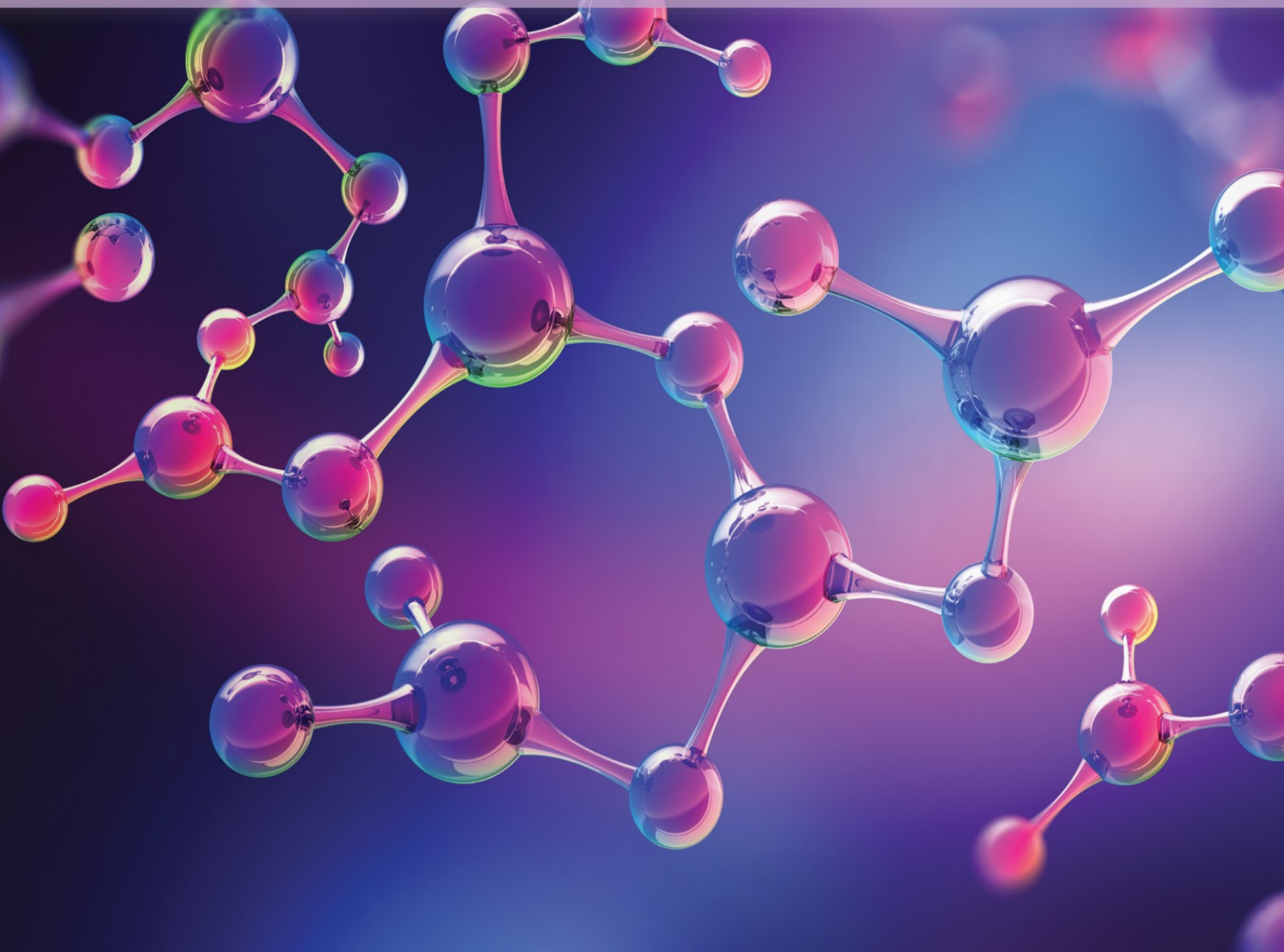
NINTH EDITION

CLINICAL CHEMISTRY

Principles, Techniques, and Correlations

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



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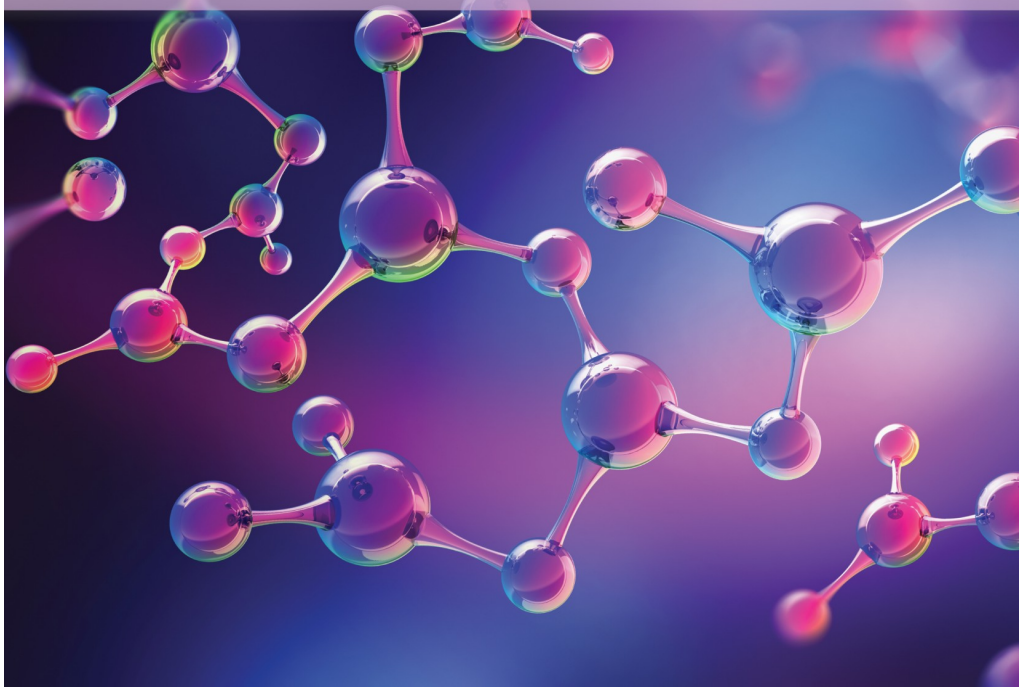

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CLINICAL CHEMISTRY

Principles, Techniques, and Correlations

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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.

Brief Contents

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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

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

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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.

