chromatids, 52
- Skin disinfection, solutions for, 881.e16
- Skin puncture, 881.e20
 collection sites, 881.e20, 881.e20f
 equipment for, 881.e20, 881.e21f
 order of draw, 881.e21b
 precautions with, 881.e20
 procedure, 881.e12
 preparation of peripheral blood films, 881.e13
- Small lymphocytic lymphoma (SLL), 642–644
- Small-vessel bleeding in skin, 735
- Smoldering leukemia, 619
- Smooth endoplasmic reticulum (SER), 46t, 47
- Smudged eosinophils, 482
- Social determinants of health, 12
- Sodium butyrate, 424
- Sodium citrate, 227, 813
 volume adjustment for elevated hematocrits, 813–814, 814f
- Sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), 101, 101f, 358
- Sodium lauryl sulfate (SLS), 119, 203
- Sodium-potassium ATPase, 49
- Solenoid, 553
- Solid tumor cytogenetics, 561–562, 562f
- Soluble fibrin monomers, 775–776
- Soluble transferrin receptor, 132t, 134, 280, 281f
- Soluble transferrin receptor/log ferritin (sTfR), 132t, 134
- Sonic estimation of elasticity by resonance (SEER), 834
- Sonorheometry, 834
- Sons of mothers against decapentaplegic (SMAD) protein, 127t
- Sorting, cell, 515
- Southeast Asian ovalocytosis (SAO), 354–355, 361
 clinical and laboratory findings, 361
 pathophysiology, 361
- Specimen collection, 179–180
 anticoagulants for, 813–814
 citrate theophylline adenosine dipyridamole, 814
 EDTA, 814
 sodium citrate as, 813
- blood
 clotted, 815
 materials for, 813–814
 collection tubes for, 813
 needle selection in, 813–814, 813t
 procedure for, 814–815
 with butterfly set, 814
 with syringe, 815
 venipuncture and, 814–815
 short draw in, 814
 using capillary puncture, 815
 from vascular access devices, 815
- bone marrow, 250
 errors in, 814t
 heparinized, 813
 patient management during, 812
 for peripheral blood films, 226–227, 226f
 platelet function tests for, 817–821
 sites, bone marrow, 246
 transport and storage of, 816t
- Specimen integrity, 10–11, 219
- Specimen management, 815–817
 nucleic acid isolation, 527–529
 preparation, 816–817
 transport and storage, 815–816
- Specimen quality set points, 849
- Specimen rejection, reasons for, 881.e22, 881.e23b
- Spectrin stabilization, 103–104
- Spectrophotometry, for hemoglobin determination, 203
- S phase checkpoint, 53
- Spheric aberrations, 881.e28
- Spherocytes, 267t, 269f, 344, 357f, 359
- Sphingolipidoses, 470–474, 472f
- Sphingomyelin (SP), 100
- Spinous process of vertebrae or ribs, 246
- Spleen, 64–66, 65f–66f
 pathophysiology of, 65f, 66
- Splenectomy, 66, 359, 359f
- Splenic artery, 66
- Splenic marginal zone lymphoma (SMZL), 650–651, 651f
- Splenomegaly, 66
 in acute myeloid leukemia, 570
- Spur cells, 267t
 anemia, 363
- Spurious thrombocytopenia, 219
- SRA. *See* Serotonin release assay
- S (DNA synthesis) stage, cell cycle, 52
- Stability and reactivity, 881.e7
- Stage, microscope, 881.e28
- Staining of peripheral blood films, 228–229
 automated, 228–229
 features of proper, 230, 231b
 manual technique, 229, 230f
 quick, 230
- Standard deviation, 21, 22f
- Standard precautions, 881.e2, 881.e12
 hepatitis B virus vaccination, 881.e5
 housekeeping, 881.e5
 laundry, 881.e5
 regulated medical waste management, 881.e6
