

NINTH EDITION

CLINICAL CHEMISTRY

Principles, Techniques, and Correlations

Michael L. Bishop | Edward P. Fody
Carleen Van Siclen | James March Mistler | Michelle Moy

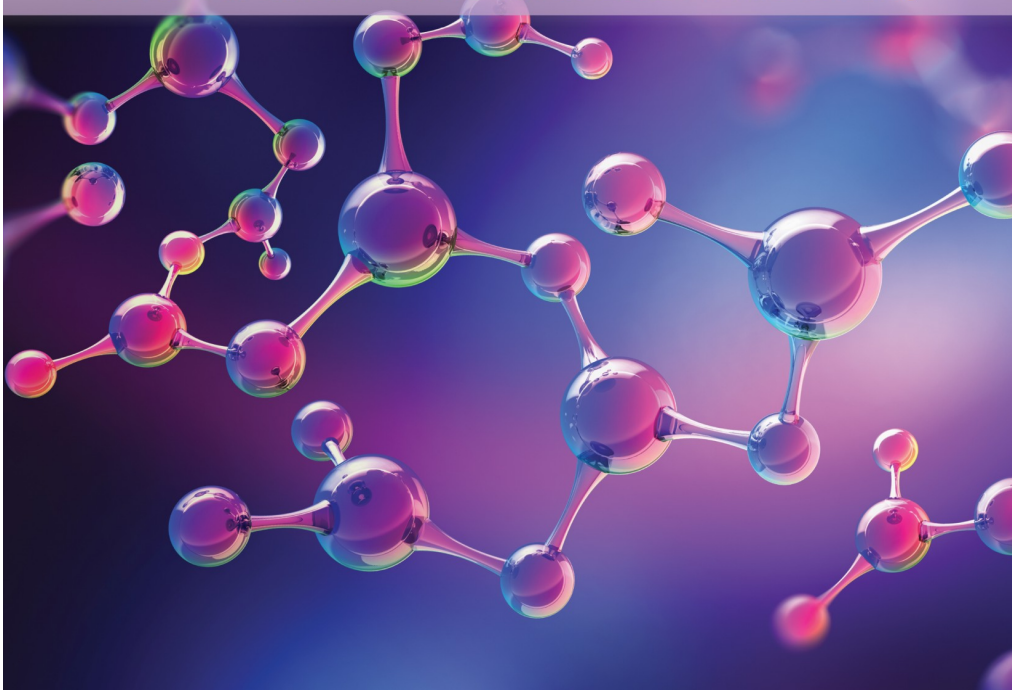


NINTH EDITION

CLINICAL CHEMISTRY

Principles, Techniques, and Correlations

Michael L. Bishop | Edward P. Fody
Carleen Van Sicken | James March Mistler | Michelle Moy



NINTH EDITION

CLINICAL CHEMISTRY

Principles, Techniques, and Correlations

Michael L. Bishop, MS, MLS(ASCP)

Adjunct Faculty, Medical Laboratory Scientist Program, Santa Fe College, Alachua FL
Retired Faculty, Medical Technology Program, Duke University Medical Center, Durham, North Carolina
Retired Program Director and University Department Chair, Medical Laboratory Science
and Medical Laboratory Technician Program, Keiser University, Orlando, Florida

Edward P. Fody, MD

Clinical Professor, Department of Pathology, Microbiology and Immunology, Vanderbilt University School of Medicine,
Nashville, Tennessee
Pathologist, Holland Hospital, Holland, Michigan

Carleen Van Siclen, MS,MLS(ASCP)^{CM},TS(ABB)

Assistant Professor of Laboratory Medicine and Pathology, MCSHS Medical Laboratory Science Program
Department of Laboratory Medicine and Pathology, Mayo Clinic, Jacksonville, Florida

James March Mistler, ABD, MS, MLS(ASCP)^{CM}

Program Director and Fulltime Lecturer, Department of Medical Laboratory Science, University of Massachusetts Dartmouth,
North Dartmouth, Massachusetts

Michelle Moy, MAdEd, MT(ASCP) SC

Assistant Professor of Medical Laboratory Science, Program Director, Biomedical Science, Department of Natural Science
and Mathematics, College of Arts and Sciences, Madonna University, Livonia, Michigan





World Headquarters
Jones & Bartlett Learning
25 Mall Road
Burlington, MA 01803
978-443-5000

Jones & Bartlett Learning books and products are available through most bookstores and online booksellers. To contact Jones & Bartlett Learning directly, call 800-832-0034, fax 978-443-8000, or visit our website, www.jblearning.com.

Substantial discounts on bulk quantities of Jones & Bartlett Learning publications are available to corporations, professional associations, and other qualified organizations. For details and specific discount information, contact the special sales department at Jones & Bartlett Learning via the above contact information or send an email to specialsales@jblearning.com.

Copyright © 2023 by Jones & Bartlett Learning, LLC, an Ascend Learning Company

All rights reserved. No part of the material protected by this copyright may be reproduced or utilized in any form, electronic or mechanical, including photocopying, recording, or by any information storage and retrieval system, without written permission from the copyright owner.

The content, statements, views, and opinions herein are the sole expression of the respective authors and not that of Jones & Bartlett Learning, LLC. Reference herein to any specific commercial product, process, or service by trade name, trademark, manufacturer, or otherwise does not constitute or imply its endorsement or recommendation by Jones & Bartlett Learning, LLC and such reference shall not be used for advertising or product endorsement purposes. All trademarks displayed are the trademarks of the parties noted herein. *Clinical Chemistry: Principles, Techniques, and Correlations, Ninth Edition* is an independent publication and has not been authorized, sponsored, or otherwise approved by the owners of the trademarks or service marks referenced in this product.

There may be images in this book that feature models; these models do not necessarily endorse, represent, or participate in the activities represented in the images. Any screenshots in this product are for educational and instructive purposes only. Any individuals and scenarios featured in the case

studies throughout this product may be real or fictitious but are used for instructional purposes only.

23886-0

Production Credits

Vice President, Product Management: Marisa R. Urbano
Vice President, Content Strategy and Implementation: Christine Emerton
Director of Product Management: Matt Kane
Product Manager: William Lawrensen
Content Strategist: Carol Brewer Guerrero
Content Coordinator: Samantha Gillespie
Director, Project Management and Content Services: Karen Scott
Manager, Project Management: Kristen Rogers
Project Specialist: Daniel Stone
Senior Digital Project Specialist: Angela Dooley
Marketing Manager: Mark Adamiak
Composition: Exela Technologies
Project Management: Exela Technologies
Cover Design: Kristin Parker
Senior Media Development Editor: Troy Liston
Rights & Permissions Manager: John Rusk
Rights Specialist: Rebecca Damon
Rights Specialist: Liz Kincaid
Cover Image (Title Page, Part Opener, Chapter Opener): © Yurchanka
Siarhei/Shutterstock
Printing and Binding: LSC Communications

Library of Congress Cataloging-in-Publication Data

Names: Bishop, Michael L., editor. | Fody, Edward P., editor. | Siclen, Carleen Van, editor. | Mistler, James March, editor. | Moy, Michelle, editor.
Title: Clinical chemistry: principles, techniques, and correlations / [edited by] Michael L. Bishop, Edward P. Fody, Carleen Van Siclen, James March Mistler, Michelle Moy.
Other titles: Clinical chemistry (Bishop)
Description: Ninth edition. | Burlington, MA : Jones & Bartlett Learning, [2023] | Includes bibliographical references and index.
Identifiers: LCCN 2021034082 | ISBN 9781284238860 (paperback)
Subjects: LCSH: Clinical chemistry.
Classification: LCC RB40 .C576 2023 | DDC 616.07/56—dc23
LC record available at <https://lcn.loc.gov/2021034082>

6048

Printed in the United States of America
26 25 24 23 22 10 9 8 7 6 5 4 3 2 1



© Yevhen Vitte/Shutterstock.

Disclaimer

Care has been taken to confirm the accuracy of the information presented and to describe generally accepted practices. However, the authors, editors, and publisher are not responsible for errors or omissions or for any consequences from application of the information in this book and make no warranty, expressed or implied, with respect to the currency, completeness, or accuracy of the contents of the publication. Application of this information in a particular situation remains the professional responsibility of the practitioner; the clinical treatments described and recommended may not be considered absolute and universal recommendations.

The authors, editors, and publisher have exerted every effort to ensure that drug selection and dosage set forth in this text are in accordance with the current recommendations and practice at the time of publication. However, in view of ongoing research, changes in government regulations, and the constant flow of information relating to drug therapy and drug reactions, the reader is urged to check the package insert for each drug for any change in indications and dosage and for added warnings and precautions. This is particularly important when the recommended agent is a new or infrequently employed drug.

Some drugs and medical devices presented in this publication have Health Canada clearance for limited use in restricted research settings. It is the responsibility of the health care provider

to ascertain the Health Canada status of each drug or device planned for use in his or her clinical practice.



© Yevhen Vitte/Shutterstock.