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 deathstatistics. 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 interdisciplinaryteamwork. 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.

Theninth 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 accesscontains 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 Siclen
James March Mistler
Michelle Moy

*Modified from Harvey Specter in *Suits*.

New to This Edition

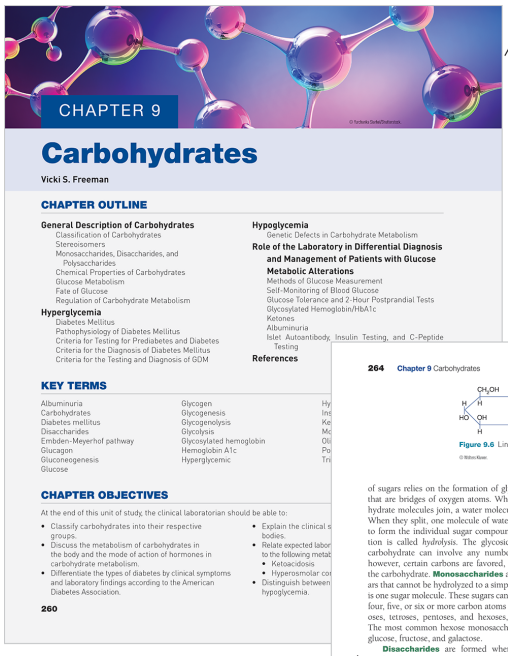
Medical laboratory Science students need a strong foundation in applied chemistry to meet the requirements of certifying bodies and accreditation organizations that ensure students are prepared for employment.

