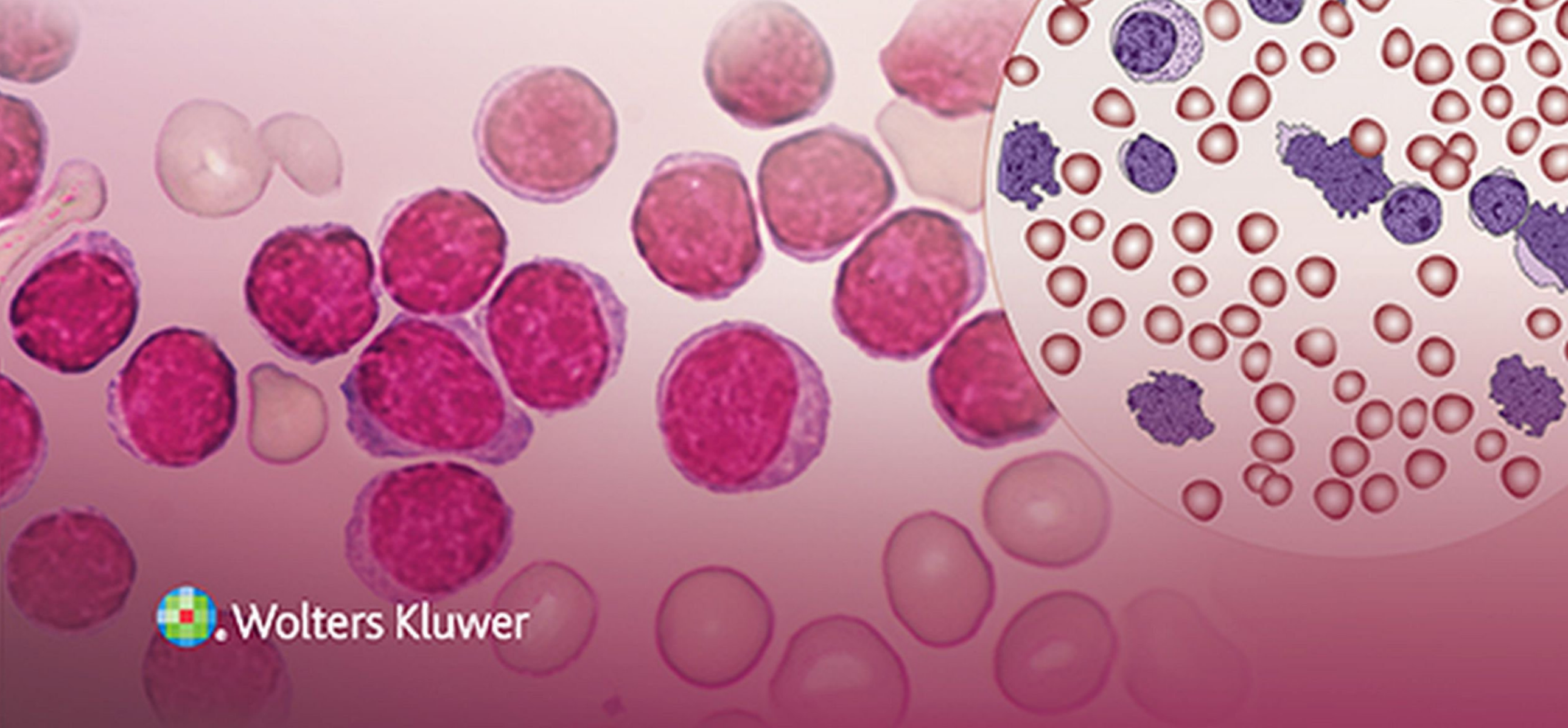
MARY LOUISE TURGEON

CLINICAL HEMATOLOGY

THEORY AND PRACTICE

SIXTH EDITION



Wolters Kluwer

Clinical Hematology

Theory and Procedures

SIXTH EDITION

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*T*o my husband, Dick Mordaunt
May we continue to love exploring and
learning

ABOUT THE AUTHOR

Mary Louise Turgeon, EdD, MLS(ASCP)^{CM}, is an educator, author, and consultant in medical laboratory science education. Her career as an educator includes 15 years as a community college professor and medical laboratory technician (MLT) program director, and 14 years as an undergraduate and graduate university professor, medical laboratory science (MLS) program director, and departmental chairperson. She is an educational consultant at Northeastern University, Boston.

Dr. Turgeon is the author of medical laboratory science books (sold in more than 45 countries):

- Linné & Ringsrud's Clinical Laboratory Science, 6th ed. (2016)
- Immunology and Serology in Laboratory Medicine, 5th ed. (2014)
- Clinical Hematology, 5th ed. (2012)
- Fundamentals *of* Immunohematology, 2nd ed. (1995)

Clinical Hematology has been translated into Spanish. Immunology and Serology in Laboratory Medicine has been translated into Italian and Chinese. Dr. Turgeon is the author of numerous professional journal articles.

Presentation of professional workshops and lectures complement the author's teaching and writing activities. Her consulting practice, Mary L. Turgeon & Associates focuses on new program development, curriculum revision, and increasing teaching effectiveness through the use of technology.

Dr. Turgeon's career in medical laboratory science has spanned the globe. She has met and collaborated with medical laboratory science colleagues throughout the United States and worldwide, including China, Italy, Japan, Qatar, Saudi Arabia, and the United Arab Emirates. Professional volunteer activities have taken her to Cambodia and Lesotho, Africa.

PREFACE

The goal of the sixth edition of Clinical Hematology is to facilitate mastery of the principles and practice of hematology needed by medical laboratory technician (MLT) and medical laboratory science (MLS) students to achieve board certification or licensure upon graduation and the entry-level professional competencies for career success. Clinical Hematology has been classroom and laboratory "field tested" by MLT and MLS students, instructors, and the author for almost 30 years. Presentation of content with high visual impact is designed to meet the preferences of today's students and to promote effective learning. Since the first edition of Clinical Hematology, each new edition has continued to capture the excitement of the latest knowledge and emerging practices of the ever-changing field of clinical hematology and hemostasis.

Clinical Hematology encompasses the professional knowledge and practice guidelines recommended by the newest ASCLS Entry Level Curriculum and ASCLS Professional Body of Knowledge documents in hematology, hemostasis and coagulation, and molecular applications. In addition, the current ASCP Board of Certification Examination Content Guideline & Outline for Medical Laboratory Technician, MLT(ASCP), and ASCP Board of Certification Examination Content Guideline & Outline for Medical Laboratory Scientist, MLS(ASCP), categories of certification are used as reference documents.

Beyond recommendations for competency in core content, the sixth edition continues with the expansion of exciting molecular discoveries such as Next Generation Sequencing (NGS) that initially assumed importance in the fifth edition. Molecular diagnosis has become a more visible inclusion and has been integrated throughout the book because it reflects the importance of molecular diagnostics in today's medical laboratories as well as continuing to be the "wave of the future."

T is edition of Clinical Hematology strengthens the robust pedagogy that has set the quality benchmark since the first edition. Some traditional content has been retained in the book or transferred to the LWW web-based, thePoint, because some questions related to classic content may appear on certification or licensure examinations for the next several years.

Clinical Hematology clearly addresses the changes in clinical hematology and the challenges for students to learn more and for instructors to teach more in a fixed time frame. Each chapter in this edition capitalizes on the strengths of previous editions based on up-to-date information presented at annual meetings and conferences, publications in the professional literature, and comments received from students, faculty, faculty book reviewers, and working professionals from around the globe.

Hands-on presentation of the information and techniques discussed in Clinical Hematology underscores the importance of clarity, conciseness, and continuity of information for the entry-level student. T e sole authorship of this textbook ensures a smooth transition from chapter to chapter without unnecessary redundancy or changes in writing style.

THE AUDIENCE

Clinical Hematology, sixth edition, is primarily intended to fulfill the needs of medical laboratory science (MLS) and medical laboratory technician (MLT) students and faculty as a time-tested book. MLT students may select portions of the book depending on the length of the curriculum. Other health professionals can use the book as an instructional or reference guide.

WHAT'S NEW IN GENERAL OVERALL FEATURES OF THE SIXTH EDITION THAT FACILITATE MORE EFFECTIVE LEARNING?

- **More Full-Color Images** offer student desired visual guides to the concepts, procedures, and cellular structures and functions.
- **More Visual Learning Content** to meet the needs of today's students and to promote effective learning.
- **Additional Algorithms** and other student desired visual learning formats (figures, tables, and boxes) clarify key points.
- **Expanded Basic and Advanced Outcomes c**larify what MLT and MLS students should know upon successful completion of each chapter.
- **Bulleted Chapter Highlights** facilitate quick review of each chapter's material.
- **Revised In-Text Learning Aids** (Chapter Highlights and Review Questions) are now clustered by major topic to facilitate concept mastery.
- **Numerous Updated End-of-Chapter Certif cation-Style Review Questions** help students assess their knowledge as they advance through each chapter.
- **More than 70 Case Studies** with etiology, pathophysiology, laboratory findings, and critical thinking questions to link key concepts and procedures with a disorder, disease, or condition.
- **Dedicated Lab Manual Chapter** provides step-by-step procedure instructions, enabling students to confidently perform important clinical procedures for clarification of concepts or skill set development.
- **Key Terms Italicized in the Text and Defined in the Glossary** help students master the vocabulary of hematology.

ORGANIZATIONAL PHILOSOPHY

T e eight-part organization of Clinical Hematology follows the original profile for a logical combination of textbook with fully developed case studies, a cellular morphology images, and a procedure manual.

PART I Hematology Basics discusses the newest fundamental concepts including safety, quality assessment, and specimen collection. Chapter 3, Molecular Genetics and Cellular Morphology, continues to be of extreme importance in understanding the pathophysiology and diagnosis of many blood disorders and related therapy.

PART II Hematopoiesis and Cellular Maturation presents the normal development of blood cells in humans. T is is essential basic information.