Brief Contents

Foreword
Preface
New to This Edition
Acknowledgments
Contributors
Ancillary Contributors
Reviewers

Part 1 Basic Principles and Practice in Clinical Chemistry

Chapter 1 Basic Principles and Practices of Clinical Chemistry

Chapter 2 Laboratory Safety and Regulations

Chapter 3 Quality Management in the Clinical Laboratory

Chapter 4 Analytic Techniques

Chapter 5 Clinical Chemistry Automation

Part 2 Analytic Procedures and Clinical Correlation

- Chapter 6** Proteins and Heme Derivatives
- Chapter 7** Nonprotein Nitrogen Compounds
- Chapter 8** Enzymes
- Chapter 9** Carbohydrates
- Chapter 10** Lipids and Lipoproteins
- Chapter 11** Electrolytes
- Chapter 12** Blood Gases, pH, and Buffer Systems
- Part 3** Endocrinology and Clinical Correlation
 - Chapter 13** Basic Endocrinology
 - Chapter 14** Thyroid Function
 - Chapter 15** Hypothalamic and Pituitary Function
 - Chapter 16** Adrenal Function
 - Chapter 17** Gonadal Function
 - Chapter 18** Parathyroid Function
- Part 4** Organ Systems and Clinical Correlation
 - Chapter 19** Liver Function
 - Chapter 20** Cardiac Function
 - Chapter 21** Renal Function

Chapter 22 Pancreatic Function

Part 5 Specialty Areas of Clinical Chemistry

Chapter 23 Body Fluid Analysis

Chapter 24 Pregnancy and Prenatal Testing

Chapter 25 Therapeutic Drug Monitoring

Chapter 26 Toxicology

Chapter 27 Trace Elements, Toxic Elements, and Vitamins

Chapter 28 Tumor Markers

Chapter 29 Point-of-Care Testing

Chapter 30 Newborn and Pediatric Clinical Chemistry

Chapter 31 Geriatric Clinical Chemistry
Appendix: Reference Range
Glossary
Index



© Yevhen Vitte/Shutterstock.

Contents

Foreword

Preface

New to This Edition

Acknowledgments

Contributors

Ancillary Contributors

Reviewers

Part 1 Basic Principles and Practice in Clinical Chemistry

Chapter 1 Basic Principles and Practices of Clinical Chemistry

Kathryn Dugan and Elizabeth Warning

Units of Measure

Reagents

Chemicals

Reference Materials

Water Specifications

Solution Properties

Concentration

Colligative Properties

Redox Potential

Conductivity

- pH and Buffers
- Laboratory Equipment
 - Heating Units
 - Glassware and Plasticware
 - Desiccators and Desiccants
 - Balances
 - Centrifuges
- Laboratory Mathematics and Calculations
 - Significant Figures
 - Logarithms
 - Concentration
 - Dilutions
 - Simple Dilutions
 - Serial Dilutions
 - Water of Hydration
 - Graphing and Beer's Law
- Specimen Collection and Handling
 - Types of Samples
 - Sample Processing
 - Sample Variables
 - Chain of Custody
 - Electronic and Paper Reporting of Results

Chapter 2 Laboratory Safety and Regulations

Brandy Greenhill

- Laboratory Safety and Regulations
 - Occupational Safety and Health Act
 - Other Regulations and Guidelines
- Safety Awareness for Clinical Laboratory Personnel
 - Safety Responsibility
 - Signage and Labeling
- Safety Equipment
 - Chemical Fume Hoods and Biosafety Cabinets
 - Chemical Storage Equipment
 - PPE and Hygiene
- Biologic Safety

- General Considerations
- Spills
- Bloodborne Pathogens
- Airborne Pathogens
- Shipping
- Chemical Safety
 - Hazard Communication
 - Safety Data Sheet
 - OSHA Laboratory Standard
 - Toxic Effects from Hazardous Substances
 - Storage and Handling of Chemicals
- Radiation Safety
 - Environmental Protection
 - Personal Protection
 - Nonionizing Radiation
- Fire Safety
 - The Chemistry of Fire
 - Classification of Fires
 - Types and Applications of Fire Extinguishers
- Control of Other Hazards
 - Electrical Hazards
 - Compressed Gas Hazards
 - Cryogenic Materials Hazards
 - Mechanical Hazards
 - Ergonomic Hazards
- Disposal of Hazardous Materials
 - Chemical Waste
 - Radioactive Waste
 - Biohazardous Waste
- Accident Documentation and Investigation

Chapter 3 Quality Management in the Clinical Laboratory

Yun L. Trull, Michael W. Rogers, Cyndy B. Levtzow, Matthew P. A. Henderson, Christopher R. McCudden, and Monte S. Willis

Basic Concepts

Descriptive Statistics: Measures of Center, Spread, and Shape

Measurement of Precision

Descriptive Statistics of Groups of Paired Observations

Measurement of Bias

Inferential Statistics

Quality Control and Quality Improvement

QC Charts

Operation of a QC System

Multi-Rules Rule!

Proficiency Testing

Lean Six Sigma

Quality Assessment

Individual Quality Control Program (IQCP): An Option to Streamline QCP

Reference Range Studies

Establishing Reference Ranges

Determining Whether to Establish or Transfer and Verify Reference Ranges

Data Analysis to Establish a Reference Range

Data Analysis to Transfer and Verify a Reference Range

Method Evaluation

Regulatory Aspects of Method Evaluation

Allowable Analytical Error

Method Evaluation Acceptance Criteria

Diagnostic Efficiency

Measures of Diagnostic Efficiency

Chapter 4 Analytic Techniques

Karen K. Apolloni

Spectrophotometry

Beer's Law

Spectrophotometric Instruments

Components of a Spectrophotometer

Spectrophotometer Quality Assurance

Atomic Absorption Spectrophotometry

Fluorometry

- Fluorometry Instrumentation
- Fluorescence Polarization
- Advantages and Disadvantages of Fluorometry
- Chemiluminescence
- Turbidimetry
- Nephelometry
- Laser Applications

Electrochemistry

- Galvanic and Electrolytic Cells
- Half-Cells
- Ion-Selective Electrodes
- pH Electrodes
- Gas-Sensing Electrodes
- Enzyme Electrodes
- Coulometric Titration
- Anodic Stripping Voltammetry

Electrophoresis

- Procedure
- Support Materials
- Treatment and Application of Sample
- Detection and Quantitation
- Electroendosmosis
- Isoelectric Focusing
- Immunofixation Electrophoresis
- Capillary Electrophoresis
- Two-Dimensional Electrophoresis

Osmometry

- Freezing Point Osmometer

Newer Optical Techniques

Chromatography

- Modes of Separation
- Chromatographic Procedures
- High-Performance Liquid Chromatography
- Gas Chromatography

Mass Spectrometry

- Sample Introduction and Ionization

Mass Spectrometer Analyzer
Detector
Applications of MS in the Clinical Laboratory
Small Molecule Analysis
Mass Spectrometry in Proteomics and Pathogen
Identification
Mass Spectrometry at the Point of Care

Chapter 5 Clinical Chemistry Automation

Nikola A. Baumann and Brooke M. Katzman

History and Evolution of Automated Analyzers
Driving Forces and Benefits of Automation
Steps in Automated Analysis
Specimen Preparation and Identification
Specimen Measurement and Delivery
Reagent Systems and Delivery
Chemical Reaction Phase
Measurement Phase
Signal Processing and Data Handling
Additional Considerations for Automated Immunoassays
Immunoassay Basics
Turbidimetry and Nephelometry
Labeled Immunoassays
Total Laboratory Automation
Pre-analytic Phase
Analytic Phase
Post-analytic Phase
Future Trends in Automation

Part 2 Analytic Procedures and Clinical Correlation

Chapter 6 Proteins and Heme Derivatives

Takara L. Blamires and Kristina Jackson Behan

Amino Acids
Overview
Basic Structure

- Metabolism
- Classification
- Aminoacidopathies
- Methods of Analysis

Proteins

- Overview
- Basic Structure
- General Chemical Properties
- Synthesis
- Catabolism and Nitrogen Balance
- Hormonal Regulation of Protein Metabolism
- Classification

Plasma Proteins

- Prealbumin
- Albumin
- Globulins

Other Proteins of Clinical Significance

- Troponin
- Natriuretic Peptides
- Fibronectin
- Cross-Linked C-Telopeptide
- Cystatin C

Plasma Total Protein Abnormalities

- Hypoproteinemia
- Hyperproteinemia

Methods of Analysis

- Sample Requirements
- Total Protein
- Albumin
- Immunochemical Assays
- Electrophoresis

Proteins in Other Body Fluids

- Urine
- Cerebrospinal Fluid

Hemoglobin

- Synthesis and Degradation of Hemoglobin

Myoglobin

Heme

Synthesis of Heme

Disorders of Heme Biosynthesis

Clinical Application

Analytical Methods

Chapter 7 Nonprotein Nitrogen Compounds

Shawn H.W. Luby

Urea

Biochemistry

Clinical Application

Analytical Methods

Pathophysiology

Uric Acid

Biochemistry

Clinical Application

Analytical Methods

Pathophysiology

Creatinine/Creatine

Biochemistry

Clinical Application

Analytical Methods

Pathophysiology

Ammonia

Biochemistry

Clinical Application

Analytical Methods

Pathophysiology

Chapter 8 Enzymes

Donna J. Spannaus-Martin

General Properties and Definitions

Enzyme Classification and Nomenclature

Enzyme Kinetics

Enzyme Catalysis

- Factors That Influence Enzymatic Reactions
- Measurement of Enzyme Activity
- Calculation of Enzyme Activity
- Measurement of Enzyme Mass
- Enzymes as Reagents
- Enzymes of Clinical Significance
 - Creatine Kinase
 - Lactate Dehydrogenase
 - Aspartate Aminotransferase
 - Alanine Aminotransferase
 - Alkaline Phosphatase
 - Acid Phosphatase
 - γ -Glutamyltransferase
 - 5'-Nucleotidase
 - Amylase
 - Lipase
 - Glucose-6-Phosphate Dehydrogenase
 - Macroenzymes
 - Drug-Metabolizing Enzymes