 training and documentation, 881.e6
- Stand, microscope, 881.e27
- Statistical significance, 19–20, 20t
- Stem cell factor, 163
- Stem cells
 cycle kinetics, 70, 70f
 hematopoietic stem cell (HSC), 59, 68–69
 transplantation, 319
 phenotypic and functional characterization, 70
 theory, 68–70, 69f, 69t
 therapeutic applications, 73, 73t–74t
 transplantation, 319, 496–497
- Stem cell transplant, 423–424
- Sternum, 246
- Stomatocytes, 267t, 269f
- Stomatocytosis, acquired, 363
- Stool analysis, for parasites, 306
- Storage artifacts, in leukocytes, 479
- Storage pool disorders, 717, 718b
- Stormorken syndrome, 721
- Stress, 220
- Stromal cells, 56, 61–62
- Structural chromosome abnormalities, 558–559, 558f
- Student *t*-test, 19–20, 20t, 23–24, 24t
- Succinyl coenzyme A, 112–113, 113f
- Sudan Black B staining, 573, 574f, 578, 578f
- Sulfhemoglobin, 119
- Superficial veins of the antecubital fossa, 881.e16, 881.e16f
- Superwarfarin, 692
- Supravital staining, 454f, 456
- Surface carbohydrates, 101
- Surface-connected canalicular system (SCCS), 165, 165f
- SUSTAIN clinical trial, 425
- Symports, plasma membrane, 49
- Synovial cells, 881.e44, 881.e45f
- Synovial fluid, 881.e43, 881.e44f, 881.e46f
 crystals, 881.e44, 881.e45f
 differential cell counts of, 881.e43, 881.e44f
 gross examination of, 881.e43
- Syringe, 881.e15
- Sysmex, 207–210, 208f
 fluorescence flow cytometry, for WBC count, WBC differential, NRBCs, and reticulocyte analyses, 207–210, 209f–210f
 hemoglobin determination, 207
 RBC analyses and platelet distribution, DC detection system for, 207, 208f
- Sysmex XN-3100, 204t
- Systemic body iron kinetics, 124–128, 124f
 absorption, ionic, 125–126, 125f
 regulation, 126–128, 126f, 127t
 transport, 126
- Systemic body iron regulation, 281–282
- Systemic fibrinolysis, 776
- Systemic fibrinolytic therapy, for COVID-19, 776
- Systemic (mucocutaneous) hemorrhage, 735, 735f
- T**
- TACO. *See* Transfusion-associated circulatory overload
- Tapeworm, fish, 303
- Taqman assays, 534–535
- Taq polymerase, 529
- Target cells, 49, 269f
- Targeted therapy, for leukocyte neoplasms, 495–496
- TAR syndrome, 737
RBM8A gene mutation, 737
- T cell
 neoplasms, mature, 512–513, 514f
 production of, 60
- Teamwork, 13
- Teardrop cells, 267t, 269f
- TEG 5000 Thromboelastograph System, 854
- Telomere biology disorders (TBDs), 319–320
- Telophase, 53
- 10x objective examination of blood film, 231
- Tenase complex, factor VIII, 701
- Tenecteplase (TNKase) (Genentech), 804

- Ten eleven translocation 2 (*TET2*), 596–597
- Terminal megakaryocyte differentiation, 160–162, 161f, 162t
- Tertiary structure, hemoglobin, 111–112
- Tetramer, 112
- Tetraploidy (4n), 557
- Thalassemias, 332, 414f, 440–463
 - categories of, 443
 - definitions and history of, 441
 - diagnosis of, 455–459
 - alkali denaturation test in, 458
 - assessment of hemolysis in, 456
 - assessment of normal and variant hemoglobins in, 456–457, 456f–457f
 - complete blood count with peripheral blood film review, 455
 - differential, 459
 - high performance liquid chromatography (HPLC), 457, 457f
 - history and physical examination in, 455
 - laboratory methods for, 455–459
 - molecular genetic testing in, 457–458