PART III Hematology Laboratory Assessments focuses on erythrocytes and leukocytes. T e content progresses from normal structure and function to specific abnormalities in each grouping.

PART IV Erythrocyte Disorders focuses on a wide variety of disorders related to red blood cells with many types of anemia.

PART V Nonmalignant Leukocyte Disorders presents on a wide variety of nonmalignant disorders related to white blood cells.

PART VI Neoplastic Disorders focuses on a wide variety of malignant disorders related to white blood cells including many types of leukemias and lymphomas.

PART VII Principles and Disorders of Hemostasis and T rombosis presents a distinct specialty in hematology: hemostasis and blood coagulation. An abundance of new knowledge about platelets and coagulation factors continues to emerge, particularly with a genetics emphasis.

PART VIII Fundamentals of Hematological Analysis focuses on hematological analysis. T is section includes diversified types of analysis including body fluid analysis, manual procedures, and instrumentation. T is part is conveniently located at the end of the book for easy reference when reading other parts of the book.

HIGHLIGHTS OF SIGNIFICANT CONTENT ADDITIONS OR EXPANSIONS

PART I: Hematology Basics (Chapters 1–3)

- Additions include the latest safety information associated with National Patient Safety Goals as well as clinical personal safety in the laboratory including WHO's 5 Moments of Hand Hygiene.
- T e newest changes in the Hazard Communication have been added.
- A streamlined Phlebotomy chapter focusing on special patient considerations for adults a significant revision of anticoagulants in evacuated tubes, EDTA specimen storage, expanded test requisition data, and neonatal blood spot screening.

PART II: Hematopoiesis and Cellular Maturation (Chapters 4–9)

- Additions include nutritional and regulatory factors related to erythropoiesis.
- Expanded content related to tense and relaxed structure of hemoglobin, genetic hemoglobin abnormalities, the principle of the hemiglobincyanide (cyanmethemoglobin) assay, and molecular testing—as a method for studying hemoglobin.
- Content expansion includes the addition of granulocytic growth factors and granulocytic growth inhibitors and leukocyte surface markers. Monocyte subsets phenotypes and functions, the kinetics life span of monocytes-blood and tissue phases and functional properties of monocytes/macrophages are new additions.
- Phagocytosis and Neutrophils Extracellular Traps (NETs) content has been added.
- Lymphocyte content revisions and additions focus on lymphocyte recirculation, B lymphocytes in the bone marrow, functional division of B lymphocytes, antibody-independent role of B lymphocytes, and recirculation of lymphocytes.
- Expansion of plasma cell development content.

PART III: Hematology Laboratory Assessments (Chapters 10–11)

- Chapter 10 is a newly organized introductory chapter that combines basic theory and practice transferred from other existing chapters. Content includes quantitative assessment of erythrocytes, reticulocyte count, assessment of bone marrow response, quantitative assessment of leukocytes, and blood smear preparation and differential evaluation, including platelet assessment.
- Additional procedures are in the Lab Manual, Chapter 32.

PART IV: Erythrocyte Disorders (Chapters 12–17)

- Expanded content related to iron deficiency and iron overload such as absolute iron deficiency compared to functional iron deficiency has been added.
- Primary overload disorders compared to secondary iron overload disorders is another addition.
- Expanded coverage of hepcidin and disorders related to hemoglobin biosynthesis: sideroblastic anemia, hemochromatosis, heme (porphyrin) synthesis, and globulin have been added.
- Comparison of macrocytic anemias and nonmegaloblastic macrocytosis.
- Differentiation of the pathophysiology and peripheral blood smear appear of nonmegaloblastic anemia from megaloblastic anemia.
- Assessment of an algorithm of clinical chemistry laboratory tests used to distinguish megaloblastic anemias.
- Expanded explanation of the body's requirements for folate and the physiologic role of folate including the

process of folic acid metabolism and explain how a deficiency can result in megaloblastosis.
- Expansion of hemolytic anemia: acquired anemias, disorders of erythrocyte hydration, hemolytic disease of the fetus and newborn (HDFN), and cold agglutinin disease.
- Presentation of novel pharmaceutical therapies.

PART V: Nonmalignant Leukocyte Disorders (Chapters 18–19)

- Expanded content addressing neutrophilia and neutrophilia work-up
- New additions of cyclical neutropenia, chronic benign neutropenia

PART VI: Neoplastic Disorders (Chapters 20–24)

- Expanded information on clonal heterogeneity
- Addition of extensive information on molecular analysis
- Inclusions of extensive World Health Organization (WHO) Classification Revisions
- Addition of key laboratory findings in acute myelogenous leukemia (AML)
- Expanded information on acute myelogenous leukemia (AML) prognosis
- Updated transplantation content
- Presentation of new acute myelogenous leukemia (AML) therapies
- Addition of pathogenesis of acute lymphoblastic leukemia (ALL)
- Updated and expanded content on leukemias versus lymphomas
- New content chronic lymphocytic leukemia (CLL) treatments
- New content monoclonal B-cell lymphocytosis (MLD), B-cell prolymphocytic leukemias (PLLs), T-cell prolymphocytic leukemia, Sézary syndrome, T-cell large granular lymphocytic leukemia, adult T-cell leukemia/lymphoma
- Expanded content on lymphomas and non-Hodgkin's lymphoma
- New and expanded leukemic phase of non-Hodgkin's lymphomas
- Expanded content for Burkitt's lymphoma
- Updated content on multiple myeloma treatments
- Additions with a strong emphasis on molecular diagnosis
- Chronic neutrophilic leukemia and atypical chronic myeloid leukemia
- Chronic eosinophilic leukemias including PDGFRA-associated chronic eosinophilic leukemia and chronic eosinophilic leukemia, not otherwise specified (CEL-NOS)
- Mastocytosis
- Myeloproliferative Neoplasm, Unclassifiable (MPN-U)
- Seven subtypes of MDS are classified, and the combined MDS/MPN category has five subtypes with new molecular genetic criteria and a new entity, RARS-T. RARS-T (refractory anemia with ringed sideroblasts and thrombocytosis) has been added in 2016 WHO revision of Tumors and Hematopoietic and Lymphoid Tissues
- Increased emphasis on cytogenetic findings

PART VII: Principles and Disorders of Hemostasis and Thrombosis (Chapters 25–28)

- Updated international prognostic scoring system
- Addition of antiplatelet drugs
- Complete revision with additions to vascular abnormalities
- Updated MYH-9–related thrombocytopenia syndromes (May-Hegglin anomaly)
- Updated heparin-induced thrombocytopenia (HIT)
- Addition of hemolytic uremic syndrome (HUS and HELLP syndrome)
- Addition of cell-based mechanism of coagulation, ecarin clotting time, clot waveform analysis (CWA), and global assays
- Expanded content related to factor Leiden, less common hereditary clotting deficiencies, circulating inhibitors, and antiphospholipid syndrome (APS)
- Updated content related to anticoagulation therapy including new oral anticoagulants

PART VIII: Fundamentals of Hematological Analysis (Chapters 29–32)

- Addition of seminal fluid—fertility studies
- Addition of fetal lung maturity—lamellar body count
- New male infertility case study
- Reinstated manual cell counts for RBCs and platelets
- Added mixing studies to coagulation procedures

CHAPTER STRUCTURE AND FEATURES

Each chapter of Clinical Hematology provides the following elements to enhance the usability of the text:

- **Learning outcomes** separated into core and advanced content provide a quick overview of the content.
- **Multiple full-color images and visual learning aids** such as figures, graphs, charts, and algorithms clarify complex concepts.
- **Case studies** with full development of information to reinforce concepts with real-world applications.
- **Procedure boxes** provide step-by-step information for key processes.
- **Key terms** that emphasize important concepts are italicized and defined in the end-of-book glossary.
- **Chapter highlights** enable a quick review of material learned in each chapter.
- **Review questions** reinforce the student's understanding of key concepts and aid in test preparation.

ADDITIONAL RESOURCES

Clinical Hematology includes additional resources for both instructors and students that are available on the book's companion Web site at http://thePoint.lww.com/Turgeon6e.

Instructor Resources

Approved adopting instructors will be given access to the following additional resources:

- Two test banks—one contains more than 800 unique questions; the other contains all the review questions from the book
- PowerPoint slides for each chapter
- Answers to Critical T inking Group Discussion Questions
- An image bank of all the figures and tables in the book
- And more

Student Resources

Students who have purchased Clinical Hematology, sixth edition have access to the following additional resources:

- A quiz bank of 270 questions
- A lab manual of additional procedures
- New flash cards for review

ACKNOWLEDGMENTS

My objective in writing Clinical Hematology, sixth edition, continues to be to share basic scientific concepts, procedural theory, and clinical applications with colleagues and students. Because the knowledge base and technology in hematology continues to expand, writing and revising a book that addresses the need of teachers and students at multiple levels in hematology continues to be a challenge. In addition, this book continues to provide me with the opportunity to learn and share my working and teaching experience, and insight as an educator, with others.

A special thanks to Demetra C. Castillo, MAdEd, MLS(ASCP)^{CM}, Assistant Professor, Department of Medical Laboratory Science, Rush University, Chicago, IL. for her editing and updating of the ancillaries associated with this edition.

T ank you to Jonathan Joyce, for his leadership throughout this project, and John Larkin, who has managed the smooth organizational flow of the project.

Comments from instructors and students are welcome at Turgeonbooks@gmail.com.

Mary L. *T*urgeon
St. Petersburg, Florida

CONTENTS

PART ONE

Hematology Basics

CHAPTER 1

Safety Practices and Quality in the Hematology Laboratory

KEY TERMS

accuracy
biohazard
calibration
coefficient of variation (CV)
control specimen
delta check
disinfection
dispersion
drift
Hazard Communication Standard
human immunodeficiency virus (HIV)
infectious waste
Levey-Jennings chart
nosocomial infection
pathogen
precision
proficiency testing
quality control (QC)
Safety Data Sheets
standard deviation
standard precautions
standards
trend
variance

LEARNING OUTCOMES

An overview of the hematology laboratory

- Explain the role of the hematology laboratory staff in providing quality patient care.
- List five basic functions of the hematology laboratory.