Chapter 9 Carbohydrates

Vicki S. Freeman

- General Description of Carbohydrates
 - Classification of Carbohydrates
 - Stereoisomers
 - Monosaccharides, Disaccharides, and Polysaccharides
 - Chemical Properties of Carbohydrates
 - Glucose Metabolism
 - Fate of Glucose
 - Regulation of Carbohydrate Metabolism
- Hyperglycemia
 - Diabetes Mellitus
 - Pathophysiology of Diabetes Mellitus
 - Criteria for Testing for Prediabetes and Diabetes
 - Criteria for the Diagnosis of Diabetes Mellitus
 - Criteria for the Testing and Diagnosis of GDM

Hypoglycemia

Genetic Defects in Carbohydrate Metabolism

Role of the Laboratory in Differential Diagnosis and Management of Patients with Glucose Metabolic Alterations

Methods of Glucose Measurement

Self-Monitoring of Blood Glucose

Glucose Tolerance and 2-Hour Postprandial Tests

Glycosylated Hemoglobin/HbA1c

Ketones

Albuminuria

Islet Autoantibody, Insulin Testing and C-Peptide Testing

Chapter 10 Lipids and Lipoproteins

Kathleen M. Kenwright

Lipid Chemistry

Fatty Acids

Triglycerides

Phospholipids

Cholesterol

General Lipoprotein Structure

Chylomicrons

Very-Low-Density Lipoprotein

Intermediate-Density Lipoproteins

Low-Density Lipoproteins

Lipoprotein (a)

High-Density Lipoproteins

Lipoprotein X

Lipoprotein Physiology and Metabolism

Lipid Absorption

Exogenous Pathway

Endogenous Pathway

Reverse Cholesterol Transport Pathway

Lipid and Lipoprotein Population Distributions

National Cholesterol Education Program

Dyslipidemia and Children

National Heart, Lung, and Blood Institute

Diagnosis and Treatment of Lipid Disorders

Arteriosclerosis

Hyperlipoproteinemia

Hypercholesterolemia

PCSK9

Hypertriglyceridemia

Combined Hyperlipidemia

Lp(a) Elevation

Non-HDL Cholesterol

Hypobetalipoproteinemia

Hypoalphalipoproteinemia

Lipid and Lipoprotein Analyses

Lipid Measurement

Cholesterol Measurement

Triglyceride Measurement

Lipoprotein Methods

HDL Methods

LDL Methods

Apolipoprotein Methods

Phospholipid Measurement

Fatty Acid Measurement

Standardization of Lipid and Lipoprotein Assays

Precision

Accuracy

Matrix Interactions

CDC Cholesterol Reference Method Laboratory Network

Analytic Performance Goals

Quality Control

Specimen Collection

Chapter 11 Electrolytes

James March Mistler

Water

Osmolality

The Electrolytes

Sodium

- Potassium
- Chloride
- Bicarbonate
- Calcium
- Magnesium
- Phosphate
- Lactate
- Anion Gap
- Electrolytes and Renal Function

Chapter 12 Blood Gases, pH, and Buffer Systems

Kyle B. Riding

- Acid–Base Balance

 - Maintenance of H⁺

 - Buffer Systems: Regulation of H⁺ and the Henderson-Hasselbalch Equation

 - Regulation of Acid–Base Balance: Lungs and Kidneys (Transport of Carbon Dioxide)

- Assessment of Acid–Base Homeostasis

 - The Bicarbonate Buffering System

 - Acid–Base Disorders: Acidosis and Alkalosis

 - Determining Patient Acid–Base Status

- Oxygen and Gas Exchange

 - Oxygen and Carbon Dioxide

 - Oxygen Transport

 - Assessment of a Patient's Oxygen Status

 - Hemoglobin–Oxygen Dissociation

- Measurement

 - Blood Gas Analyzers: pH, $p\text{CO}_2$, and $p\text{O}_2$

 - Measurement of $p\text{O}_2$

 - Measurement of pH and $p\text{CO}_2$

 - Types of Sensors

 - Calibration

 - Correction for Temperature

 - Calculated Parameters

Spectrophotometric Determination of Oxygen Saturation
(Co-Oximetry)

Quality Assurance

Preanalytic Considerations

Analytic Assessments: Quality Control and Proficiency
Testing

Part 3 Endocrinology and Clinical Correlation

Chapter 13 Basic Endocrinology

Scott Moore

Hormone Classification

Amine

Peptide

Protein

Glycoprotein

Steroid

Fatty Acid

Introduction to Hormones

Growth Hormone (GH)

Adrenocorticotrophic Hormone (ACTH) and the Adrenal
Cortical Hormones

Follicle Stimulating Hormone and Luteinizing Hormone

Prolactin (PRL)

Androgens

Progesterone

Estrogens/Estradiol/Estriol

Catecholamines

Thyroid Hormone (T_3 , T_4) and Thyroid Stimulating
Hormone (TSH)

Posterior Pituitary Hormones

Calcitonin and Procalcitonin

Parathyroid Hormone (PTH)

Insulin

Glucagon

Gastrin and Secretin

Human Chorionic Gonadotropin (hCG)

- Serotonin/5-hydroxyindolacetic Acid (5-HIAA)
- Hormone Metabolism
 - Alcohol Consumption
 - Adrenal Steroid Hormone Synthesis
- Mechanisms of Elimination
- Hormone Transport
 - Solubility
 - Carrier Proteins
 - Micelles
- Feedback Mechanisms
 - Negative Feedback Mechanisms
 - Positive Feedback Mechanisms
- Primary, Secondary, and Tertiary Disorders
- Other Factors That Affect Hormone Levels
 - Emotional Stress
 - Time of Day
 - Menstrual Cycle
 - Menopause
 - Food Intake/Diet
 - Drugs

Chapter 14 Thyroid Function

Yukari Nishizawa-Brennen

- The Thyroid
 - Thyroid Anatomy and Development
 - Thyroid Hormone Synthesis
 - Protein Binding of Thyroid Hormone
 - Control of Thyroid Function
 - Actions of Thyroid Hormones
- Tests for Thyroid Function
 - Thyroid-Stimulating Hormone
 - Thyroxine (T_4)
 - Triiodothyronine (T_3)
 - Free Thyroxine (FT_4)
 - Free Triiodothyronine (FT_3)
 - Thyroglobulin Antibody

- Thyroperoxidase Antibody
- Thyrotropin Receptor Antibody
- Other Tools for Thyroid Evaluation
 - Nuclear Medicine Evaluation
 - Thyroid Ultrasound
 - Fine-Needle Aspiration
- Disorders of the Thyroid
 - Hypothyroidism
 - Thyrotoxicosis
 - Hyperthyroidism
 - Toxic Adenoma and Multinodular Goiter
- Drug-Induced Thyroid Dysfunction
 - Amiodarone-Induced Thyroid Disease
- Subacute Thyroiditis
- Nonthyroidal Illness
- Thyroid Nodules

Chapter 15 Hypothalamic and Pituitary Function

Stephanie L. Jacobson

- Embryology and Anatomy
- Functional Aspects of the Hypothalamic–Hypophyseal Unit
- Pituitary Tumors
- Hypophysiotropic or Hypothalamic Hormones
- Anterior Pituitary Hormones
- Growth Hormone
 - Actions of GH
 - Testing
 - GH Excess
 - GH Deficiency
- Prolactin
 - Prolactinoma
 - Other Causes of Hyperprolactinemia
 - Clinical Evaluation of Hyperprolactinemia
 - Management of Prolactinoma
 - Idiopathic Galactorrhea
- Hypopituitarism

- Etiology of Hypopituitarism
- Treatment of Panhypopituitarism
- Posterior Pituitary Hormones
 - Oxytocin
 - Arginine Vasopressin

Chapter 16 Adrenal Function

Stephanie L. Jacobson

- Embryology and Anatomy
- The Adrenal Cortex
 - Glucocorticoid Physiology
 - Cortex Steroidogenesis
 - Congenital Adrenal Hyperplasia
- Primary Aldosteronism
 - Etiology
 - Diagnosis
 - Treatment
- Adrenal Insufficiency
 - Symptoms
 - Diagnosis
 - Treatment
 - Isolated Hypoaldosteronism
- Hypercortisolism (Cushing's Syndrome)
 - Etiology
 - Diagnosis
 - Treatment
- Adrenal Androgens
 - Androgen Excess
 - Diagnosis
 - Treatment
- The Adrenal Medulla
 - Embryology
 - Biosynthesis, Storage, and Secretion of Catecholamines
 - Metabolism and Excretion of Catecholamines
- Pheochromocytoma and Paraganglioma
 - Epidemiology

Clinical Presentation
Diagnosis
Result Interpretation
Treatment
Adrenal Incidentaloma

Chapter 17 Gonadal Function

Jane R. Semler

The Testes

Functional Anatomy of the Male Reproductive Tract
Physiology of the Testicles
Disorders of Sexual Development and Testicular Hypofunction
Diagnosis of Hypogonadism
Testosterone Replacement Therapy
Monitoring Testosterone Replacement Therapy

The Ovaries

Early Ovarian Development
Functional Anatomy of the Ovaries
Hormonal Production by the Ovaries
The Menstrual Cycle
Hormonal Control of Ovulation
Pubertal Development in the Female
Precocious Sexual Development
Menstrual Cycle Abnormalities
Evaluation of Female Infertility
Hirsutism
Estrogen Replacement Therapy

Chapter 18 Parathyroid Function

Rebecca Silva

Parathyroid Glands

Parathyroid Hormone
Vitamin D

Effects of the Parathyroid Hormone
GI Regulation

- Role of Kidneys
- Bone Physiology
- Parathyroid Disorders
 - Primary Hyperparathyroidism
 - Secondary Hyperparathyroidism
 - Secondary and Tertiary Hyperparathyroidism in Renal Failure
 - Familial Hypocalciuric Hypercalcemia
- Hyperthyroidism
- Addison's Disease
- Medications That Cause Hypercalcemia
- Hypervitaminosis
- Parathyroid Hormone–related Protein
- Hypoparathyroidism
- Metabolic Bone Diseases
 - Rickets and Osteomalacia
 - Osteoporosis