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

KEY TERMS

Albuminuria
Carbohydrates
Diabetes mellitus
Disaccharides
Embden-Meyerhof pathway
Glucagon
Gluconeogenesis
Glucose
Glycogen
Glycogenesis
Glycogenolysis
Glycolysis
Glycosylated hemoglobin
Hemoglobin A1c
Hyperglycemic

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 s bodies.
- Relate expected labor to the following metal
  - Ketoacidosis
  - Hyperosmolar co
- Distinguish between hypoglycemia.

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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.

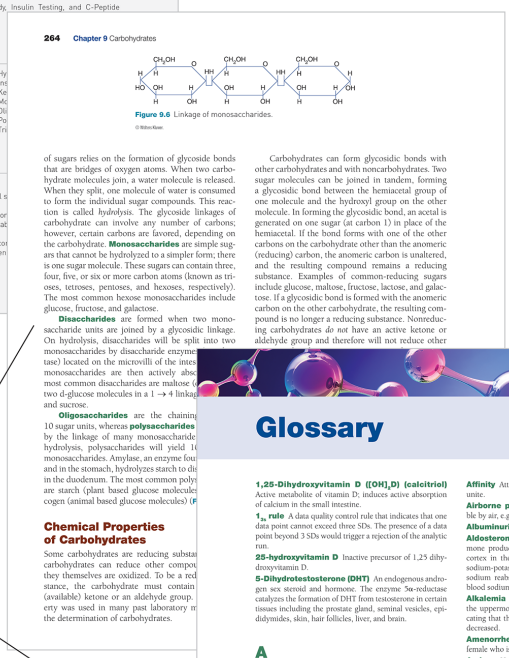

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Figure 9.6 Linkage of monosaccharides.

of sugars relies on the formation of glycoside 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 glycoside 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 disaccharide enzyme
tase) located on the microvilli of the intes
monosaccharides are then actively abso
most common disaccharides are maltose (
two d-glucose molecules in a 1 → 4 linkag
and sucrose.

Oligosaccharides are the chaining
10 sugar units, whereas **polysaccharides**
by the linkage of many monosaccharide
hydrolysis, polysaccharides will yield 1
monosaccharides. Amylase, an enzyme fou
and in the stomach, hydrolyzes starch to di
in the duodenum. The most common polys
are starch (plant based glucose molecules
cogen (animal based glucose molecules) (F

Chemical Properties of Carbohydrates

Some carbohydrates are reducing substa
carbohydrates can reduce other compou
they themselves are oxidized. To be a red
stance, the carbohydrate must contain
(available) ketone or an aldehyde group.
erty was used in many past laboratory m
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]$_2$D) (calcitriol) Active metabolite of vitamin D; induces active absorption of calcium in the small intestine.

1_{ss} 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.

5-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 thrombi. 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 particle, 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 (>7.45), 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: NH_3 or H_3N.

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

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

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?

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.

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?

A

Used with permission from Helena Laboratories.

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?

B

Used with permission from Helena Laboratories.

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.