Patient safety

- Name and describe the Institute of Medicine's six goals for health care delivery to improve the quality of American healthcare.
- Name and explain goal areas cited by the Joint Commission that have specific applications for the clinical laboratory.

Safety for laboratory personnel

- Explain the basic techniques for safety in the hematology laboratory.
- Explain the basic techniques in the prevention of disease transmission.
- Compare the features of general safety regulations governing the clinical laboratory, including components of the Occupational Safety and Health Administration (OSHA)–mandated plans for chemical hygiene and for occupational exposure to bloodborne pathogens, and the importance of the laboratory safety manual.
- List and describe the basic aspects of infection control policies and practices, including how and when to use personal protective equipment or devices (e.g., gowns, gloves, goggles), and the reasons for using standard precautions.
- Explain the purpose and correct procedure of handwashing.
- Describe the contents of the laboratory procedures manual.
- Given a Safety Data Sheet, identify critical information.

Quality assessment and quality control in the hematology laboratory

- Summarize the essential nonanalytical factors in quality assessment.
- Explain the delta check as a quality control method.
- Define terms used in quality control and basic statistical terms.
- Define accuracy, precision, control material, mean, and standard deviation.
- Given the appropriate data, calculate the mean and standard deviation and create a quality control chart.
- Describe the basic terms and state the formulas for the standard deviation, coefficient of variation, and z score.
- Describe the use of a Levey-Jennings quality control chart.
- Compare three types of changes that can be observed in a quality control chart.
- Assess the most frequent application of a histogram.
- Appraise the Westgard Rules and use of the Multirule Procedure

NOTE:
- ■ indicates MLT and MLS core content
- • indicates MLT (optional) and MLS advanced content

AN OVERVIEW OF THE HEMATOLOGY LABORATORY

Hematology, the discipline that studies the development and diseases of blood, is an essential medical science. In this field, the fundamental concepts of biology and chemistry are applied to the medical diagnosis and treatment of various disorders or diseases related to or manifested in the blood and bone marrow.

The Study of Hematology

Basic procedures performed in the hematology laboratory, such as the complete blood cell count (CBC), which includes the measurement and examination of red blood cells (erythrocytes), white blood cells (leukocytes), and platelets (thrombocytes), and the erythrocyte sedimentation rate (ESR), frequently guide the primary care provider in establishing a patient's differential diagnosis. Molecular diagnostics, flow cell cytometry, and digital imaging are modern techniques that have revolutionized the laboratory diagnosis and monitoring of many blood disorders, for example, acute leukemias and inherited blood disorders. T e field of hematology encompasses the study of blood coagulation—hemostasis and thrombosis.

Functions of the Hematology Laboratory

Medical laboratory scientists, medical laboratory technicians, laboratory assistants, and phlebotomists employed in the hematology laboratory play a major role in patient care.

T e assays and examinations that are performed in the laboratory can do the following:

- Establish a diagnosis or rule out a diagnosis
- Confirm a physician's clinical impression of a possible hematological disorder
- Detect an unsuspected disorder
- Monitor the effects of therapy
- Detect minimal residual disease following therapy

Although the CBC is the most frequently requested procedure, a laboratory professional must be familiar with the theory and practice of a wide variety of automated and manual tests performed in the laboratory to provide quality patient care. Continuing education is a necessity to keep up with continually changing knowledge and instrumentation in the field.

NOTE: Now is a good time to review key term definitions in the Glossary and flash cards on thePoint®.

PATIENT SAFETY

Safety standards for patients are initiated, governed, and reviewed by governmental agencies and professional organizations (see Box 1.1).

BOX 1.1

Safety Agencies and Organizations

- U.S. Department of Labor's Occupational Safety and Health Administration (OSHA)
- Clinical and Laboratory Standards Institute (CLSI)
- Centers for Disease Control and Prevention (CDC), Department of Health and Human Services (DHHS)
- College of American Pathologists (CAP)
- T e Joint Commission

T e Joint Commission's National Patient Safety Goals[1] has several goal areas that have specific applications for clinical laboratories. T ese goals are part of the overall quality improvement requirements for accreditation of hospitals by the Joint Commission. T e topics of each of the applicable goals are

- Correct patient identification. At least, two methods of patient identification are required. T ese methods require the use of the patient's name, an assigned ID number, date of birth, or other person-specific information.
- Improved staff communication. T is area of interest includes communicating patient issues, for example, nonfasting state, related to blood collection to appropriate medical personnel. Reporting critical test results on a timely basis falls in this category.
- Reduce the risk of hospital-acquired, nosocomial infection. T is goal area requires the use of handwashing guidelines from the Centers for Disease Control and Prevention (CDC) or the World Health Organization (WHO). T e National Nosocomial Infections Surveillance (NNIS) System of the CDC performed a survey from October 1986 to April 1998. T e highest rates of infection occurred in the burn intensive care unit (ICU), the neonatal ICU, and the pediatric ICU. Risk factors include pathogens on the hands of medical personnel. Patient risk factors include the severity of illness, underlying immunocompromised state, and length of stay. Many hospitals have reorganized the physical layout of handwashing stations and have adopted patient cohorts to prevent the spread of pathogens.

SAFETY IN THE HEMATOLOGY LABORATORY

T e practice of safety should be uppermost in the mind of all persons working in a clinical hematology laboratory. Accidents do not just happen; they are caused by carelessness, lack of attention to detail, or lack of proper communication. Most laboratory accidents are preventable by exercising good technique, staying alert, and using common sense.

Safety standards for patients and/or clinical laboratories are initiated, governed, and reviewed by several agencies.

1. U.S. Department of Labor's Occupational Safety and Health Administration (OSHA)
2. Clinical and Laboratory Standards Institute (CLSI)
3. Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services (DHHS)
4. College of American Pathologists (CAP)

Laboratory safety includes OSHA standards and CDC guidelines that are designed to protect laboratory personnel from potential hazards in the clinical laboratory. Ensuring safety in the clinical laboratory includes the following measures:

- A formal safety program
- Specifically mandated plans (e.g., chemical hygiene, bloodborne pathogens)
- Identification of various hazards (e.g., fire, electrical, chemical, biological)

The Safety Officer

A designated safety of cer is a critical part of a laboratory safety program. T is individual has many duties affecting staff including compliance with existing regulations affecting the laboratory and staff, for example, labeling of chemicals and providing supplies for the proper handling and disposal of hazardous materials.

Occupational Safety and Health Administration Acts and Standards

Laboratory safety includes Occupational Safety and Health Administration (OSHA) standards and CDC guidelines that are designed to protect laboratory personnel from potential hazards in the clinical laboratory. To ensure safe and healthful working conditions for workers, the US federal government created a system of safeguards and regulations under the Occupational Safety and Health Act of 1970. In 1988, the Act expanded the Hazard Communication Standard to apply to hospital staff. T e programs deal with many aspects of safety and health protection and place responsibility for compliance on management and employees.

OSHA standards include systems for alerting all workers to potential hazards, suitable protective equipment, exposure control procedures, and implementation of training and education programs. T e primary purpose of OSHA standards is to ensure safe and healthful working conditions for every US worker.

OSHA and the CDC have published numerous safety standards and regulations that are applicable to clinical laboratories. Ensuring safety in the clinical laboratory includes the following measures:

- A formal safety program
- Specifically mandated plans (e.g., chemical hygiene, bloodborne pathogens)
- Identification of various hazards (e.g., chemical, biological)

Chemical Hygiene Plan

In 1991, OSHA mandated that all clinical laboratories must implement a chemical hygiene plan (CHP) and an exposure control plan.

T e Hazard Communication Standard (HCS) (29 CFR 1910.1200(g)), revised in 2012, requires that the chemical manufacturer, distributor, or importer provide Safety Data Sheets (SDSs) (formerly Material Safety Data Sheets) for each hazardous chemical to downstream users to communicate information on these hazards. T e information contained in the SDS is largely the same as the MSDS, except now the SDSs are required to be presented in a consistent user-friendly, 16-section format.

> Safety Data Sheets must be readily accessible and available to all employees at all times. T is document ensures that laboratory workers are fully aware of the hazards associated with chemicals in their workplaces. T e SDS describes hazards, safe handling, storage, and disposal of hazardous chemicals. T e information is provided by chemical manufacturers and suppliers about each chemical and accompanies the shipment of each chemical.

New changes, initiated in 2013, to the Occupational Safety and Health Administration's (OSHA) Hazard Communication Standard are bringing the United States into alignment with the Globally Harmonized System of Classification and Labeling of Chemicals (GHS), further improving safety and health protections for America's workers. OSHA's current Hazard Communication Standard is expected to prevent injuries and illnesses, save lives, and improve trade conditions for chemical manufacturers. T e Hazard Communication Standard in 1983 gave the workers the "right to know," but the new Globally Harmonized System gives workers the "right to understand."

Occupational Exposure to Bloodborne Pathogens

T e OSHA-mandated program, Occupational Exposure to Bloodborne Pathogens, became law in March 1992. T is regulation requires that laboratories develop, implement, and comply with a plan that ensures the protective safety of laboratory staff to potential infectious bloodborne pathogens, hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV). T e law further specifies the rules for managing and handling medical waste in a safe and effective manner.

T e CDC also recommends safety precautions concerning the handling of all patient specimens, known as standard precautions. T e CLSI has also issued guidelines for the laboratory worker in regard to protection from bloodborne disease spread through contact with patient specimens. In addition, the CDC provides recommendations for treatment after occupational exposure to potentially infectious material.