Part 4 Organ Systems and Clinical Correlation

Chapter 19 Liver Function

Janelle M. Chiasera

- Anatomy
 - Gross Anatomy
 - Microscopic Anatomy
- Biochemical Functions
 - Excretory and Secretory Functions
 - Metabolism
 - Detoxification and Drug Metabolism
- Liver Function Alterations During Disease
 - Jaundice
 - Cirrhosis
 - Tumors
 - Reye's Syndrome
 - Drug- and Alcohol-Related Disorders
- Assessment of Liver Function/Liver Function Tests

Bilirubin

Methods

Urobilinogen in Urine and Feces

Serum Bile Acids

Enzymes

Tests Measuring Hepatic Synthetic Ability

Tests Measuring Nitrogen Metabolism

Hepatitis

Chapter 20 Cardiac Function

Teresa A. Mortier

Pathophysiology of Atherosclerosis

Cardiac Ischemia, Angina, and Heart Attacks

Markers of Cardiac Damage

Initial Markers of Cardiac Damage

Cardiac Troponins

Myoglobin

Cardiac Injury

Cardiac Biomarkers in Heart Failure

Diagnosis and Risk Stratification of Heart Failure

Cardiac Troponins

Markers of Coronary Heart Disease Risk and Plaque

Instability

C-Reactive Protein

Homocysteine

Markers of Pulmonary Embolism

Use of d-Dimer Detection in PE

Value of Assaying Troponin and BNP in Acute PE

Coronary Heart Disease

Chapter 21 Renal Function

Peter O'Brien

Renal Anatomy

Renal Physiology

Glomerular Filtration

Tubular Function

Elimination of Nonprotein Nitrogen Compounds
Water, Electrolyte, and Acid–Base Homeostasis
Endocrine Function

Analytic Procedures

Creatinine Clearance

Estimated GFR

Cystatin C

β_2 -Microglobulin

Myoglobin

Albuminuria

Neutrophil Gelatinase–Associated Lipocalin

NephroCheck

Urinalysis

Pathophysiology

Glomerular Diseases

Tubular Diseases

Urinary Tract Infection/Obstruction

Renal Calculi

Renal Failure

Chapter 22 Pancreatic Function

Gerald D. Redwine, John E. Lee Sang, and Amanda Rivera-Begeman

Physiology of Pancreatic Function

Diseases of the Pancreas

Tests of Pancreatic Function

Cholecystokinin (CCK) Test

Fecal Fat Analysis

Fecal Enzymes

Sweat Electrolyte Testing

Serum Enzymes

Tests of Gastric Secretion and Intestinal Function

Part 5 Specialty Areas of Clinical Chemistry

Chapter 23 Body Fluid Analysis

Kyle B. Riding

- Cerebrospinal Fluid
- Serous Fluids
 - Pleural Fluid
 - Pericardial Fluid
 - Peritoneal Fluid
- Amniotic Fluid
 - Hemolytic Disease of the Fetus and Newborn
 - Neural Tube Defects
 - Fetal Lung Maturity
 - Phosphatidylglycerol
 - Lamellar Body Counts
- Sweat
- Synovial Fluid

Chapter 24 Pregnancy and Prenatal Testing

Heather L. Phillips and Michelle R. Campbell

- Pregnancy
 - Conception and Embryonic Development
 - Fetal Development
 - Delivery
- Transformation During Pregnancy
 - Plasma Volume Increase
 - Renin–Angiotensin–Aldosterone System
 - Natural Decreases in Analytes
 - Upregulation of Hormones and Steroids
 - Increased Glomerular Filtration Rate
 - Hyperventilation
 - Endocrine
 - Cholesterols
 - Immune System
 - Neuroactive Hormones
- Analytes for Maternal and Fetal Health Assessment
 - Human Chorionic Gonadotropin
 - α -Fetoprotein (AFP)
 - Fetal Amniotic Fluid α -Fetoprotein
 - Unconjugated Estriol

- Inhibin A
- The Triple and Quadruple Screen Test
- Acetylcholinesterase
- Pregnancy Associated Plasma Protein A (PAPP-A)
- Progesterone
- Glucose
- Fetal Fibronectin
- Common Diseases Associated with the Developing Fetus
 - Neural Tube Defects
 - Down Syndrome
 - Trisomy 18
 - Isoimmunization
 - Preterm Delivery
- Common Diseases Associated with the Mother and Pregnancy
 - Preeclampsia
 - Hyperemesis Gravidarum
 - Ectopic Pregnancy
 - Analyte Deficiency
 - Other Clinical Impairments

Chapter 25 Therapeutic Drug Monitoring

Jie Gao and Floyd Josephat

- Pharmacokinetics
- Routes of Administration
- Drug Absorption
- Drug Distribution
- Free Versus Bound Drugs
- Drug Metabolism
- Drug Elimination
 - Elimination Example
- Pharmacodynamics
- Specimen Collection
- Pharmacogenomics
- Cardioactive Drugs
 - Digoxin

Quinidine

Procainamide and *N*-acetylprocainamide

Disopyramide

Antibiotics

Aminoglycosides

Gentamicin

Tobramycin

Amikacin

Vancomycin

Antiepileptic Drugs

Primidone

Phenobarbital

Phenytoin and Free Phenytoin

Valproic Acid

Carbamazepine

Ethosuximide

Felbamate

Gabapentin

Lamotrigine

Levetiracetam

Oxcarbazepine

Tiagabine

Topiramate

Zonisamide

Psychoactive Drugs

Lithium

Tricyclic Antidepressants

Clozapine

Olanzapine

Immunosuppressive Drugs

Cyclosporine

Tacrolimus

Sirolimus

Everolimus

Mycophenolic Acid

Antineoplastics

Methotrexate
Bronchodilators
Theophylline

Chapter 26 Toxicology

Christopher R. Swartz

Xenobiotics, Poisons, and Toxins
Routes of Exposure
Dose–Response Relationship
 Acute and Chronic Toxicity
Analysis of Toxic Agents
Toxicology of Specific Agents
 Alcohols
 Carbon Monoxide
 Caustic Agents
 Cyanide
 Metals and Metalloids
 Pesticides
Toxicology of Therapeutic Drugs
 Salicylates
 Acetaminophen
Toxicology of Drugs of Abuse
 Amphetamines
 Sedatives–Hypnotics
 Barbiturates
 Benzodiazepines
 Cannabinoids: Tetrahydrocannabinol (THC)
 Cocaine
 Opioids
 Tricyclic Antidepressants
 Methylenedioxymethamphetamine
 Phencyclidine
 Anabolic Steroids

Chapter 27 Trace Elements, Toxic Elements, and Vitamins

Michelle R. Campbell

Trace and Toxic Elements

Instrumentation and Methods

Aluminum

Arsenic

Cadmium

Chromium

Copper

Iron

Lead

Manganese

Mercury

Molybdenum

Selenium

Zinc

Vitamins

Overview

Fat-Soluble Vitamins

Water-Soluble Vitamins

Chapter 28 Tumor Markers

Carleen Van Siclen

Types of Tumor Markers

Applications of Tumor Marker Detection

Screening and Risk Assessment

Prognosis

Monitoring Effectiveness of Therapy and Disease
Recurrence

Laboratory Considerations for Tumor Marker Measurement

Immunoassays

High-Performance Liquid Chromatography

Immunohistochemistry and Immunofluorescence

Enzyme Assays

Tumor Marker Tests

α -Fetoprotein

Cancer Antigen 125 (CA-125)

Carcinoembryonic Antigen (CEA)

Human Chorionic Gonadotropin (hCG)
Prostate-Specific Antigen
Cancer Antigen 15-3
Carbohydrate Antigen 19-9 (CA 19-9)
Immunoglobulin Free Light Chains
Human Epididymis Protein 4 (HE4)
Neuron-Specific Enolase (NSE)

Chapter 29 Point-of-Care Testing

Heather Blalock McNasby

Laboratory Regulations
Accreditation
POCT Complexity
Implementation
Establishing Need
POCT Implementation Protocol
Personnel Requirements
Quality Management
Accuracy Requirements
QC and Proficiency Testing
POC Applications
Informatics and POCT

Chapter 30 Newborn and Pediatric Clinical Chemistry

Khushbu Patel and Tracey G. Polsky

Developmental Changes from Neonate to Adult
Respiration and Circulation
Growth
Organ Development
Problems of Prematurity and Immaturity
Pediatric Sample Collection and Handling
Phlebotomy
Preanalytic Concerns
Choice of Analyzer
Point-of-Care Analysis in Pediatrics
Turnaround Time

- Evaluation of POCT Devices
 - Device Limitations for Pediatric Use
- Regulation of Blood Gases and pH in Neonates and Infants
 - Blood Gas and Acid–Base Measurement
- Regulation of Electrolytes and Water: Renal Function
 - Disorders Affecting Electrolytes and Water Balance
- Development of Liver Function
 - Physiologic Jaundice
 - Energy Metabolism
 - Diabetes
 - Nitrogen Metabolism
 - Nitrogenous End Products as Markers of Renal Function
 - Liver Function Tests
- Calcium and Bone Metabolism in Pediatrics
 - Hypocalcemia and Hypercalcemia
- Endocrine Function in Pediatrics
 - Hormone Secretion
 - Hypothalamic–Pituitary–Thyroid System
 - Hypothalamic–Pituitary–Adrenal Cortex System
 - Growth Factors
 - Endocrine Control of Sexual Maturation
- Development of the Immune System
 - Basic Concepts of Immunity
 - Components of the Immune System
 - Neonatal and Infant Antibody Production
 - Immunity Disorders
- Genetic Diseases
 - Cystic Fibrosis
 - Newborn Screening for Whole Populations
 - Diagnosis of Metabolic Disease in the Clinical Setting
- Drug Metabolism and Pharmacokinetics
 - Therapeutic Drug Monitoring
 - Toxicologic Issues in Pediatric Clinical Chemistry