 - polymerase chain reaction and, 457–458
 - reticulocyte count in, 456
 - supravital staining in, 454f, 456
- epidemiology of, 441
- genetic defects causing, 443, 444f
- genetic designations in, 443t
- genetics of globin synthesis, 442, 442f, 442t
- hemoglobin C-, 455
- hemoglobin E-, 455
- hemoglobin Lepore, 451
- hemoglobin S-, 454–455
- hemoglobin S- β -, 431
- with increased levels of fetal hemoglobin, 451
- pathophysiology of, 444–445
- α -, 441, 452–454
 - clinical syndromes of, 452–454, 453t
 - mechanisms in, 445
 - minor, 452–453
 - silent carrier state, 452
- β -, 443
 - caused by defects in the β -globin gene cluster, 451
 - clinical syndromes of, 445–451, 447t
 - intermedia, 450–451
 - major, 447–450, 448f–449f
 - mechanisms in, 444–445, 445f
 - minor, 447, 447f
 - screening for, 451–452
 - pathophysiology of, 446f
 - silent carrier state of, 446–447
- β -globin gene cluster, 445–452
- Thawed plasma, 689
- The Joint Commission (TJC), 9
- Therapeutic range development, 29–31, 31f
- Therapeutic target range, 30
- Thermal sensitivity, 360–361
- Thermocycler, 529
- Thomas plot, 134, 134f
- Three-part differential, 200
- Thrombin, 168, 672, 819–820
 - time, 5
- Thrombin activatable fibrinolysis inhibitor, 681
- Thrombinantithrombin complex (TAT), 677
- Thrombin receptor-activating peptide, 819–820
- Thrombin time, 826–827
 - procedure for, 826–827
 - quality control for, 827
 - reagent and principle for, 826, 826f
 - reporting of, 827
- Thrombocytes, 4
- Thrombocythemia, essential, 4, 599–601
 - clinical presentation of, 599
 - diagnosis of, 599
 - incidence of, 599
 - pathogenetic mechanism of, 599
- Thrombocythemia, essential (*Continued*)
 - peripheral blood and bone marrow, 599–600, 600f, 600t
 - treatment and prognosis of, 600–601
- Thrombocytopenia, 4, 221, 380, 735–751, 776
 - with absent radii syndrome, 720
 - alcohol consumption and, 739
 - artifact, 735
 - bacterial infections associated with, 739
 - and bleeding, 735
 - classification of
 - increased platelet destruction, 739b
 - platelet production, impaired or decreased, 735–739, 736b
 - platelet sequestration, 751b
 - inherited, 735–737
 - associated with chromosomal abnormalities, 735–737
 - Fanconi anemia, 737
 - list of, 736t
 - May-Hegglin anomaly, 737, 737f
 - neonatal thrombocytopenia and, 738, 738t
 - TAR syndrome, 737
 - mechanical platelet destruction, 751
 - neonatal, 738
 - causes of, 738
 - and fetal thrombocytopenia, classification of, 738t
 - pathophysiologic processes in, 735
 - in pregnancy, 870, 870t
 - hemolytic disease of newborn, 746
 - idiopathic thrombocytopenic purpura (ITP), 740
 - incidental thrombocytopenia of pregnancy, 746
 - preeclampsia, 745b, 746
 - thrombotic thrombocytopenic purpura, 746–749
 - systemic (mucocutaneous) hemorrhage, 735, 735f
 - viruses associated with, 739
- Thrombocytopoiesis, 161f–162f, 162
- Thrombocytosis, 4, 751–754, 752b
 - associated with myeloproliferative disorders, 753–754
 - essential thrombocythemia, 753–754
 - definition of, 751–752
 - reactive, 752–753. *See also* Reactive thrombocytosis
- Thromboelastography (TEG), 833–834, 842, 854, 854f
- Thromboinflammation, 764t, 781–782