Avoiding Transmission of Infectious Diseases

A laboratory-acquired infection (LAI) is defined as an infection acquired through laboratory or laboratory-related

activities regardless whether they are symptomatic or asymptomatic in nature.

Transmission of various bloodborne pathogens has always been a concern for laboratory staff, but with the identification of human immunodeficiency virus (HIV), a new awareness was created. Specific regulations in regard to the handling of blood and body fluids from patients suspected or known to be infected with a bloodborne pathogen were originally issued in 1983.

The recognition of HIV-1 generated new policies from the CDC and mandated regulations by the OSHA. Current safety guidelines for the control of infectious disease are based on the original CDC publication, "Recommendations for Prevention of HIV Transmission in Health-Care Settings" (MMWR, Suppl 2S, 1987) with subsequent clarifications.

The purpose of the standards for bloodborne pathogens and occupational exposure is to provide a safe work environment. OSHA mandates that an employer does the following:

- Educate and train all health care workers in standard precautions and in preventing bloodborne infections
- Provide proper equipment and supplies, for example, gloves
- Monitor compliance with the protective biosafety policies

Occupational Exposure Related to HIV, HBV, and HCV Transmission

Blood is the most frequently implicated infected body fluid in HIV and HBV exposure in the occupational setting.

Occupational Exposure

According to safeneedle.org, there are approximately 38,400 reported needlestick injuries to US hospital professionals annually. The Needlestick Prevention and Safety Act of 2000 (see Chapter 2) should have a significant impact on reducing the number of injuries because of hollow-bore devices, for example, needles.

An occupational exposure is defined as a percutaneous injury, for example, needlestick or cut with a sharp object, or contact by mucous membranes or nonintact skin (especially when the skin is chapped, abraded, or affected with dermatitis), or the contact is prolonged or involves an extensive area with blood, tissues, blood-stained body fluids, body fluids to which standard precautions apply, or concentrated virus.

Among health care personnel with documented occupationally acquired HIV infection, prior percutaneous exposure is the most common source of infection. Certain percutaneous injuries carry a higher risk of infection. Risk of infection is greater with

- A deep injury
- Late-stage HIV disease in the source patient
- Visible blood on the device that caused the injury
- Injury with a needle that had been placed in a source patient's artery or vein

There are a small number of cases when HIV has been acquired through contact with nonintact skin or mucous membranes (i.e., splashes of infected blood in the eye or aerosols). The risk of infection not only varies with the type of exposure but also may be influenced by

- Amount of infected blood in the exposure
- Length of contact with infectious material
- Amount of virus in the patient's blood or body fluid or tissue at the time of exposure
- Presence of skin lesions or abrasions on the hands or exposed skin of the health care worker

Exposure to HIV is uncommon, but cases of occupational transmission to health care personnel with no other known high-risk factors have been documented. HIV has been isolated from blood and body fluids. Sperm cells themselves have been discovered to be capable of transmitting HIV. Evidence for the role of saliva in the transmission of virus is unclear, but standard precautions do not apply to saliva uncontaminated with blood. HIV retains infectivity for more than 3 days in dried specimens at room temperature and for more than 1 week in an aqueous environment at room temperature.

The transmission of HIV through occupational exposure is among the least likely to occur, if proper safety practices are followed. The latest statistics on acquired immunodeficiency syndrome (AIDS) and HIV in the United States were published in 2012 by the CDC.[2] Since the beginning of the HIV/AIDS epidemic, health care workers across the world have become infected with HIV. The main cause of infection in occupational settings is exposure to HIV-infected blood via a percutaneous injury (i.e., from needles, instruments, bites that break the skin, etc.). Occupational transmission of HIV to health care workers is extremely rare.

No confirmed cases of occupational HIV transmission to health care workers have been reported since 1999. Underreporting of cases to CDC is possible, however, because case reporting is voluntary. Health care workers who are exposed to HIV-infected blood at work have a 0.3% risk of becoming infected. In other words, 3 of every 1,000 such injuries, if untreated, will result in infection.[3]

The risk of transmission of HBV and hepatitis C (HCV) from an occupational exposure is greater than the risk of HIV transmission. The likelihood of infection after exposure to blood infected with HBV depends on the concentration of HBV in the blood and the immune status of the health care worker for HBV. Between 1990 and 2002, the incidence of acute hepatitis B declined to 67%. Although the number of cases has sharply declined since hepatitis B vaccine became available, unvaccinated health care workers can become infected with HBV following occupational exposure.

HBV can be present in extraordinarily high concentrations in blood. HBV may be stable in dried blood and blood products at 25°C for up to 7 days. The average risk of HBV infection ranges from 1% to 30% depending on the presence of hepatitis e antigen. If HBe antigen is positive, the average risk of infection is 22.0% to 30%; If HBe antigen is negative, the average risk of infection is 1.0% to 6%).

FIGURE 1.1 Puncture-resistant sharps containers. (Courtesy of Becton Dickinson, Franklin Lakes, New Jersey.)

T e source of hepatitis C infection is not as definitive as either HIV or HBV. Exposure to blood is one of the known ways of exposure. T e risk of HCV infection following a needlestick is 1.8%.[4,5]

Sharps Prevention

T e most widespread control measure required by OSHA and CLSI is the use of puncture-resistant sharps containers (Fig. 1.1). T ese containers must be

- Closable, puncture-resistant, and leakproof on sides and bottom
- Accessible, maintained upright, and not allowed to overfill
- Labeled or color coded according to 29 CFR 1910.1030(g)(1)(i)
- Colored red or labeled with the biohazard symbol
- Labeled in fluorescent orange or orange-red, with lettering and symbols in a contrasting color 29 CFR 1910.1030(g)(1)(i)(C). Red bags or containers may be substituted 29 CFR 1910.1030(g)(1)(i)(E)

T e primary reason for using these containers is to eliminate the need for anyone to transport needles and other sharps while looking for a place to discard them. Sharps containers are to be located in the patient areas as well as conveniently placed in the laboratory.

Phlebotomists should carry these red, puncture-resistant containers in their collection trays. Needle containers should not project from the top of the container. Use of the special sharps container permits quick disposal of a needle without recapping as well as of other sharp devices that may be contaminated with blood. T is supports the recommendation against recapping, bending, breaking, or otherwise manipulating any sharp needle or lancet device by hand. Most needlestick accidents have occurred during recapping of a needle after a phlebotomy. Injuries also can occur to housekeeping personnel when contaminated sharps are left on a bed, concealed in linen, or disposed of improperly in a waste receptacle. Most accidental disposal-related exposures can be eliminated by the use of sharps containers. To discard sharps, containers are closed and placed in the biohazard waste. A needlestick injury must be reported to the supervisor or other designated individual.

Blood-borne Virus Postexposure Issues

Although the most important strategy for reducing the risk of occupational HIV transmission is to prevent occupational exposures, plans for postexposure management of health care personnel should be in place. T e CDC has issued guidelines for the management of health care personnel exposures to HIV and recommendations for a postexposure plan (PEP). (Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Postexposure Prophylaxis, MMWR, 50[RR-11], 2001).

An occupational exposure should be considered to be an urgent medical concern to ensure timely postexposure management. If an accidental occupational exposure does occur, laboratory staff members should be informed of options for treatment. Because a needlestick can trigger an emotional response, it is wise to think about a course of action before the occurrence of an actual incident. If a "source patient" can be identified, part of the workup could involve testing the patient for various infectious diseases. Laws addressing the patient's rights in regard to testing of a source patient can vary from state to state.

If a known or suspected parenteral exposure takes place, a laboratory professional may request follow-up monitoring for hepatitis or HIV antibodies. T is monitoring and follow-up counseling must be provided free of charge. If voluntary informed consent is obtained, the source of the potentially infectious material and the technician/technologist should be tested immediately. T e laboratory professional should also be tested at intervals after exposure. An injury report must be filed after parenteral exposure.

Immune Status: Screening and Vaccination

Screening is available for the detection of many occupationally acquired bloodborne pathogens including HBV. Before the advent of the hepatitis B vaccine, the leading occupational infection in health care workers was hepatitis B.

Preemployment health profiles with baseline screening of students and laboratory staff should include an immune status evaluation for hepatitis B. If antibodies to HBV are not demonstrable, vaccination is necessary. OSHA issued a federal standard in 1991 mandating employers to provide the hepatitis B vaccine to all employees who have or may have occupational exposure to blood or other potentially infective materials. T e vaccine is to be offered at no expense to the employee, and if the employee refuses the vaccine, a declination form must be signed.

A well-planned and properly implemented immunization program is an important component of a health care organization's infection prevention and control program. T e risk of nosocomial transmission of HBV and some other bloodborne pathogens can be minimized if laboratory personnel are vaccinated and comply with essential safety guidelines.

SAFE WORK PRACTICES AND PROTECTIVE TECHNIQUES FOR INFECTION CONTROL

Safety Manual, Policies, and Practices

Each laboratory must have an up-to-date safety manual. T is manual contains a comprehensive listing of approved policies, acceptable practices, and precautions including standard precautions. Specific regulations that conform to current state and federal requirements such as OSHA regulations must be included in the manual. Other sources of mandatory and voluntary standards include the Joint Commission (TJC), the College of American Pathologists (CAP), and the CDC.

Each laboratory is required to evaluate the effectiveness of its safety plan at least annually and to update it as necessary. T e written plan must be available to employees. A laboratory's written plan must include the purpose and scope of the plan, references, definitions of terms and responsibilities, and detailed procedural steps to follow.

Because many hazards in the clinical laboratory are unique, a special term biohazard was devised. T is word is posted throughout the laboratory to denote infectious materials or agents that present a risk or even a potential risk to the health of humans or animals in the laboratory.

T e potential risk can be either through direct infection or through the environment. Infection can occur during the process of specimen collection or from handling, transporting, or testing the specimen.

Laboratory policies are included in a laboratory reference manual that is available to all hospital personnel. Such manuals that are frequently published online contain information regarding patient preparation for laboratory tests. Approved policies regarding the reporting of abnormal values are clearly stated in this document.