Chapter 31 Geriatric Clinical Chemistry

Laura M. Hickes and J. Marvin McBride

The Aging of America

Aging and Medical Science

General Physiologic Changes with Aging

Muscle

Bone

Gastrointestinal System

Kidney/Urinary System

Immune System

Endocrine System

Sex Hormones

Glucose Metabolism

Effects of Age on Laboratory Testing

Muscle

Bone

Gastrointestinal System

Urinary System

Immune System

Endocrine System

Sex Hormones

Glucose Metabolism

Establishing Reference Ranges for the Elderly

Preanalytical Variables Unique to Geriatric Patients

Diseases Prevalent in the Elderly

Age-Associated Changes in Drug Metabolism

Absorption

Distribution

Metabolism

Elimination

Atypical Presentations of Common Diseases

Geriatric Syndromes

The Impact of Exercise and Nutrition on Chemistry Results
in the Geriatric Population

Appendix: Reference Range

Glossary

Index

To all Clinical Laboratory practitioners, educators and healthcare professionals for their previous and continuing extraordinary commitment, service and professionalism during the Covid-19 pandemic.

MLB, EPF, CVS, JMM, MM

In memory of my mother and father, Betty Beck Bishop and William Stewart Bishop, Sr for support, guidance and encouragement.

To Sheila, Chris and Carson for their support, patience and inspiration.

MLB

To Nancy, my wife, for continuing support and dedication.

EPF

To Gary, my husband, for his support of my professional goals and to all the laboratory professionals, including my students, who have contributed to my knowledge and passion for lifelong learning.

CVS

To my husband, Keith, for everything.

JMM

**To my college mentors: Pete Gebauer and Herb
Miller I thank you for believing in me.**

In memory of my mother SG (1940-2021)

MM



© Oxygen/Moment/Getty Images.

Foreword

Many years ago, I wrote the Foreword to some earlier editions of this text. A 9th edition seems like an unbelievably long time until I reflect that this year is the 40th anniversary of the paper that introduced a multi-rule Shewhart control chart,¹ more commonly known as “Westgard Rules.” That paper was written early in my career, but now in my retirement we have updated that approach to provide “Westgard Sigma Rules” in order to customize the QC design on the basis of the quality required by a test and the Sigma performance observed for a method.² Even well established “standard” laboratory practices need periodic review and updating to keep current with the improvements in testing processes. Likewise, this 9th edition of the standard clinical chemistry text reflects the latest knowledge and improvements for laboratory science. That is a testament to the authors’ commitment and dedication to providing an up-to-date knowledge base for the professionals in clinical laboratory science.

I am writing this on the one-year anniversary of the declaration of a global pandemic, a year during which over half a million Americans died of COVID19. This pandemic has revealed the importance of laboratory testing for the health of the nation. Laboratory testing has often been viewed as a behind-the-scenes service in healthcare. During the pandemic, laboratory testing has been center stage as an essential service for assessing the state

of disease, diagnosing those with infection, monitoring those under treatment, and monitoring the immunity and the health of the community.

Laboratory scientists were on the front line in introducing new diagnostic tests, validating their performance, and implementing testing in many diverse settings, including central laboratories, clinic laboratories, and point-of-care settings, including drive-through testing services. Understanding the performance of qualitative tests brought new importance to ideas such as clinical sensitivity, clinical specificity, and predictive value of laboratory tests. That also meant new protocols for validating new tests to characterize test performance, including adaptations for the nature of molecular tests, such as the real-time Reverse Transcription Polymerase Chain Reaction (rRT-PCR) methods that were critical in the early diagnosis and management of patients. Antibody tests flooded the market and required care and attention by laboratories, especially during the early phases when the FDA exercised very limited control of the companies introducing the new tests. Antigen tests emerged later and more slowly, but were critical for providing more widespread diagnostic testing. All in all, this year provided the lessons of a lifetime and demonstrated the importance of what you will be learning in your studies.

This new edition of *Clinical Chemistry: Principles, Techniques, and Correlations continues* continues its mission of addressing the formal education needs of students in clinical laboratory science, as well as the ongoing needs of professionals in the field. It facilitates the educational process by identifying the learning objectives, focusing on key concepts and ideas, and applying the theory through case studies. It covers the basics of laboratory testing, as well as many special areas of testing. And it is still possible to carry this text with you to class, to the laboratory, to the office, or home to study!

Having personally worked with some of the editors and contributors, I know they have high standards both in the laboratory and in the classroom. Their interests and background provide an excellent balance between the academic and the

practical, ensuring that students are exposed to a well-developed base of knowledge that has been carefully refined by experience.

For the many students for whom this book is intended, let me offer some advice from my close friend and mentor, Hagar the Horrible. It seems his young Viking son was embarking on a voyage to the real world of work. Needing advice, he asked “How do I get to the top?” Hagar’s response, “You have to start at the bottom and work your way up.” After pondering this for a moment, his son then asked, “How do I get to the bottom?” Hagar replied, “You have to know somebody.” The people you need to know are the authors of this book, as well as the instructors in your courses and your bench teachers in the laboratory. You need to seek them out to profit from their learning and experiences. They are the professionals who know the state of laboratory practice, possess the current knowledge of the field, and are dedicated to helping you become a successful laboratory scientist.

—James O. Westgard
Madison, WI

REFERENCES

1. Westgard JO, Barry PL, Hunt MR, Groth T. A multi-rule Shewhart chart for quality control in clinical chemistry. *Clin Chem* 1981;27:493-501.
2. Westgard JO, Westgard SA. Establishing evidence-based statistical quality control practices. *Am J Clin Pathol* 2019;151:364-370.



© Oxygen/Moment/Getty Images.

Preface

The events with the worldwide pandemic have placed an extraordinary burden on our health care system. Facing staffing, PPE, and diagnostic supply shortages, healthcare professionals stepped up with effort, critical process evaluation, and extraordinary dedication to providing quality patient care with compassion and empathy. Initially, the nightly news became a presentation of CDC guidelines, mask mandates, business shutdowns, travel restrictions, metrics, trends, positivity rates, hospitalization and death statistics. Months later, the metrics related to more positive information—initial results of vaccine clinical trials, emergency use authorizations, vaccine shipments and “shots in arms.” Through it all, the healthcare system functioned as effectively as possible due to individual efforts and interdisciplinary teamwork. Healthcare professionals have improved communication with each other as well as with the patient and their families. Collaborative efforts between healthcare disciplines are emerging across the patient care spectrum landscape.

Since the initial idea for this textbook was discussed in a meeting of the Biochemistry/Urinalysis section of ASMT (now ASCLS) in the late 1970s, the only constant has been change and the never wavering commitment of the clinical laboratory professionals. Now almost 45 years since the initiation of this

effort, the editors have had the privilege of completing the ninth edition with another diverse team of dedicated clinical laboratory professionals. In this era of focusing on metrics, the editors would like to share the following information. The 401 contributions in the 9 editions and supporting material represent 115 clinical laboratory science education programs, 83 clinical laboratories, 28 medical device companies, 4 government agencies, and 3 professional societies representing 40 states and territories. One hundred and sixty-four contributors were clinical laboratory scientists with advanced degrees. These contributors have produced 289 chapters citing 12,054 references for a total of 5,708 pages that included 2,158 figures and 691 case studies. With today's global focus, the previous editions of the text have been translated into at least six languages. By definition, a profession is a calling requiring specialized knowledge and intensive academic preparation to define its scope of practice and produce its own literature. The Clinical Laboratory Science professions has evolved significantly over these past four and a half decades.

Clinical chemistry continues to be one of the most rapidly advancing areas of laboratory medicine. New technologies and analytical techniques have been introduced, with a dramatic impact on the practice of clinical chemistry and laboratory medicine. In addition, the healthcare system itself is rapidly changing. There is ever increasing emphasis on improving the quality of patient care, individualized medicine, patient outcomes, financial responsibility, and total quality management. Now, more than ever, clinical laboratorians need to be concerned with disease correlations, result interpretations, problem solving, quality assurance, and cost-effectiveness. Laboratory professionals need to know not only the *how* of tests but more importantly be able to communicate the *what, why, and when* to the patient and the healthcare team. The editors of *Clinical Chemistry: Principles, Techniques, and Correlations* have designed the ninth edition to be an even more valuable resource to both students and practitioners.

The ninth edition of *Clinical Chemistry: Principles, Techniques, and Correlations* is comprehensive, up-to-date, and easy to

understand for students and at all entry levels. It is also intended to be a practically organized resource for both instructors and practitioners. The editors have tried to maintain the book's readability and further improve its content while rearranging content and focusing on the scaffolding provided by the ASCLS MLT and MLS Entry Level Curriculum and the ASCP BOC guidelines. Because clinical laboratorians use their interpretative and analytic skills in the practice of clinical chemistry, an effort has been made to maintain an appropriate balance between analytic principles, techniques, and the correlation of results with disease states.