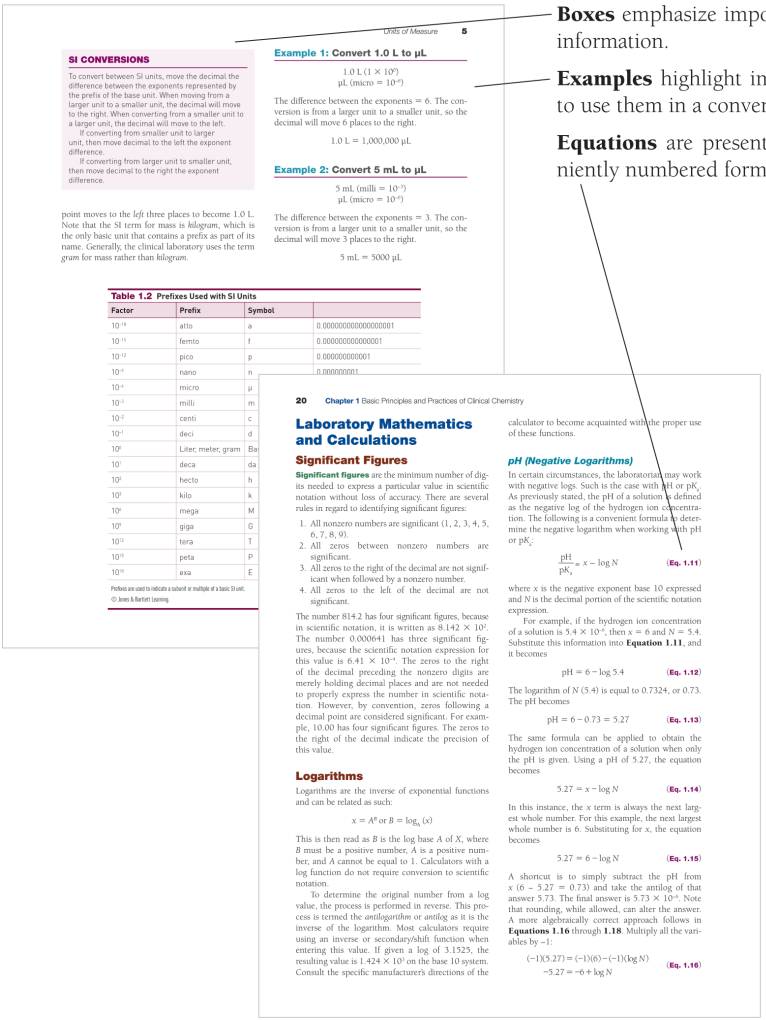
4. Evaluate the image of Guillermo's serum immunofixation electrophoresis in Figure C. Figure A is the serum protein electrophoresis (SPE). If you turn Figure C 90° to the right, it will look like the SPE pattern in Figure A. What immunoglobulin heavy chain is prominent? What light chain is in the same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

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 basic unit that contains a prefix as part of its name. Generally, the clinical laboratory uses the term *gram* for mass rather than *kilogram*.

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.

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

Table 1.2 Prefixes Used with SI Units

Factor	Prefix	Symbol	
10^{-18}	atto	a	0.000000000000000001
10^{-15}	femto	f	0.000000000000001
10^{-12}	pico	p	0.000000000001
10^{-9}	nano	n	0.000000001
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 subunit or multiple of a basic SI unit.

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:

$$x = A^{B} \text{ or } B = \log_{A}(x)$$

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 3.1525, 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 laboratorian 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:

$$\frac{\text{pH}}{\text{pK}_a} = x - \log N \qquad \text{(Eq. 1.11)}$$

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

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

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

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

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

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

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

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

A shortcut is to simply subtract the pH from x ($6 - 5.27 = 0.73$) 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:

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

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 conveniently numbered format.

Figures and **Tables** provide dynamic visuals and populate the new edition throughout, including illustrations, photos, charts, and graphs.

Table 5.4 Competitive Binding Assay Example

AG	+	AG*	+	AB	→	AGAB	+	AG*AB	+	AG*
CONCENTRATION OF REACTANTS						CONCENTRATION OF PRODUCTS				
AG		AG*		AB		AGAB		AG*AB		AG*
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	$\frac{100}{200} = 50$	$\frac{100}{100} = 1$
50	$\frac{80}{200} = 40$	$\frac{80}{200} = 67$
100	$\frac{66}{200} = 33$	$\frac{66}{134} = 33$
200	$\frac{50}{200} = 25$	$\frac{50}{150} = 33$
400	$\frac{34}{200} = 17$	$\frac{34}{166} = 20$

Ab, unlabeled antigen; Ab*, labeled antigen; AB, antibody; AGAB, antigen–antibody complex; Ab*AB, labeled ant

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/B_0 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 (B_0) multiplied by 100. Logit B/B_0 transformation is the natural log of $(B/B_0)/(1 - B/B_0)$. When B/B_0 is plotted

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

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

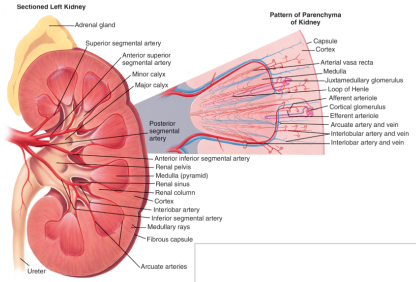


Figure 21.1 Anatomy of the kidney.