Standard Precautions

Standard precautions are intended to prevent occupational exposures to bloodborne pathogens. T is approach eliminates the need for separate isolation procedures for patients known or suspected to be infectious. T e application of standard precautions also eliminates the need for warning labels on specimens. According to the CDC concept of standard precautions, all human blood and other body fluids are treated as potentially infectious for HIV, HBV, and other bloodborne microorganisms that can cause disease in humans. Standard precautions are intended to supplement rather than replace handwashing recommendations for routine infection control.

Handwashing

Frequent handwashing is an important safety precaution. It must be performed after contact with patients and laboratory specimens. Gloves should be used as an adjunct to, not a substitute for, handwashing.

BOX 1.2

Your 5 Moments of Hand Hygiene

BEFORE PATIENT CONTACT
WHEN? Clean your hands before touching a patient when approaching him or her
WHY? To protect the patient against harmful germs carried on your hands

BEFORE AN ASEPTIC TASK
WHEN? Clean your hands immediately before any aseptic task
WHY? To protect the patient against harmful germs, including the patient's own germs, entering his or her body

AFTER BODY FLUID EXPOSURE RISK
WHEN? Clean your hands immediately after an exposure risk to body fluids (and after glove removal)
WHY? To protect yourself and the health care environment from harmful patient germs

AFTER PATIENT CONTACT
WHEN? Clean your hands after touching a patient and his or her immediate surroundings when leaving
WHY? To protect yourself and the health care environment from harmful patient germs

AFTER CONTACT WITH PATIENT SURROUNDINGS
WHEN? Clean your hands after touching any object or furniture in the patient's immediate surroundings, when leaving—even without touching the patient
WHY? To protect yourself and the health care environment from harmful patient germs.

Source: World Health Organization (WHO). www.who.int retrieved September 13, 2015.

According to the WHO (see Box 1.2), clean your hands by rubbing them with an alcohol-based formulation, as the preferred mean for routine hygienic hand antisepsis if hands are not visibly soiled. It is faster, more effective, and better tolerated by your hands than washing with soap and water.

Wash your hands with soap and water when hands are visibly dirty or visibly soiled with blood or other body fluids or after using the toilet. If exposure to potential spore-forming pathogens is strongly suspected or proven, including outbreaks of Clostridium dif cile, handwashing with soap and water is the preferred means.

T e Department of Health and Human Services (CDC) issued a guide in 2002 for Hand Hygiene in Healthcare Settings see Box 1.3). T e ef cacy of handwashing in reducing transmission of microbial organisms has been demonstrated. Handwashing is particularly important after removing gloves. T e Association for Professionals in Infection Control and Epidemiology reports extreme variability in the quality

BOX 1.3

Guidelines for Handwashing and Hand Antisepsis in Healthcare Settings

1. Wash hands with a nonantimicrobial soap and water or an antimicrobial soap and water when hands are visibly dirty or contaminated with proteinaceous material.
2. Use an alcohol-based waterless antiseptic agent for routine decontamination of hands, if not visibly soiled.
3. Waterless antiseptic agents are highly preferable, but hand antisepsis using antimicrobial soap may be considered in certain circumstances.
4. Decontaminate hands after contact with the patient's skin.
5. Decontaminate hands after contact with blood and body fluids.
6. Decontaminate hands if moving from a contaminated area to clean body site during patient care.
7. Decontaminate hands after contact with inanimate objects in the immediate vicinity of a patient.
8. Decontaminate hands after removing gloves.

Modified from Centers for Disease Control and Prevention, U.S. Department of Health and Human Services. Guideline for Hand Hygiene in Healthcare Settings, MMWR Morb Mortal Wkly Rep, 51 (RR-16):1, 2002.

of gloves, with leakage in 4% to 63% of vinyl gloves and in 3% to 52% of latex gloves.

Handwashing is essential mmediately after accidental skin contact with blood, body fluids, or tissues. If the contact occurs through breaks in gloves, the gloves should be removed immediately and the hands thoroughly washed. If accidental contamination occurs to an exposed area of the skin or because of a break in gloves, one must wash first with a liquid soap, rinse well with water, and apply a 1:10 dilution of bleach or 50% isopropyl or ethyl alcohol. T e bleach or alcohol is left on the skin for at least 1 minute before final washing with liquid soap and water.

In addition to the CDC guidelines, additional precautions include:

- After completing laboratory work and before leaving the laboratory.
- Before eating, drinking, applying makeup, and changing contact lenses as well as before and after using the lavatory.

Two important points in the practice of hand hygiene technique are:

- When decontaminating hands with a waterless antiseptic agent (e.g., an alcohol-based handrub), apply product to the palm of one hand and rub hands together, covering all surfaces of hands and fingers, until hands are dry. Follow the manufacturer's recommendations on the volume of product to use. If an adequate volume of an alcohol-based handrub is used, it should take 15 to 25 seconds for hands to dry.
- When washing with a nonantimicrobial or antimicrobial soap, wet hands first with warm water, apply 3 to 5 mL of detergent to hands, and rub hands together vigorously for at least 15 seconds, covering all surfaces of the hands and fingers. Rinse hands with warm water and dry thoroughly with a disposable towel. Use the towel to turn off the faucet.

Personal Protective Equipment

OSHA requires laboratories to have a personal protective equipment (PPE) program. T e components of this regulation include the following:

- A workplace hazard assessment with a written hazard certification
- Proper equipment selection
- Employee information and training, with written competency certification
- Regular reassessment of work hazards

Laboratory personnel should not rely solely on devices for PPE to protect themselves against hazards. T ey also should apply PPE standards when using various forms of safety protection. A clear policy on institutionally required standard precautions is needed. For usual laboratory activities, PPE consists of gloves and a laboratory coat or gown. In a hematology laboratory, splash shields are also used.

Selection and Use of Gloves

Gloves for phlebotomy and laboratory work are nonsterile and made of vinyl or latex. T ere are no reported differences in barrier effectiveness between intact latex and intact vinyl gloves. Either type is usually satisfactory for phlebotomy and as a protective barrier when performing technical procedures. Latex-free gloves should be available for personnel with sensitivity to the typical glove material. In some laboratories, latex-free gloves are available for everyone to use.

Care must be taken to avoid indirect contamination of work surfaces or objects in the work area. Gloves should be properly placed on the hands and removed (see Fig. 1.2). An uncontaminated glove or paper towel is required before answering the telephone, handling laboratory equipment, or touching doorknobs.

T e guidelines for the use of gloves during phlebotomy procedures are the following:

- Must be worn when performing fingersticks or heelsticks on infants and children
- Must be worn when receiving phlebotomy training
- Should be changed between each patient contact
- Must be worn when processing specimens

Facial Barrier Protection and Occlusive Bandages

Facial barrier protection (shields) should be used if there is a potential for splashing or spraying of blood or certain body fluids. Masks and facial protection should be worn if mucous