In this edition, the editors have maintained features in response to requests from our readers, students, instructors, and practitioners. Ancillary materials have been updated and expanded. Chapters now include current, more frequently encountered case studies modelled after the nursing PICOT initiative in a structured unfolding style. To provide a thorough, up-to-date study of clinical chemistry, all chapters have been updated and reviewed by professionals who practice clinical chemistry and laboratory medicine on a daily basis. The basic principles of the analytic procedures discussed in the chapters reflect the most recent or commonly performed techniques in the clinical chemistry laboratory. Detailed procedures have been omitted because of the variety of equipment and commercial kits used in today's clinical laboratories. Instrument manuals and analyte package inserts are the most reliable reference for detailed instructions on current analytic procedures. All chapter material has been updated, improved, and rearranged for better continuity and readability. The **Navigate 2 Advantage** digital access contains additional case studies, review questions, teaching resources, teaching tips, additional references, and teaching aids for instructors and students; it is included with the purchase of this textbook, and is available for separate purchase from the publisher.

One last piece of advice to make you successful in the field of clinical laboratory science:

Work with compassion, empathy, and professionalism until you no longer have to introduce yourself.*

Michael L. Bishop
Edward P. Fody
Carleen Van Sicen
James March Mistler
Michelle Moy

*Modified from Harvey Specter in *Suits*.



© Oxygen/Moment/Getty Images.

New to This Edition

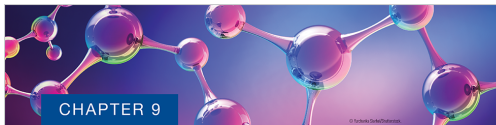
Medical laboratory Science students need a strong foundation in applied chemistry to meet the requirements of certifying bodies and accreditation organizations that ensure students are prepared for employment.

This textbook provides clear explanations that balance analytic principles, techniques, and correlation of results with coverage of disease states, helping students develop interpretive and analytic skills for their future careers.

Updates to this edition include:

- Chapter content based on the ASCLS Entry Level Curriculum and current ASCP Content Guidelines
- Reorganization of chapter order to reflect clinical chemistry flow in most courses today.
- Over 60 unique case studies that evolve throughout the chapters
- NEW Chapter 13: Basic Endocrinology
- NEW Chapter 24: Pregnancy and Prenatal Testing
- Reference range table is included as an Appendix in the printed book and online.

A map of how the textbook correlates to the ASCLS curriculum and ASCP guidelines is provided as an instructor resource.



CHAPTER 9

Carbohydrates

Vicki S. Freeman

CHAPTER OUTLINE

General Description of Carbohydrates

- Classification of Carbohydrates
- Stereoisomers
- Monosaccharides, Disaccharides, and Polysaccharides
- Chemical Properties of Carbohydrates
- Glucose Metabolism
- Fate of Glucose
- Regulation of Carbohydrate Metabolism

Hyperglycemia

- Diabetes Mellitus
- Pathophysiology of Diabetes Mellitus
- Criteria for Testing for Prediabetes and Diabetes
- Criteria for the Diagnosis of Diabetes Mellitus
- Criteria for the Testing and Diagnosis of GDM

KEY TERMS

| | | |
|--------------------------|-------------------------|-----|
| Albuminuria | Glycogen | Hy |
| Carbohydrates | Glycogenesis | Int |
| Diabetes mellitus | Glycogenolysis | Ke |
| Disaccharides | Glycolysis | Me |
| Ehrlich-Meyerhof pathway | Glycosylated hemoglobin | Of |
| Glucagon | Hemoglobin A1c | Pe |
| Glucosuria | Hyperglycemic | Tr |
| Glucose | | |

CHAPTER OBJECTIVES

At the end of this unit of study, the clinical laboratorian should be able to:

- Classify carbohydrates into their respective groups.
- Discuss the metabolism of carbohydrates in the body and the mode of action of hormones in carbohydrate metabolism.
- Differentiate the types of diabetes by clinical symptoms and laboratory findings according to the American Diabetes Association.
- Explain the clinical codes.
- Relate expected labor to the following metabolic conditions:
 - Metabolic acidosis
 - Hyperosmolar coma
- Distinguish between hyperglycemia.

260

Each chapter opens with a **Chapter Outline**, **Key Terms**, and **Chapter Objectives** that correlate to the ASCLS entry-level curriculum and current ASCP content guidelines.

Key Terms are also highlighted within the chapter and defined in the book's Glossary.

264 Chapter 9 Carbohydrates

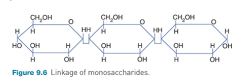


Figure 9.9 Linkage of monosaccharides.

of sugars relies on the formation of glycosidic bonds that are bridges of oxygen atoms. When two carbohydrate molecules join, a water molecule is released. When they split, one molecule of water is consumed to form the individual sugar compounds. This reaction is called hydrolysis. The glycosidic linkages of carbohydrate can involve any number of carbons; however, certain carbons are favored, depending on the carbohydrate. **Monosaccharides** are simple sugars that cannot be hydrolyzed to a simpler form; there is one sugar molecule. These sugars can contain three, four, five, or six or more carbon atoms (known as trioses, tetroses, pentoses, and hexoses, respectively). The most common hexose monosaccharides include glucose, fructose, and galactose.


Disaccharides are formed when two monosaccharide units are joined by a glycosidic linkage. On hydrolysis, disaccharides will be split into two monosaccharides by disaccharidase enzyme (lactase) located on the microvilli of the intestinal mucosa. The most common disaccharides are maltose (two d-glucose molecules in a 1 → 4 linkage) and sucrose.

Oligosaccharides are the chains of 10 sugar units, whereas **polysaccharides** are formed by the linkage of many monosaccharide units. On hydrolysis, polysaccharides will yield 10 monosaccharides. Amylase, an enzyme found in the salivary gland, hydrolyzes starch to d-glucose in the duodenum. The most common polysaccharide is starch (plant based glucose molecules) and glycogen (animal based glucose molecules) (Figure 9.10).

Chemical Properties of Carbohydrates

Some carbohydrates are reducing substances. Carbohydrates can reduce other compounds if they themselves are oxidized. To be a reducing sugar, the carbohydrate must contain a free (available) ketone or an aldehyde group. This property was used in many past laboratory tests for the determination of carbohydrates.

Carbohydrates can form glycosidic bonds with other carbohydrates and with noncarbohydrates. Two sugar molecules can be joined in tandem, forming a glycosidic bond between the hemiacetal group of one molecule and the hydroxyl group on the other molecule. In forming the glycosidic bond, an acetal is generated on one sugar (at carbon 1) in place of the hemiacetal. If the bond forms with one of the other carbons on the carbohydrate other than the anomeric (reducing) carbon, the anomeric carbon is unaltered, and the resulting compound remains a reducing substance. Examples of common-reducing sugars include glucose, maltose, fructose, lactose, and galactose. If a glycosidic bond is formed with the anomeric carbon on the other carbohydrate, the resulting compound is no longer a reducing substance. Nonreducing carbohydrates do not have an active ketone or aldehyde group and therefore will not reduce other



Glossary

1,25-Dihydroxyvitamin D ([OH]₂D) (calcitriol) Active metabolite of vitamin D; induces active absorption of calcium in the small intestine.

1_s rule A data quality control rule that indicates that one data point cannot exceed three SDs. The presence of a data point beyond 3 SDs would trigger a rejection of the analytic run.

25-hydroxyvitamin D Inactive precursor of 1,25 dihydroxyvitamin D.

8-Dihydrotestosterone (DHT) An endogenous androgen sex steroid and hormone. The enzyme 5α-reductase catalyzes the formation of DHT from testosterone in certain tissues including the prostate gland, seminal vesicles, epididymides, skin, hair follicles, liver, and brain.

A

Accuracy How close the measured value is to the true value due to systematic error, which can be either constant or proportional.

Acidemia A condition in which the pH of blood is below the lower limit of the reference range (7.35), indicating that the hydrogen ion concentration in the blood is increased.

Activation energy The excess energy needed to form the transition state of a reaction.

Activators Inorganic cofactors, such as metal ions, needed for enzyme activity.

Active transport Use of energy to move ions or substances across cell membranes.

Acute coronary syndrome (ACS) A progression of pathologic conditions involved in ischemic heart disease, including erosion and rupture of coronary artery plaques, activation of platelets, and thrombosis. This progression ranges from unstable angina to extensive tissue necrosis in acute myocardial infarction.

Acute kidney injury (AKI) A sudden, sharp decline in renal function as a result of an acute toxic or hypoxic insult.

Affinity Attraction or force causing two substances to unite.

Airborne pathogens Any infectious agent transmissible by air, e.g., tuberculosis, virus particles, etc.

Albuminuria The presence of albumin in the urine.

Aldosterone The main mineralocorticoid steroid hormone produced by the zona glomerulosa of the adrenal cortex in the adrenal gland. This hormone controls the sodium-potassium pump, the primary mechanism for sodium reabsorption in the kidney and regulator of the blood sodium and potassium levels.

Alkalemia A condition in which blood pH is greater than the uppermost limit of the reference range (7.43), indicating that the hydrogen ion concentration in the blood is decreased.

Amenorrhea Temporary cessation of menstruation in a female who is past menarche but not yet in menopause.

Amines Hormones that are derived directly from amino acids.

Amino acid Simple organic compounds that serve as the building blocks of proteins, contain at least one amine functional group, one carboxyl function group, and a unique R group.

Aminoacidopathies Inborn errors of metabolism that inhibit the body's ability to metabolize specific amino acids.

Ammonia A compound consisting of nitrogen and hydrogen. Formula: NH₃ or H₃N.

Amniocentesis Puncture of the amniotic sac to obtain fluid for analysis.

Amniotic fluid (AF) A fluid in which the fetus is suspended; it provides a cushioning medium for the fetus and serves as a matrix for influx and efflux of constituents.