- Thrombolytic therapy, 790
- Thrombomodulin, 664, 670, 771
- Thrombophilia, 762
 - laboratory evaluation of, 765–773, 766t
 - activated protein C resistance and factor V Leiden mutation, 769–770
 - antiphospholipid antibodies, 765–769
 - antithrombin, 770–771
 - protein C control pathway, 771–773
 - prothrombin G20210A, 770
 - molecular diagnostics in, 857–858
 - during pregnancy, 869–870
- Thrombosis, 4, 778
 - antithrombotic therapy and, 790
 - arterial, 790
 - disseminated intravascular coagulation and, 775–778
 - causes of, 775, 776t
 - differential diagnosis of, 777–778
 - laboratory diagnosis of, 776–778, 777t
 - pathophysiology of, 775–776
 - specialized laboratory tests for, 777, 777t
 - symptoms of, 776
 - treatment, 778
 - predictors of, 773–774
 - C-reactive protein, 773
- Thrombosis (*Continued*)
 - factor VIII, 774
 - fibrinogen activity, 773–774, 773f
 - lipoprotein (a), 773
 - prevalence of, 762–763
 - etiology and prevalence of, 762–763
 - in neonates, 868
 - predictors, of arterial, 773–774
 - in pregnancy, 869–870
 - risk factors, 763–765
 - acquired, 763–764, 763t
 - congenital, 764, 765t
 - double hit, 764–765
 - risk testing
 - developments, 762
 - future, 782
- Thrombotic disorders, 761–788
- Thrombotic microangiopathies (TMAs), 234, 380, 745, 745b
- Thrombotic thrombocytopenic purpura (TTP), 381–382, 382f, 746–749, 870
 - ADAMTS13 and, 746, 748
 - attributes of, 747t
 - clinical monitoring of, 746
 - differential diagnosis, 383
 - differentiation, 749t
 - mechanism for, 749f
 - and thrombosis, 747
 - treatment of, 748–749
- Thromboxane A₂ (TXA₂), 168, 172–173
- Thromboxane pathway disorders, 720–721
- Thymine, 523–524
- Thymus, 66–68, 67f–68f
 - at birth, 67–68, 67f
 - pathophysiology, 68
- Ticagrelor, 723, 791t
 - for oral antiplatelet therapeutic drugs, 803
- Tilt-tube technique, 842
- Timely hematology, and hemostasis testing, 12
- Timely laboratory testing, 12
- Tirofiban, 724, 791t
- Tirofiban hydrochloride, 803
- Tissue factor, 670
 - pathway inhibitor, 677, 678f
- Tissue plasminogen activator (TPA), 665, 678f, 680, 804, 832–833
 - principle of, 833, 833f
 - specimen collection for, 833
- T lymphoblastic leukemia/lymphoma, 511, 513f
- T lymphocytes, 64–65, 151–152
 - development, 153
 - functions, 153–154
 - maturation of, 153, 154f
- To Err Is Human*, 8–9
- Tolbutamide, cytotoxic effect of, 738
- Tolerance, 151
- Total iron-binding capacity (TIBC), 132, 132t, 133f
- Total Symptom Score (TSS), 598
- Total Testing Process, in clinical laboratory, 9, 10f
- Total Thrombus Formation Analyzer System, 857
- Total voteout, 206
- Touch preparations, bone marrow, 250–251
- Tourniquet, 881.e12
- Towelettes, 881.e12
- Toxic granulation, 480
- Toxic methemoglobinemia, 118–119
- Toxicological information, 881.e7
- Toxic vacuoles, 480
- TP53, 54
- T-prolymphocytic leukemia (T-PLL), 644–645, 645f
 - laboratory findings, 645
 - treatment, 645
- Trabeculae, 60–61
- Trabecular veins, 65
- Traditional complete blood count, 219

- Training and documentation, 881.e6
 Transcription activator-like effector nucleases (TALENS), 425
 Transcription, DNA, 524–525
 Transferrin, 113–114
 saturation, 132, 132t, 279–280