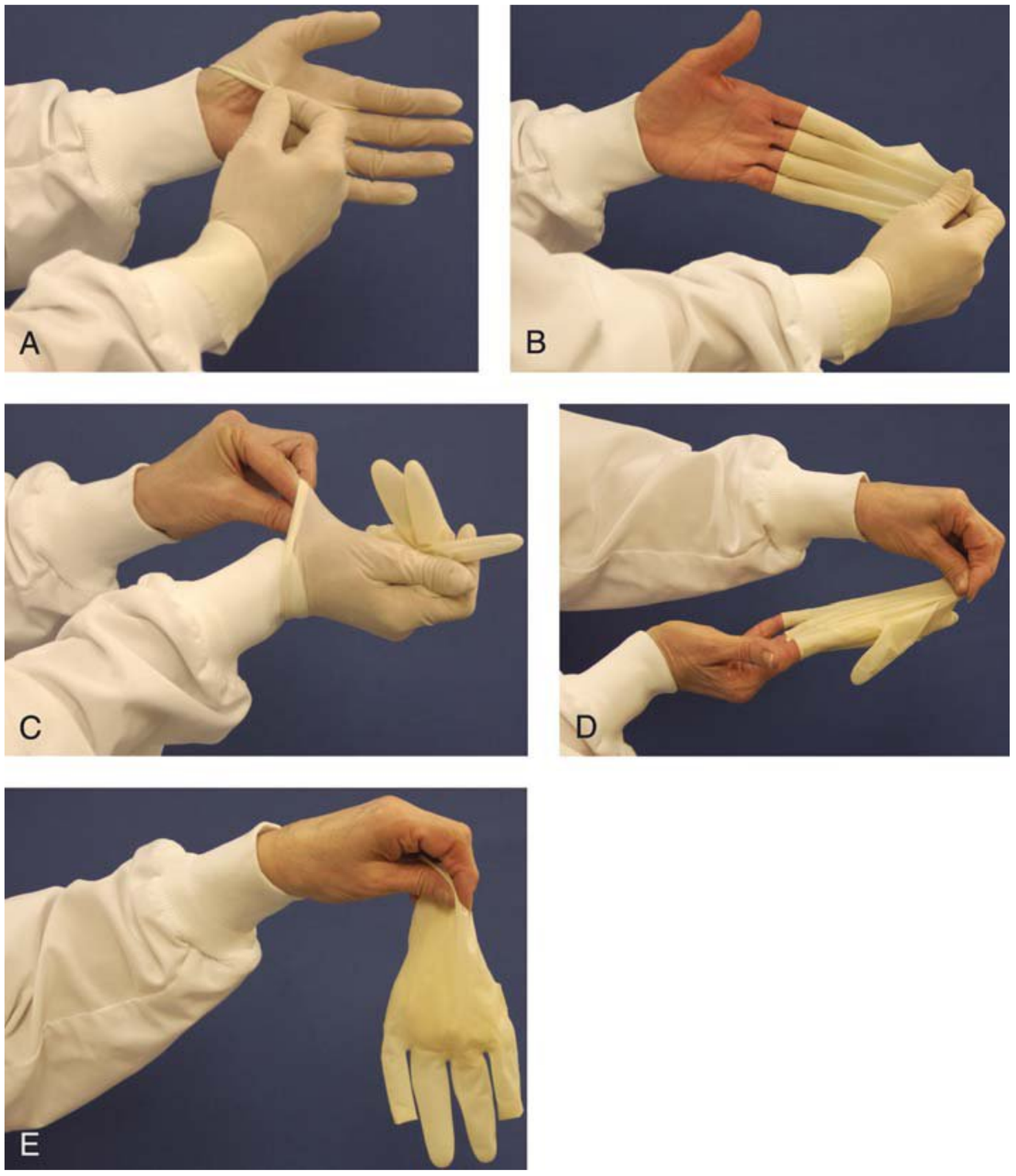

FIGURE 1.2 Glove removal. **A.** T e wrist of one glove is grasped with the opposite gloved hand. **B.** T e glove is pulled inside out, over, and off the hand. **C.** With the first glove held in the gloved hand, the fingers of the non-gloved hand are slipped under the wrist of the remaining glove without touching the exterior surfaces. **D.** T e glove is then pulled inside out over the hand so that the first glove ends up inside the second glove, with no exterior glove surfaces exposed. **E.** Contaminated gloves ready to be dropped into the proper waste receptacle. (Reprinted from McCall RE, Tankersley CM. Phlebotomy Essentials, 6th ed, Baltimore, MD: Lippincott Williams & Wilkins, 2016:69, with permission.)

membrane contact with blood or certain body fluid is anticipated. All disruptions of exposed skin should be covered with a water-impermeable occlusive bandage. T is includes defects on the arms, face, and neck.

Laboratory Coats or Gowns as Barrier Protection

A color-coded, two–laboratory coat or equivalent system should be used whenever laboratory personnel are working with potentially infectious specimens. T e coat worn in the laboratory must be changed or covered with an uncontaminated coat when leaving the immediate work area. Coats should be changed immediately if grossly contaminated with blood or body fluids, to prevent seepage through street clothes to skin. Contaminated coats or gowns should be placed in an appropriately designated biohazard bag for laundering.

Disposable laboratory coats are available. Coats should be discarded into a biohazard container.

Nail Care

According to the CDC, to promote infection control, nails should be no longer than one quarter inch beyond the tip of the finger. Longer nails do not fit into gloves properly and can cause problems with blood collection and analysis.

Shoes

According to CLSI document GP17-A2, shoes worn in the clinical laboratory and phlebotomy services should be rubber-soled and cover the entire foot. Unless covered with shoe covers, canvas shoes are not recommended. Fluid-impermeable material, for example, leather or synthetic, is recommended.

Electronic Devices

Electronic devices, for example, mobile phones, Ipods, MP3 players, and tablet computers, should not be exposed to potential sources of infectious contamination.

Decontamination of Work Surfaces, Equipment, and Spills

All work surfaces are cleaned and sanitized at the beginning and end of the shift with a freshly prepared 1:10 dilution of household bleach (Table 1.1) or an EPA-registered disinfectant.

TABLE 1.1 Preparation of Diluted Household Bleach

Volume of Bleach	Volume of H_2O	Ratio	% Sodium Hypochlorite	% Solution
1 mL	9 mL	1:10	0.5	10

Note: A 10% solution of bleach is stable for 1 week at room temperature when diluted with tap water.

Disinfection describes a process that eliminates many or all pathogenic microorganisms, except bacterial spores, on inanimate objects. In health care settings, objects usually are disinfected by liquid chemicals or wet pasteurization. T e effective use of disinfectants is part of a multibarrier strategy to prevent health care–associated infections. Surfaces are considered noncritical items because they contact intact skin. Use of noncritical items or contact with noncritical surfaces carries little risk of causing an infection in patients or staff.

Disinfecting Solutions

Sodim hypochlorites are the most widely used of the chlorine disinfectants. T e most prevalent chlorine products in the United States are aqueous solutions of 5.25% to 6.15% sodium hypochlorite, usually called household bleach. Bleach, a broad spectrum of antimicrobial activity, does not leave a toxic residue and is unaffected by water hardness. In addition, bleach is inexpensive and fast acting, removes dried or fixed microorganisms from surfaces, and has a low incidence of serious toxicity. A hazard is that sodium hypochlorite at the concentration used in household bleach can produce ocular irritation or oropharyngeal, esophageal, and gastric burns. T e Environmental Protection Agency (EPA) has determined that the currently registered uses of hypochlorites will not result in unreasonable adverse effects to the environment.

Hypochlorites are widely used in health care facilities in a variety of settings. Inorganic chlorine solution is used for spot disinfection of countertops and floors. A 1:10 to 1:100 dilution of household bleach can be used.

Concentrations of 1:10 to 1:100 free chlorine are effective, depending on the amount of organic material present on the surface to be cleaned and disinfected. For small spills of blood (i.e., drops of blood) on noncritical surfaces, the area can be disinfected with freshly diluted household bleach or an EPA-registered tuberculocidal disinfectant. Because hypochlorites and other germicides are substantially inactivated in the presence of blood, large spills of blood require that the surface be cleaned before an EPA-registered disinfectant or a solution of household bleach is applied. If a sharps injury is possible, the surface initially should be decontaminated and then cleaned and disinfected (1:10 final concentration).

An important issue concerning use of disinfectants for noncritical surfaces in health care settings is that the contact time specified on the label of the product is often too long to be practically followed. T e labels of most products registered by EPA for use against HBV, HIV, or Mycobacterium tuberculosis specify a contact time of 10 minutes. Such a long contact time is not practical for disinfection of environmental surfaces in a health care setting because most health care facilities apply a disinfectant and allow it to dry (approximately 1 minute). Multiple scientific papers have demonstrated significant microbial reduction with contact times of 30 to 60 seconds.

Hypochlorite solutions in tap water at a pH > 8 stored at room temperature (23°C) in closed, opaque plastic containers can lose up to 40% to 50% of their free available chlorine level over 1 month. Sodium hypochlorite solution does not decompose after 30 days when stored in a closed brown bottle.

Disinfecting Procedure

Although wearing gloves, employees should clean and sanitize all work surfaces at the beginning and end of their shift with a 1:10 dilution of household bleach. Instruments such as scissors or centrifuge carriages should be sanitized daily with a diluted solution of bleach. It is equally important to clean and disinfect work areas frequently during the workday as well as before and after the workday. Studies have demonstrated that HIV is inactivated rapidly after being exposed to common chemical germicides at concentrations that are much lower than those used in practice. Disposable materials contaminated with blood must be placed in containers marked “Biohazard” and properly discarded.

Neither HBV, HCV or HIV has ever been documented as being transmitted from a housekeeping surface (e.g., countertops). However, an area contaminated by either blood or body fluids needs to be treated as potentially hazardous, with prompt removal and surface disinfection. Strategies differ for decontaminating spills of blood and other body fluids; the cleanup procedure depends on the setting (e.g., porosity of the surface) and volume of the spill. T e following protocol is recommended for managing spills in a clinical laboratory:

1. Wear gloves and a laboratory coat.
2. Absorb the blood with disposable towels. Remove as much liquid blood or serum as possible before decontamination.
3. Using a diluted bleach (1:10) solution, clean the spill site of all visible blood.
4. Wipe down the spill site with paper towels soaked with diluted bleach.

5. Place all disposable materials used for decontamination into a biohazard container.
6. Decontaminate nondisposable equipment by soaking overnight in a dilute bleach (1:10) solution and rinsing with methyl alcohol and water before reuse. Disposable glassware or supplies that have come in contact with the blood should be autoclaved or incinerated.

General Infection Control Safety Practices

All laboratories need programs to minimize risks to the health and safety of employees, volunteers, and patients. Suitable physical arrangements, an acceptable work environment, and appropriate equipment need to be available to maintain safe operations.

A variety of other safety practices should be adhered to, to reduce the risk of inadvertent contamination with blood or certain body fluids. T ese practices include the following:

1. All devices in contact with blood that are capable of transmitting infection to the donor or recipient must be sterile and nonreusable.
2. Food and drinks should not be consumed in work areas or stored in the same area as specimens. Containers, refrigerators, or freezers used for specimens should be marked as containing a biohazard.
3. Specimens needing centrifugation should be capped and placed into a centrifuge with a sealed dome.
4. Rubber-stoppered test tubes are opened slowly and carefully with a gauze square over the stopper to minimize aerosol production (the introduction of substances into the air).
5. Autodilutors or safety bulbs are used for pipetting. Pipetting of any clinical material by mouth is strictly forbidden (see the following discussion).
6. No tobacco products can be used in the laboratory.
7. No manipulation of contact lenses or teeth-whitening strips should be done with gloved or potentially infectious hands.
8. Do not apply lipstick or makeup.
9. All personnel should be familiar with the location and use of eyewash stations and safety showers.

Pipetting Safeguards: Automatic Devices

Pipetting must be done by mechanical means. Such a device is a bottle top dispenser that can be used to deliver repetitive aliquots of reagents. It is designed as a bottle-mounted system that can dispense selected volumes in an easy, precise manner. It is usually trouble free and requires minimal maintenance.

Specimen-Processing Protection

Protective gloves should always be worn for handling any type of biological specimen. Specimens should be transported to the laboratory in plastic leakproof bags. Protective gloves should always be worn for handling any type of biological specimen.

FIGURE 1.3 Biohazard symbol. (Reprinted from McCall RE, Tankersley CM. Phlebotomy Essentials, 6th ed, Baltimore, MD: Lippincott Williams & Wilkins, 2016:79, with permission.)

Infection can occur during the process of specimen collection or from handling, transporting, or testing the specimen. Biohazard symbols are used in a clinical laboratory for additional notification (see Figs. 1.3 and 1.4). T e presence of pathogenic organisms is not limited to the culture plates in the microbiology laboratory. Airborne infectious particles, or aerosols, can be found in all areas of the laboratory where human specimens are used.