Amperometry The measurement of amperes. It is the unit of measure for electric current. The reduction of oxygen produces a current that is proportional to the amount of oxygen present in the sample.

Amphoteric A molecule that is both an acid and a base.

Analyte Substance of interest being measured.

Analytic Introduced during the phase of processing and

Case Studies with patient visuals progress through the chapter and pose critical-thinking questions, prompting students to synthesize and apply their new knowledge. A case study answer key is available to instructors.

CASE STUDY 4.1, PART 1

Remember Miles and Mia from Chapter 1? The laboratory is placing a spectrophotometer back in service after being in storage for 6 months. The instrument manuals are no longer available for this model. Miles and Mia, who manage quality control for the laboratory, are tasked with getting it ready for use.

1. What procedures should Miles and Mia develop to validate that the instrument is working properly for clinical use?



© iStockphoto.com



© Art Taylor/Getty Images

CASE STUDY 6.2, PART 1

Guillermo, a 47-year-old man, had fallen and broken his leg. In the emergency department, he explained his complicated medical history, with type 2 diabetes, peripheral neuropathy, and chronic renal insufficiency. His complete blood count (CBC) showed a normochromic, normocytic anemia.



© Rosalind Wiseman/The Image Bank/Getty Images

CASE STUDY 6.2, PART 2

Remember Guillermo, the 47-year-old man who had fallen and broken his leg. The radiograph of his ankle showed bone loss. Based on admitting chemistry test results, the provider ordered a serum protein electrophoresis.

1. Compare the image of the electrophoresis gel (Figure A) to the reference pattern in Figure 6.9. What protein fraction shows an increase?
2. What additional test should be ordered to identify the increased protein?



Used with permission from Miles Laboratories.

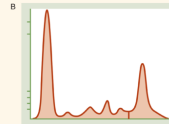


© Rosalind Wiseman/The Image Bank/Getty Images

CASE STUDY 6.2, PART 3

Remember Guillermo, the 47-year-old man who had fallen and broken his leg.

3. Compare the image of Guillermo's electropherogram from the densitometer (Figure B) to the reference patterns in Figure 6.10. Which pattern looks the most similar?



Used with permission from Miles Laboratories.



© Rosalind Wiseman/The Image Bank/Getty Images

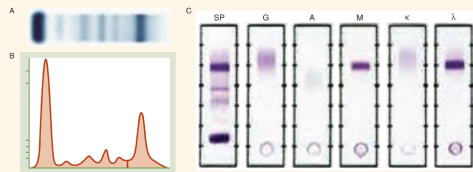
CASE STUDY 6.2, PART 4

Remember Guillermo, the 47-year-old man who had fallen and broken his leg. His provider ordered an IFE and the results are now available.

4. Evaluate the image of Guillermo's serum immunofixation electrophoresis in Figure C. Figure A is the serum protein electrophoresis (SPE). If you turn Figure C 90° to the right, it will look like the SPE pattern in Figure A. What immunoglobulin heavy chain is prominent? What light chain is in the same location and has similar staining intensity?
5. How would this gammopathy be classified?



© Rosalind Wiseman/The Image Bank/Getty Images



A

B

C

SP

G

A

M

κ

λ

SI CONVERSIONS
 To convert between SI units, move the decimal the difference between the exponents represented by the prefix of the base unit. When moving from a larger unit to a smaller unit, the decimal will move to the right. When converting from a smaller unit to a larger unit, the decimal will move to the left.
 If converting from smaller unit to larger unit, then move decimal to the left the exponent difference.
 If converting from larger unit to smaller unit, then move decimal to the right the exponent difference.

point moves to the left three places to become 1.0 L. Note that the SI term for mass is kilogram, which is the only base unit that contains a prefix as part of its name. Generally, the clinical laboratory uses the term gram for mass rather than kilogram.

Table 1.2 Prefixes Used with SI Units

| Factor | Prefix | Symbol |
|-------------------|--------------------|--------|
| 10 ⁻¹⁸ | atto | a |
| 10 ⁻¹⁵ | femto | f |
| 10 ⁻¹² | pico | p |
| 10 ⁻⁹ | nano | n |
| 10 ⁻⁶ | micro | μ |
| 10 ⁻³ | milli | m |
| 10 ⁻² | centi | c |
| 10 ⁻¹ | deci | d |
| 10 ⁰ | Liter, meter, gram | Ba |
| 10 ¹ | deca | da |
| 10 ² | hecto | h |
| 10 ³ | kilo | k |
| 10 ⁶ | mega | M |
| 10 ⁹ | giga | G |
| 10 ¹² | tera | T |
| 10 ¹⁵ | peta | P |
| 10 ¹⁸ | exa | E |

Prefixes are used to indicate a value or a multiple of a basic SI unit.
 © Jones & Bartlett Learning

Example 1: Convert 1.0 L to μL

$$1.0 \text{ L } (1 \times 10^0) \\ \mu\text{L (micro} = 10^{-6})$$

The difference between the exponents = 6. The conversion is from a larger unit to a smaller unit, so the decimal will move 6 places to the right.

$$1.0 \text{ L} = 1,000,000 \mu\text{L}$$

Example 2: Convert 5 mL to μL

$$5 \text{ mL (milli} = 10^{-3}) \\ \mu\text{L (micro} = 10^{-6})$$

The difference between the exponents = 3. The conversion is from a larger unit to a smaller unit, so the decimal will move 3 places to the right.

$$5 \text{ mL} = 5000 \mu\text{L}$$

20 Chapter 1 Basic Principles and Practices of Clinical Chemistry

Laboratory Mathematics and Calculations

Significant Figures

Significant figures are the minimum number of digits needed to express a particular value in scientific notation without loss of accuracy. There are several rules in regard to identifying significant figures:

1. All nonzero numbers are significant (1, 2, 3, 4, 5, 6, 7, 8, 9).
2. All zeros between nonzero numbers are significant.
3. All zeros to the right of the decimal are not significant when followed by a nonzero number.
4. All zeros to the left of the decimal are not significant.

The number 814.2 has four significant figures, because in scientific notation, it is written as 8.142×10^2 . The number 0.000641 has three significant figures, because the scientific notation expression for this value is 6.41×10^{-4} . The zeros to the right of the decimal preceding the nonzero digits are merely holding decimal places and are not needed to properly express the number in scientific notation. However, by convention, zeros following a decimal point are considered significant. For example, 10.00 has four significant figures. The zeros to the right of the decimal indicate the precision of this value.

Logarithms

Logarithms are the inverse of exponential functions and can be related as such:

$$x = A^y \text{ or } y = \log_A(x)$$

This is then read as B is the log base A of X, where B must be a positive number, A is a positive number, and A cannot be equal to 1. Calculators with a log function do not require conversion to scientific notation.

To determine the original number from a log value, the process is performed in reverse. This process is termed the antilogarithm or antilog as it is the inverse of the logarithm. Most calculators require using an inverse or secondary/shift function when entering this value. If given a log of 3.1225, the resulting value is 1.424×10^3 on the base 10 system. Consult the specific manufacturer's directions of the

calculator to become acquainted with the proper use of these functions.

pH (Negative Logarithms)

In certain circumstances, the laboratory may work with negative logs. Such is the case with pH or pK_a. As previously stated, the pH of a solution is defined as the negative log of the hydrogen ion concentration. The following is a convenient formula to determine the negative logarithm when working with pH or pK_a:

$$\text{pH} = -\log N \quad (\text{Eq. 1.11})$$

where x is the negative exponent base 10 expressed and N is the decimal portion of the scientific notation expression.

For example, if the hydrogen ion concentration of a solution is 5.4×10^{-6} , then x = 6 and N = 5.4. Substitute this information into Equation 1.11, and it becomes

$$\text{pH} = 6 - \log 5.4 \quad (\text{Eq. 1.12})$$

The logarithm of N (5.4) is equal to 0.7324, or 0.73. The pH becomes

$$\text{pH} = 6 - 0.73 = 5.27 \quad (\text{Eq. 1.13})$$

The same formula can be applied to obtain the hydrogen ion concentration of a solution when only the pH is given. Using a pH of 5.27, the equation becomes

$$5.27 = x - \log N \quad (\text{Eq. 1.14})$$

In this instance, the x term is always the next largest whole number. For this example, the next largest whole number is 6. Substituting for x, the equation becomes

$$5.27 = 6 - \log N \quad (\text{Eq. 1.15})$$

A shortcut is to simply subtract the pH from 6 ($6 - 5.27 = 0.73$) and take the antilog of that answer 5.73. The final answer is 5.73×10^{-6} . Note that rounding, while allowed, can alter the answer. A more algebraically correct approach follows in Equations 1.16 through 1.18. Multiply all the variables by -1:

$$(-1)(5.27) = (-1)(6) - (-1)(\log N) \\ -5.27 = -6 + \log N \quad (\text{Eq. 1.16})$$

$$-5.27 = -6 + \log N$$

Boxes emphasize important points and additional information.

Examples highlight important formulas and how to use them in a convenient, numbered format.

Equations are presented throughout in a convenient numbered format.