 Transferrin receptor 1, 127t, 129
 Transferrin receptor 2, 127t, 129
 Transfusion-associated circulatory overload (TACO), 689
 Transfusion-dependent thalassemia (TDT), 446
 Transfusion-related acute lung injury (TRALI), 689
 Transfusion-related hemosiderosis, 287
 Transfusion therapy
 for SCD, 423
 for thalassemias, 448
 Transgender populations, 874–876
 diversity in, 874
 electronic health records, 876
 hematologic parameters in, 875, 876t
 hormone therapy
 and hematopoiesis, 875
 and hemostasis, 875
 sex hormone effects on hematopoiesis, 875
 Transient erythroblastopenia of childhood (TEC), 321–322
 Translation errors, 443
 Translations, DNA/RNA, 524–525
 Translocations, chromosome, 559
 Transmembrane proteins, 45, 101–103, 102f, 103t
 blood group antigens, 102
 GPI anchor and paroxysmal nocturnal hemoglobinuria, 103
 nomenclature, 101
 Transport
 iron, 126
 mutations that alter membrane proteins in, 354–355, 355b
 Transport information, 881.e7
 Transudates, exudates *vs.*, 881.e40, 881.e41t
 Trauma-induced coagulopathy (TIC), 688–690
 Traumatic cardiac hemolytic anemia, 383, 384f
 Treatment-free remission, 592
Trichuris trichiura, 279
 Triploidy (3n), 557, 558f
 Trousseau syndrome, 775
 True thrombocytopenia, 735
 T-test, 19–20, 20t, 23–24, 24t
 Tumor cells, 881.e43f
 Tumor necrosis factor receptor 1 (TNFR1), 54
 Tumor suppressor genes (TSGs), 493–494, 494t
 Tumor suppressor proteins, 54
 Tungsten-halogen light bulbs, 881.e29
 Turnaround time, 12
 22q11.2 deletion syndrome (22DS), 466
 Two-dimensional distribution scattergram, 202, 202f
 Type A, immersion oil, 881.e30
 Type B, immersion oil, 881.e30
 Type C, immersion oil, 881.e30
 Tyrosine kinase inhibitor (TKI) therapy, 592
- U**
 Ulcers, 419
 Unconjugated bilirubin, 266
 Unesterified cholesterol, 99
 Unexplained anemia, of aging, 873
 Unfractionated heparin (UFH), 791t, 795–797
 in disseminated intravascular coagulation, 778
 heparin action, 795
 LMWH action, 797, 797f
 monitoring, 795–796
 PTT therapeutic range, 795–796, 796f
 using activated clotting time, 796–797
 using chromogenic anti-Xa assay, 796
- Unfractionated heparin (UFH) (*Continued*)
 using PTT, 796
 using viscoelastometry, 796–797
 reversing, 797
 therapy, 795
 UniCel DxH 900 system, 203
 Unifying theory in DIIHA, 404
 Unstable hemoglobin variants, 434
 Upper median-angle light scatter (UMALS), 206
 Upshaw-Schülmán syndrome, 381
 Uremia, 726
 Urinalysis, 266
 Urine hemoglobin, 342–344
 Urine hemosiderin, 342–344
 Urobilinogen, 334–335, 335f, 342
 Urokinase plasminogen activator, 680
- V**
 Vaccine-induced immune thrombotic thrombocytopenia (VITT), 742–743, 782
 Vacuolation, neutrophil, 480–481
 Vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic (VEXAS), 480–481
 Validation, 21–28
 accuracy, 22–23
 analytical measurement range, 26–28
 analytical sensitivity, 28
 analytical specificity, 28
 documentation and reliability, 28
 levels of laboratory assay approval and, 28, 29t
 linearity, 26–28, 28f
 lower limit of detection, 28
 precision, 25–26
 statistical tests, 23–25
 Valoctogene roxaparvovec (Roctavian, BioMarin Pharmaceutical), 704
 Variance, computation of, 21
 Vascular access devices, hemostasis blood specimen collection from, 815