In the hematology laboratory, centrifuge accidents, or the improper removal of rubber stoppers from test tubes, produce airborne droplets (aerosols) that can result in an occupational exposure. If these aerosol products are infectious and come in direct contact with mucous membranes or nonintact skin, direct transmission of virus can potentially result.

When the cap is being removed from a specimen tube or a blood collection tube, the top should be covered with a disposable gauze pad or a special protective pad. Gauze pads with an impermeable plastic coating on one side can reduce contamination of gloves. T e tube should be held away from the body

FIGURE 1.4 Approved plastic bags. (Reprinted from McCall RE, Tankersley CM. Phlebotomy Essentials, 4th ed, Baltimore, MD: Lippincott Williams & Wilkins, 2008, with permission.)

and the cap gently twisted to remove it. Snapping off the cap or top can cause some of the contents to aerosolize. When not in place on the tube, the cap should still be kept in the gauze and not placed directly on the work surface or countertop.

When specimens are being centrifuged, the tube caps should always be kept on the tubes. Centrifuge covers must be used and left on until the centrifuge stops. T e centrifuge should be allowed to stop by itself and should not be manually stopped by the worker.

Another step that should be taken to control the hazard from aerosols is to exercise caution in handling pipettes and other equipment used to transfer human specimens, especially pathogenic materials. T ese materials should be discarded properly and carefully.

Specially constructed plastic splash shields are used in many laboratories for the processing of blood specimens. T e tube caps are removed behind or under the shield, which acts as a barrier between the person and the specimen tube. T is is designed to prevent aerosols from entering the nose, eyes, or mouth. Laboratory safety boxes are commercially available and can be used to remove stoppers from tubes or perform other procedures that might cause spattering. Splash shields and safety boxes should be periodically decontaminated.

OSHA Medical Waste Standards

OSHA standards provide for the implementation of a waste disposal program (see Box 1.4). On the federal level, the storage and management of infectious waste is primarily regulated by OSHA. Laws and statutes are defined by the Occupational Health and Safety Act and the Clean Air Act.

NOTE: Now is a good time to complete the Review Questions related to the preceding content.

QUALITY ASSESSMENT IN THE HEMATOLOGY LABORATORY

T e assessment of quality results for the various analyses is critical and is an important component of the operation of a high-quality laboratory. Quality assessment programs monitor the following:

- Test request procedures
- Patient identification
- Specimen procurement
- Specimen labeling
- Specimen transportation and processing procedures
- Laboratory personnel performance
- Laboratory instrumentation, reagents, and analytical (examination) test procedures
- Turnaround times
- Accuracy of the final result

BOX 1.4

OSHA Regulation of Medical Waste

- Contaminated reusable sharps must be placed in containers that are puncture resistant; labeled or color coded; and leakproof on the sides and bottom. Reusable sharps that are contaminated with blood or other potentially infectious materials must not be stored or processed in a manner that requires employees to reach by hand into the containers.
- Specimens of blood or other potentially infectious material are required to be placed in a container that is labeled or color coded and closed prior to being stored, transported, or shipped. Contaminated sharps must be placed in containers that are closeable, puncture resistant, leakproof on sides and bottoms, and labeled or color coded.
- Regulated wastes (liquid or semiliquid blood or other potentially infectious materials; contaminated items that would release blood or other potentially infectious materials in a liquid or semiliquid state if compressed; items that are caked with dried blood or other potentially infectious materials and are capable of releasing these materials during handling; contaminated sharps; and pathological and microbiological wastes containing blood or other potentially infectious materials) must be placed in containers that are closeable, constructed to contain all contents and prevent leakage of fluids, labeled or color coded, and closed prior to removal (see a full discussion below of biohazard containers and biohazard bag).
- All bins, pails, cans, and similar receptacles intended for reuse, which have the likelihood of becoming contaminated with blood or other potentially infectious materials, are required to be inspected and decontaminated on a regularly scheduled basis. Waste containers must be easily accessible to personnel and must be located in the laboratory areas where they are typically used. Containers for waste should be constructed so that their contents will not be spilled if the container is tipped over accidentally.
- Labels af xed to containers of regulated waste; refrigerators and freezers containing blood or other potentially infectious materials; and other containers used to store, transport, or ship blood or other potentially infectious materials must include the biohazard symbol; be fluorescent orange or orange-red or predominantly so, with lettering and symbols in contrasting color; and be af xed as closely as possible to the container by adhesive or wire to prevent loss or removal.

Complete documentation of all procedures involved in obtaining the analytical (examination) result for the patient sample must be maintained and monitored in a systematic manner.

Regulations and Organizations Impacting Quality

Clinical Laboratory Improvement Amendments

In 1988, the U.S. Congress enacted the Clinical Laboratory Improvement Amendments of 1988 (CLIA'88) in response to the concerns about laboratory testing errors. T e final CLIA rule, Laboratory Requirements Relating to Quality Systems and Certain Personnel Qualifications, was published in the Federal Register on January 24, 2003. Enactment of CLIA established a minimum threshold for all aspects of clinical laboratory testing. CLIA'88 also incorporates **prof ciency testing** in the regulations.

Voluntary Accrediting Organizations

Voluntary accrediting agencies, for example, the Joint Commission on Accreditation of Healthcare Organization and the CAP, have set standards that include quality assessment programs.

ISO 15189

T e International Organization for Standardization (ISO), a network of the national standards institutes of 159 countries, is the world's largest developer and publisher of international standards. ISO is a nongovernmental organization that forms a bridge between the public and private sectors. ISO standards and certification are widely used by industry but now ISO 15189 has been formulated for clinical laboratories. T e standard, ISO 15189, is based on ISO/IEC 17025, the main standard used by testing and calibration laboratories, and ISO 9001. T e 15189 standard was developed with the input of the CAP and has gained acceptance as a mandatory accreditation in Australia, the Canadian province of Ontario, and many European countries. In the United States, 15189 accreditation remains optional.

ISO 15189:2007 is for use by medical laboratories in developing their quality management systems and assessing their own competence and for use by accreditation bodies in confirming or recognizing the competence of medical laboratories.

Components of Quality Assessment

A Quality assessment system is divided into two major components: nonanalytical factors and the analysis of quantitative data (quality control [QC]).

Quality assessment is used in the clinical hematology laboratory to ensure excellence in performance. A systematic approach to quality assures that correct laboratory results are obtained in the shortest possible time and at a reasonable cost.

T e total testing process (TTP) serves as the primary point of reference for focusing on quality in the clinical laboratory. TTP is defined by activities in three distinct phases related to workflow outside and inside the laboratory:

1. Preanalytical (preexamination)
2. Analytical (examination)
3. Postanalytical (postexamination)

Nonanalytical Factors in Quality Assessment

To guarantee the highest quality patient care through laboratory testing, a variety of preanalytical (preexamination) and Postanalytical (postexamination) factors in addition to analytical (examination) data must be considered. For laboratories to comply with CLIA'88 and be certified to perform testing, they must meet minimum standards. In some cases, deficiencies are noted and must be corrected.

A recent study[6] of laboratory errors showed that the preanalytical phase is where 98% of the errors in laboratory testing occurs. One specific area of improvement in laboratory testing in improvement in the blood sample collection and processing of specimens is in the preanalytical phase with phlebotomists and other professional staff who collect laboratory specimens.

Nonanalytical factors that support quality testing include the following:

1. Qualified personnel
2. Laboratory policies
3. Laboratory procedure manual
4. Test requisitioning
5. Patient identification and specimen procurement and labeling
6. Specimen collection, transport, processing, and storage
7. Preventive maintenance of equipment
8. Appropriate methodology
9. Accuracy in reporting results and documentation

Quali*fi*ed Personnel

T e entry-level examination competencies of all certified persons in hematology must be validated. Validation takes the form of both external certification and new employee orientation to the work environment.

Continuing competency is equally important. Participation in continuing education activities is essential to the maintenance of competency and is required in some instances to maintain professional certification. Personnel performance should be monitored with periodic evaluations and reports. Quality assessment demands that a supervisor monitors the results of daily work and that all analytical (examination) reports produced during a particular shift be evaluated for errors and omissions.

Laboratory Policies

Laboratory policies should be included in a laboratory reference manual that is available to all hospital personnel. Each laboratory must have an up-to-date safety manual. T is manual contains a comprehensive listing of approved policies, acceptable practices, and precautions, including standard blood and body fluid precautions. Specific regulations that conform to current state and general requirement, such as OSHA regulations, must be included in the manual. Other sources of mandatory and voluntary standards include JCAHO, CAP, and the CDC.

Laboratory Procedure Manual

Laboratory procedures should be contained in a current and complete document of laboratory procedures, including approved policies for the reporting of results. T e manual must be reviewed regularly, in some cases annually, by the supervisory staff and updated, as needed.

T e laboratory procedure manual describes each procedure performed in the hematology laboratory. T is manual must comply with the CLSI format standards for a procedure manual. CLSI is an internationally recognized group of laboratory professionals who lead Quality Assessment efforts. To support a QC program, methods for documenting laboratory results must be included in the procedure manual. Proper documentation ensures that control specimens have been properly monitored. T e procedural format found in Chapter 32 of this book follows the CLSI guidelines.

T e CLSI recommends that the procedure manual follows a specific pattern of organization. Each assay done in the hematology laboratory must be included in the manual. T e minimal components are as follows:

- Title of the assay
- Principle of the procedure and statement of clinical applications
- Protocol for specimen collection and storage
- QC information
- Reagents, supplies, and equipment
- Procedural protocol
- Reference "normal" ranges
- Technical sources of error
- Limitations of the procedure
- Proper procedures for specimen collection and storage
- Approved policies for the reporting of results

Test Requisitioning

A laboratory test can be requested by a primary care provider or, in some states, the patient. T e request, either hard copy or electronic, must include the patient identification data, the time and date of specimen collection, the source of the specimen, and the analyses to be performed. T e information on the accompanying specimen container must match exactly the patient identification on the test request. T e information needed by the physician to assist in ordering tests must be included in an online database or printed handbook.