Table 5.4 Competitive Binding Assay Example

| Ag | + | AD* | + | AB | → | AGAB | + | AD*AB | + | AD* |
|----------------------------|---|-----|---|-----|---------------------------|------|---|-------|---|-----|
| CONCENTRATION OF REACTANTS | | | | | CONCENTRATION OF PRODUCTS | | | | | |
| AD | | | | AB | | AGAB | | AD*AB | | AD* |
| 0 | | 200 | | 100 | | 0 | | 100 | | 100 |
| 50 | | 200 | | 100 | | 20 | | 80 | | 120 |
| 100 | | 200 | | 100 | | 34 | | 66 | | 134 |
| 200 | | 200 | | 100 | | 50 | | 50 | | 150 |
| 400 | | 200 | | 100 | | 66 | | 34 | | 166 |

SAMPLE CALCULATIONS

| Dose of [Ag] | % B | B/F |
|--------------|-----|---------|
| 0 | 100 | 100 = 1 |
| | 200 | 100 |
| 50 | 80 | 80 = 47 |
| | 200 | 200 |
| 100 | 66 | 66 = 33 |
| | 200 | 134 |
| 200 | 50 | 50 = 33 |
| | 200 | 150 |
| 400 | 34 | 34 = 20 |
| | 200 | 166 |

equally to the Ab. As the concentration of Ag increases in a competitive assay, the amount of tracer that complexes with the binding reagent decreases. If the tracer is of low molecular weight, free tracer is often measured. If the tracer is of high molecular weight, the bound tracer is measured. The data may be plotted in one of three ways: bound/free versus the arithmetic dose of unlabeled Ag, percentage bound versus the log dose of unlabeled Ag, and logit bound/free versus the log dose of the unlabeled Ag (Figure 5.11).

The bound fraction can be expressed in several different formats. Bound/free is counts per minute (CPM) of the bound fraction compared with the CPM of the free fraction. Percent bound (% B) is the CPM of the bound fraction compared with the CPM of maximum binding of the tracer (B₀) multiplied by 100. Logit B/B₀ transformation is the natural log of (B₀/B) / (1 - B/B₀). When B/B₀ is plotted

Renal Anatomy 541

Table 21.1 Kidney Functions

| |
|---|
| Urine formation |
| Fluid and electrolyte balance |
| Regulation of acid-base balance |
| Excretion of the waste products of protein metabolism |
| Excretion of drugs and toxins |
| Secretion of hormones |
| Renin |
| Erythropoietin |
| 1,25-Dihydroxyvitamin D ₃ |
| Prostaglandins |

© Jones & Bartlett Learning

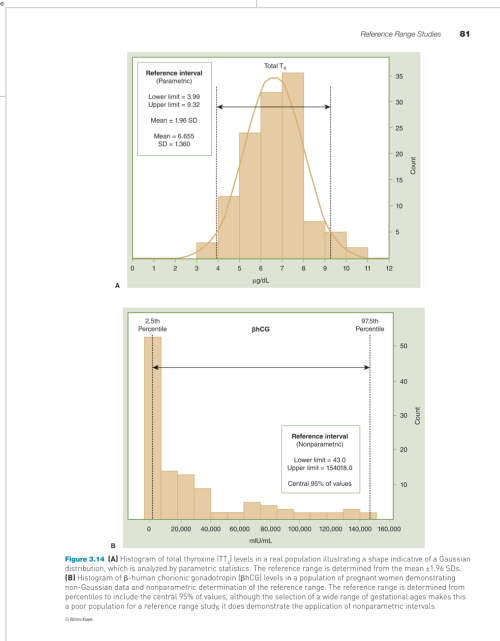
units of the kidney that can only be seen microscopically. Each kidney contains approximately 1 million nephrons. Each nephron is a complex apparatus composed of five basic parts as shown in Figure 21.2.

These five parts are:

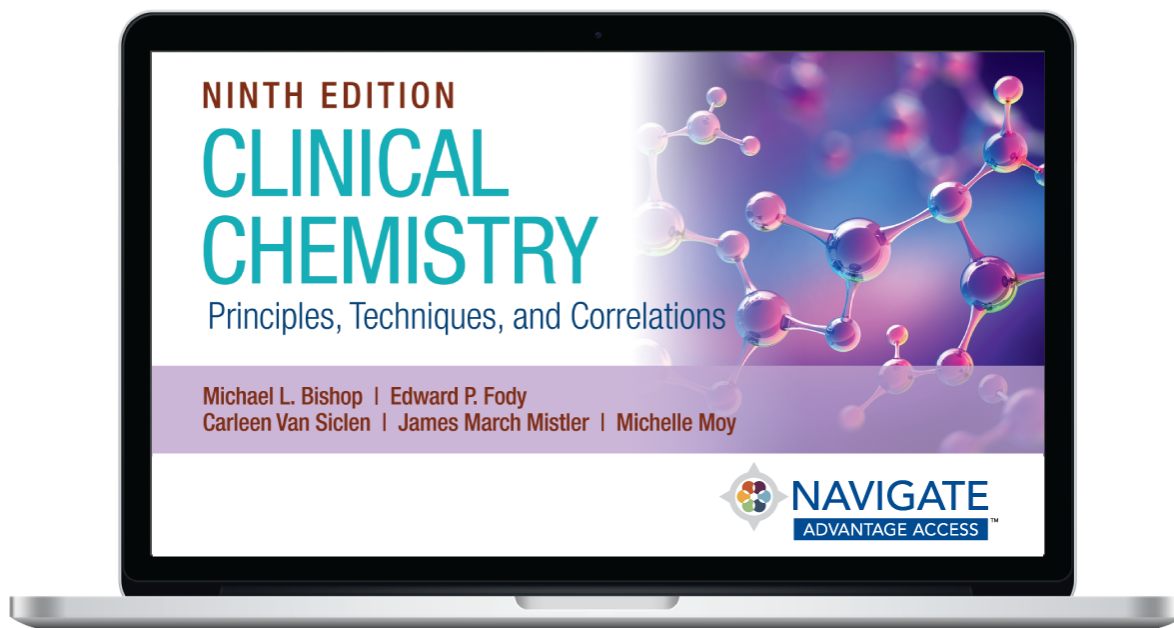
- The **glomerulus**—a capillary tuft surrounded by the expanded end of a renal **tubule** known as Bowman's capsule. Each glomerulus has an afferent arteriole that carries the blood in and an efferent arteriole carrying the blood out. The efferent arteriole branches into peritubular capillaries that supply the tubule.
- The proximal convoluted tubule—located in the cortex.
- The long loop of Henle—composed of the thin descending limb, which spans the medulla, and the ascending limb, which is located in both the medulla and the cortex, composed of a region that is thin and then thick.
- The distal convoluted tubule—located in the cortex.

the body by way of the ureter. The highlighted section in Figure 21.1 shows the arrangement of **nephrons** in the kidney; nephrons are functional

Figure 21.1 Anatomy of the kidney.



Student Resources



To support your learning, review the chapter learning objectives and complete the online activities. The **Navigate 2 Advantage Access** included with each new print copy of this book offers a wealth of resources. These include practical learning activities and study tools such as flashcards, math practice, an eBook with interactive questions, and more!

- eBook with embedded assessments
- Case Studies
- Review Questions
- Flashcards
- Reference Range Table
- General Reference Tables
- Supplemental Chapter
 - Molecular Theory and Techniques

Instructor Resources

Instructor resources, available to qualified instructors, include the following:

- Learning Objectives mapped to:
 - ASCLS Entry-Level Curriculum (MLS and MLT)
 - Current ASCP Board of Certification Content Guidelines (MLS and MLT)
- Slides in PowerPoint format
- Teaching Resources
- Test Bank (Available in LMS-compatible formats)
- Student Lab Procedures
- Image Bank
- Answer Key to Case Studies
- Answer Key to Eighth Edition Case Studies
- Answer Key to Review Questions
- Sample Syllabus



© Oxygen/Moment/Getty Images.

Acknowledgments

A project as large as this requires the assistance and support of many clinical laboratorians. The editors wish to express their appreciation to the contributors of all the editions of *Clinical Chemistry: Principles, Techniques, and Correlations*—the dedicated laboratory professionals and educators whom the editors have had the privilege of knowing and exchanging ideas with over the years. These individuals were selected because of their expertise in particular areas and their commitment to the education of clinical laboratorians. Many have spent their professional careers in the clinical laboratory, at the bench, teaching students, or consulting with clinicians. In these frontline positions, they have developed a perspective of what is important for the next generation of clinical laboratorians.

We extend appreciation to our students, colleagues, teachers, and mentors in the profession who have helped shape our ideas about clinical chemistry practice and education. Also, we want to thank the many companies and professional organizations that provided product information and photographs or granted permission to reproduce diagrams and tables from their publications. The ASCLS Entry Level Curriculum and CLSI documents have also been important sources of information. These documents are directly referenced in the appropriate chapters.

The editors would like to acknowledge the contribution and effort of all individuals to previous editions. Their efforts provided the framework for many of the current chapters. Finally, we gratefully acknowledge the cooperation and assistance of the staff at Jones & Bartlett Learning for their advice and support.

The editors are continually striving to improve future editions of this book. We again request and welcome our readers' comments, criticisms, and ideas for improvement.

MLB, EPF, CVS, JMM, MM



© Oxygen/Moment/Getty Images.

Contributors

Karen K. Apolloni, MSA, MLS(ASCP)^{CM}

Director (Academic), Clinical Laboratory Science Program
Wayne State University
Detroit, Michigan

Nikola A. Baumann, PhD, DABCC

Co-Director of Central Clinical Laboratory and Central Processing
Department of Laboratory Medicine and Pathology
Mayo Clinic
Rochester, Minnesota

Heather BlalockMcNasby, MT(ASCP), MSHS

Manager of Clinical Laboratory Services
Nemours Children's Hospital
Orlando, Florida

Takara L. Blamires, MS, MLS(ASCP)^{CM}

Associate Professor, MLS Undergraduate Program Director
Department of Pathology
University of Utah School of Medicine
Salt Lake City, Utah

Michelle R. Campbell, MS, MLS(ASCP)^{CM}MB^{CM}

Development Technologist
Department of Laboratory Medicine and Pathology
Mayo Clinic
Rochester, Minnesota
Adjunct Instructor