 Vascular disorders, 727–728, 727b
 acquired, 728
 bleeding disorders *vs.*, 735
 inherited, 727–728
 Vascular intima
 damaged, procoagulant properties of, 664
 fibrinolytic properties of, 665
 functions of, 662–663
 in hemostasis, 662–665, 663b
 intact, anticoagulant properties of, 663–664, 663f, 663t
 and platelets, 665–666
 Vasoconstriction and platelet plug formation, 662
 Vasoocclusive crisis (VOC), 416–417, 417f
 Velocardiofacial syndrome, 466
 Venipuncture, 814–815, 881.e12
 in children, 881.e18
 complications encountered in, 881.e18
 allergic reactions, 881.e19
 ecchymosis (bruise), 881.e18
 fainting (syncope), 881.e18
 hematoma, 881.e18, 881.e18f
 hemoconcentration, 881.e18
 hemolysis, 881.e19
 nerve damage, 881.e19
 petechiae, 881.e19
 seizures, 881.e19
 vomiting, 881.e19
 equipment for, 881.e12
 collection tubes, 881.e12
 needle holders, 881.e13, 881.e15f
 needles, 881.e13, 881.e15f
 solutions for skin disinfection, 881.e16
 syringe, 881.e15
 tourniquet, 881.e12
 winged blood collection set (butterfly), 881.e15, 881.e15f
- Venipuncture (*Continued*)
 inability to obtain blood specimen, 881.e19
 failure to draw blood, 881.e18f, 881.e19
 missing patient, 881.e20
 patient refusal, 881.e20
 order of draw for, 881.e17b
 procedure, 881.e16
 coagulation testing, 881.e17
 selection of vein for routine, 881.e16
 in special situations, 881.e19
 burned, damaged, scarred, and occluded veins, 881.e19
 edema, 881.e19
 intravenous therapy, 881.e19
 mastectomy, 881.e19
 obesity, 881.e19
 Venom activated assays, 827
 reptilase time, 827
 Russell viper venom test, 827
 Venoms, 388
 Venous thromboembolic disease, 790
 diagnosis of, 774
 prevalence of, 762
 Venous thromboembolism (VTE), in pregnancy, 869
 treatment of, 869
 VerifyNow system, 722, 803–804, 856–857, 857f
 Verotoxins, 382
 Vertical anchorages, 104
 Vesicles, 104
 Vesicular transport, plasma membrane, 49
 Viruses, Epstein-Barr, 315
 Viscoelastic clot detection, 844
 Viscoelastometry (VET), 804, 833–834
 assays, 854, 854f
 in unfractionated heparin, 796–797
 Vital stains, 3
 Vitamin B₁₂
 assays for, 305–306, 306b, 307f
 competition for, 303
 deficiency, 298–300, 299f
 causes of, 301–303, 302f
 in elderly adults, 873
 laboratory tests used to, 308t
 systemic manifestations of, 300–301
 failure to separate
 from haptocorrin, 303
 from proteins, 303
 Vitamin C (ascorbic acid), 99
 Vitamin deficiencies, causes of, 301–303
 Vitamin K antagonist, 792
 Vitamin K deficiency, 831
 hemorrhage and, 692
 detection of, 692
 hemorrhagic disease of the newborn, 692
 warfarin for, 692
 Vitamin K-dependent prothrombin group, 669–670, 669f–670f, 669t–670t, 669b
 Volume, conductivity, scatter (VCS) technology, 205f–207f, 206–207
 Volume distribution histogram, 199–200
 Volume/hemoglobin concentration (V/HC) cytogram, 213
 Vomiting, 881.e19
 von Willebrand disease, 693–701
 Ac platelet-binding activity, 697–699
 collagen binding assay, 699
 concentrates, 701
 diagnostic pitfalls in, 699–700
 genetic testing, 698t, 699
 laboratory diagnostic profile
 first-level phenotypic, 697–699, 697t
 second-level phenotypic, 699
 pathophysiology of, 695
 pregnancy and, 700