Patient Identification, Specimen Procurement, and Labeling

Maintaining an electronic database or handbook of specimen requirement information is one of the first steps in establishing a quality assessment program for the clinical laboratory. Current information about obtaining appropriate specimens, special collection requirements for various types of tests, ordering tests correctly, and transporting and processing specimens appropriately should be included in the database.

Patients must be carefully identified. Preanalytical (preexamination) errors are the most common source of laboratory errors (see Box 1.5). For example, identification errors, either of the patient or of the specimen, are major potential sources of error. T e use of computerized bar code identification of specimens is an asset to specimen identification. Using established specimen requirement information, the clinical specimens must be properly labeled once they have been obtained from the patient. Computer-generated bar code labels (Fig. 1.5) assist in making certain that proper patient identification is noted on each specimen container sent to the laboratory. An important rule to remember is that the analytical result can only be as good as the received specimen.

BOX 1.5

Examples of Potential Preanalytical (preexamination)/ Analytical (examination)/ Postanalytical (postexamination) Errors

PREANALYTICAL (PREEXAMINATION)

- Specimen obtained from the wrong patient
- Specimen procured at the wrong time
- Specimen collected in the wrong tube or container
- Blood specimens collected in the wrong order
- Incorrect labeling of specimen
- Improper processing of specimen

ANALYTICAL (EXAMINATION)

- Oversight of instrument flags
- Out-of-control QC results
- Wrong assay performed

POSTANALYTICAL (POSTEXAMINATION)

- Verbal reporting of results
- Instrument: Laboratory Information System (LIS) incompatibility error
- Confusion about reference ranges
- Failure to report critical values immediately

Specimen Collection, Transporting, Processing, and Storage

Strict adherence to correct procedures for specimen collection and storage is critical to the accuracy of any test.

Specimens must be ef ciently transported to the laboratory. Some assays require special handling conditions, such as placing the specimen on ice immediately after collection. Specimens should be tested within 2 hours of collection to produce accurate results. T e documentation of specimen arrival times in the laboratory as well as other specific test request data is an important aspect of the quality assessment process. It is important that the laboratory processing system is able to track a specimen.

Correct storage of specimens is critical to obtaining accurate results. Specimen integrity is an important issue when

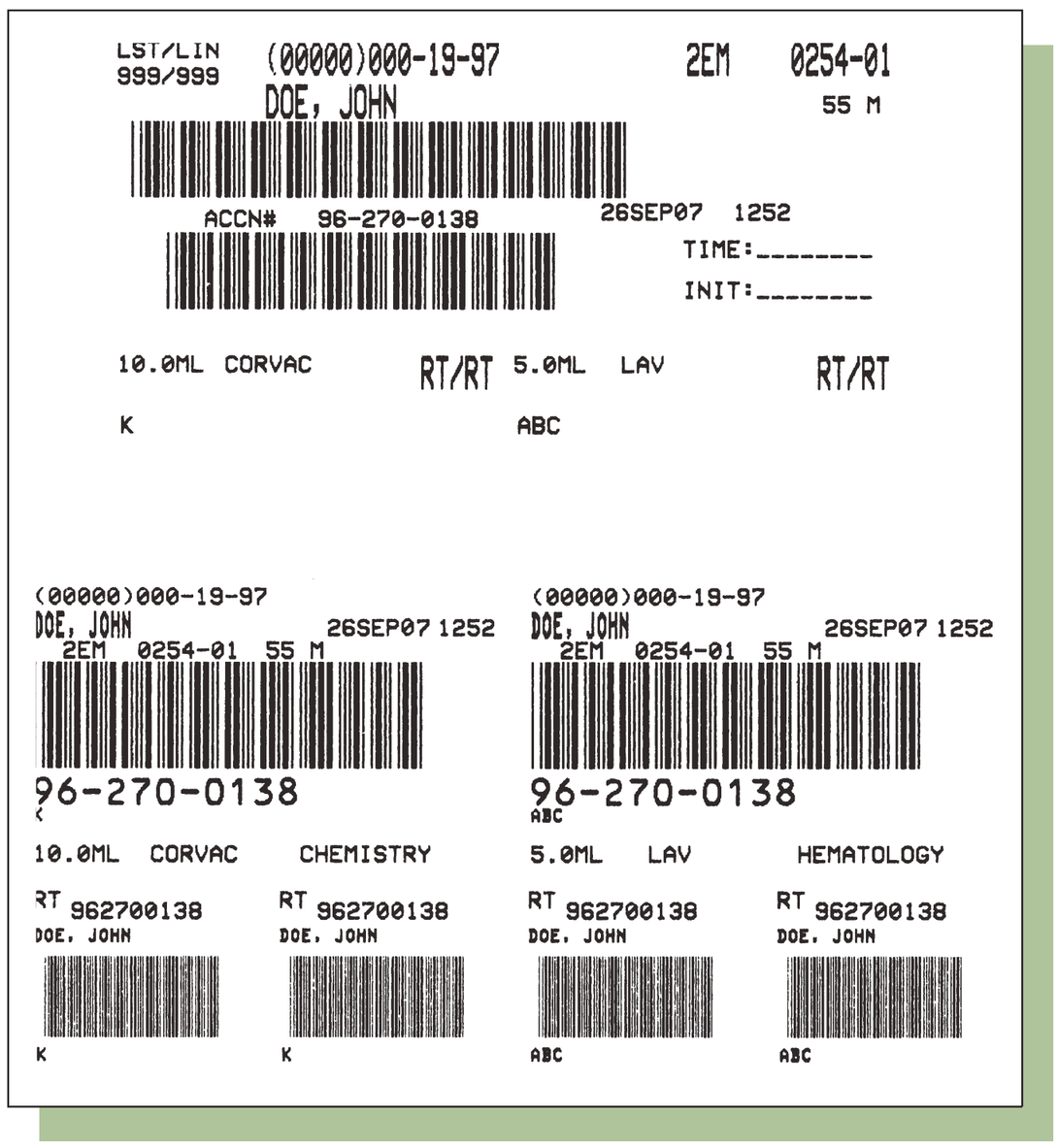

FIGURE 1.5 Bar code. (Reprinted from McCall RE, Tankersley CM. Phlebotomy Essentials, 6th ed, Baltimore, MD: Lippincott Williams & Wilkins, 2016:44, with permission.)

blood is collected at a site away from the testing facility. Samples may need to be drawn several hours before testing. In many cases, cooling of specimens on ice is critical. T is is particularly true for coagulation testing (e.g., prothrombin time [PT] and activated partial thromboplastin time [aPTT]).

According to CLSI (Collection, Transport, and Processing of Blood Specimens for Testing Plasma-Based Coagulation Assays and Molecular Hemostasis Assays; Approved Guideline—Fifth Edition), blood samples collected for PT and aPTT analysis in tubes with sodium citrate should be handled using the following sample protocol when collected off-site. T e sample tube should remain unopened before testing. Centrifugation and testing of such samples can be delayed for up to 2 hours at 22°C to 24°C (71.6°F to 75.2°F) or for up to 4 hours at 2°C to 4°C (35.6°F to 39.2°F). T e sample must be kept in a well-chilled, properly insulated cooler or a refrigerated block. Either storage device must have a thermometer to monitor its temperature to prevent overheating or partial freezing of whole blood samples. Separation of the sample upon standing should not affect sample integrity. In addition, this method of storage should be confirmed for compatibility by contacting both the manufacturer of the evacuated tube collection system and the technical supervisor of coagulation testing.

Preventive Maintenance of Equipment

Monitoring of the temperatures of equipment and refrigerators is important to the quality of test performance. Microscopes, centrifuges, and other pieces of equipment need regularly to be cleaned and checked for accuracy. A preventive maintenance schedule should be followed for all automated equipments.

Equipment such as microscopes, centrifuges, and spectrophotometers should be cleaned and checked for accuracy on a regular schedule. A preventive maintenance schedule should be followed (refer to the section "Instrument Protocol," Chapter 27, e.g.) for all pieces of automated equipment (e.g., cell-counting instruments). Failure to monitor equipment regularly can produce inaccurate test results and lead to expensive repairs.

Manufacturers will recommend a calibration frequency determined by measurement system stability and will communicate in product inserts the specific criteria for mandatory recalibration of instrument systems. T ese may include the following:

- Instrument maintenance
- Reagent lot change
- Major component replacement
- New software installation

Clinical laboratories must follow CLIA or the manufacturer's requirements for instrument calibration frequency, whichever is most stringent. CLIA requires that laboratories recalibrate an analytical (examination) method at least every 6 months.

Appropriate Methodology

When new methods are introduced, it is important to check the procedure for accuracy and variability. Replicate analyses using control specimens are recommended to check for accuracy and to eliminate factors such as day-to-day variability, reagent variability, and differences between technologists.

Accuracy in Reporting Results and Documentation

Many laboratories have established critical values or the delta check system to monitor individual patient results. T e difference between a patient's present laboratory result and consecutive previous results that exceed a predefined limit is referred to as a Delta check. An abrupt change, high or low, can trigger this computer-based warning system and needs to be investigated before reporting a patient result. Delta checks are investigated by the laboratory internally to rule out errors, for example, mislabeling of a specimen.

Highly abnormal individual test values and significant differences from previous results in the Delta check system alert the technologist to a potential problem. At times, a phone call to the primary care provider may be made by the laboratory technologist to investigate possible preanalytical (preexamination) errors such as:

1. Obtaining specimens from IV lines
2. Specimen processing error
3. Actual changes in a patient's clinical condition

Other quantitative control systems (discussed later) are also used to ensure the quality of test results.