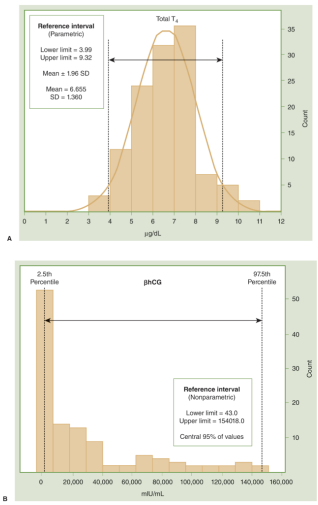
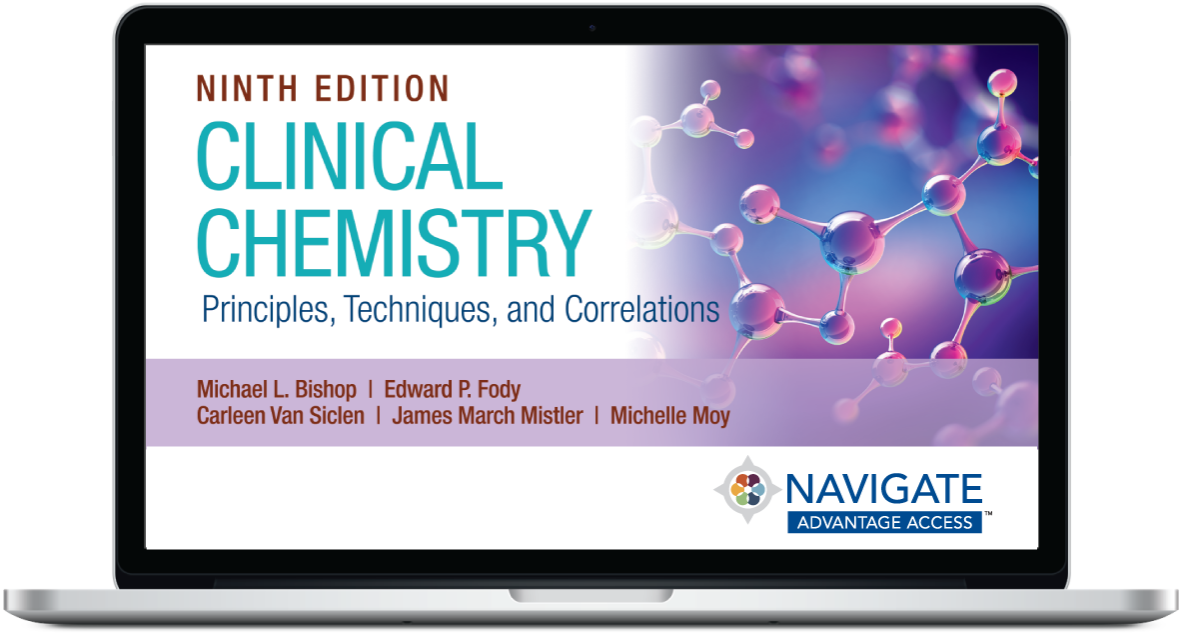


Figure 3.14 **(A)** Histogram of total thyroxine [T_4] levels in a real population illustrating a shape indicative of a Gaussian distribution, which is analyzed by parametric statistics. The reference range is determined from the mean ±1.96 SDs. **(B)** Histogram of β-human chorionic gonadotropin [βhCG] levels in a population of pregnant women demonstrating non-Gaussian data and nonparametric determination of the reference range. The reference range is determined from percentiles to include the central 95% of values, although the selection of a wide range of gestational ages makes this a poor population for a reference range study, it does demonstrate the application of nonparametric intervals.

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

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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.

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