 ristocetin cofactor, 697–699

- von Willebrand disease (*Continued*)
 subtype 1C, 695
 subtype 2A, 695
 subtype 2B, 695
 subtype 2M, 695–696
 subtype 2N, 696–697
 treatment for, 700–701, 701t
 type 1, 695, 696f
 type 2, 695
 type 3, 697
- von Willebrand factor (VWF), 169, 662, 671, 671f, 737
 activity assays, 821
 molecular biology and function of, 694–695, 694f
 nomenclature of, 695t
 thrombotic thrombocytopenic purpura and, 381
- Voting, 206
- Voxelator, 425
- VWF-cleaving protease, 169
- W**
- Waldenström macroglobulinemia, 656–657, 725
- Warfarin, 692, 790–794, 791t
 action, 790–792
 inducing skin necrosis, 771, 792
 INR therapeutic range, 793
 monitoring, 793–794
 anticoagulants in, 795
 chromogenic factor X assay in, 793–794
 diet and pharmaceutical interference, 794
 PT/INR in, 793
 prophylaxis and therapy, 792, 792f, 793t
 reversing, 794, 794t
 for venous thromboembolism, 869
 as vitamin K antagonists, 792
- Warfarin resistance, 792
- Warfarin sodium (4-hydroxycoumarin, Coumadin), 790–792
- Warm autoimmune hemolytic anemia (WAIHA), 397–399
- WAS. *See* Wiskott-Aldrich syndrome
- Wells scoring system
 in deep venous thrombosis, 774
 in pulmonary embolism, 774
- Westergren method, 191
- Westerman-Jensen needle, 247, 247f
- Westgard rules, 31–32, 32t
- White blood cell cytoplasm, uneven staining of, 621, 622f
- White blood cells (WBCs), 139, 871. *See also* Leukocytes
 count
 cytochemistry and light scatter for, 213–216, 215f
 fluorescence flow cytometry for, 207–210, 209f
 MAPSS for, 210–213, 211f–212f
 differential
 Beckman Coulter, 205–206
 blood cell analyzers, 204t
 cytochemistry and light scatter for, 213–216, 215f
 fluorescence flow cytometry for, 207–210, 209f
 MAPSS for, 210–213, 211f–212f
 volume, conductivity, scatter technology, 206–207, 206f–207f
 impedance histograms for, 200, 201f
- WHO Classification-Based Prognostic Scoring System (WPSS), 627
- Whole-blood calibration, 216
- Whole Blood/Optical Lumi-Aggregation System, 856
- Whole-blood specimens, for platelet aggregometry, 816, 818, 819f
- Winged blood collection set (butterfly), 881.e15, 881.e15f
- Wintrobe erythrocyte sedimentation rate, 190–191
- Wintrobe hematocrit tubes, 247
- Wiskott-Aldrich syndrome (WAS), 466, 719, 737
- Wiskott-Aldrich syndrome protein (WASP), 466
- Within-day variation, 25–26
- Women
 aplastic anemia in, 315
 HELLP syndrome in, 383
 iron deficiency anemia in, 279
- World Health Organization (WHO)
 classification of myelodysplastic neoplasms, 623, 624b
 tumors of hematopoietic system, 584
- Wright (Wright-Giemsa) stain, 1, 229–230
 automated slide stainers, 229–230, 230f
 manual technique, 229, 230f
 marrow smear dyes, 251
- X**
- Xerocyte, 361
- X-linked agammaglobulinemia, 466
- X-linked erythropoietic protoporphyria (XLEPP), 285t
- X-linked SCID, 465–466
- X-linked sideroblastic anemia (XLSA), 284–285
- X-linked thrombocytopenia, 737–738
- Y**
- Yellow marrow, 61
- Z**
- Z-dependent protease inhibitor (ZPI), 678
- Zenker fixative, 247
- Zidovudine, 738–739
- Zinc finger nucleases (ZFNs), 425, 450
- Zinc protoporphyrin, 132t, 134, 280, 281f
- ZPI. *See* Z-dependent protease inhibitor
- Zygosity, 411
- Zymogens, 666, 667f