Second Edition

Laboratory Medicine

The Diagnosis of Disease in the Clinical Laboratory

Michael Laposata

Mc Graw Hill Education

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Laboratory Medicine

The Diagnosis of Disease in the Clinical Laboratory

Second Edition

Edited by

Michael Laposata, MD, PhD

Chairman
Department of Pathology
University of Texas Medical Branch
Galveston, Texas

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Laboratory Medicine: The Diagnosis of Disease in the Clinical Laboratory, Second Edition

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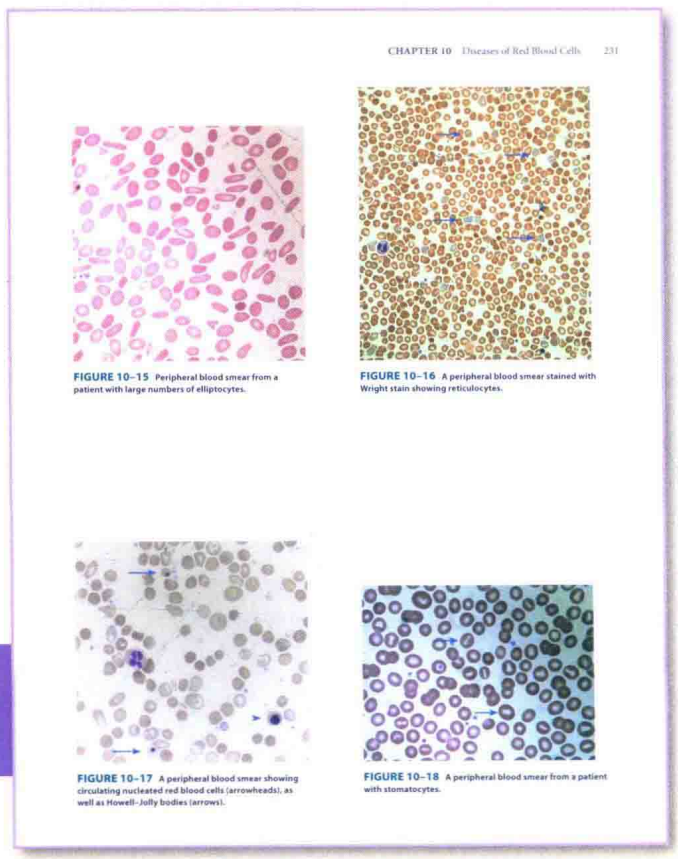
To Susan, with love

Key Features of

Laboratory Medicine

A complete full-color guide to selecting the correct laboratory test and accurately interpreting the results—covering the entire field of clinical pathology

- 46 laboratory methods presented in easy-to-understand illustrations which include information on the expense and complexity of the assays
- Features an easy-to-follow, consistent presentation for each disease discussed
- More than 200 tables and full-color algorithms encapsulate important information and facilitate understanding
- Full-color blood-smear micrographs demonstrate common abnormal morphologies of red blood cells
- Valuable learning aids in each chapter, including learning objectives, chapter outlines, and a general introduction
- Extensive table of Clinical Laboratory Reference Values showing the conversions between U.S. and SI units for each value
- An essential text for medical students and residents studying clinical pathology, medical technology students, and for practitioners working in a clinical setting
- This edition has been enhanced by coverage of genetic test options that are now commonly used in clinical practice.



Blood-smear micrographs demonstrate common abnormal morphologies of red blood cells

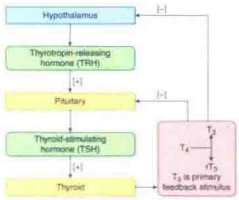


FIGURE 22–2 Hypothalamic–pituitary–thyroid interactions. [+] Stimulation; [–] inhibition.

hormone replacement in hypothyroid patients. Third-generation assays are essential for monitoring TSH suppression therapy in patients with a TSH-responsive thyroid tumor.

The relationship between TSH and the thyroid hormones, particularly free T_4, is an inverse, log-linear one, such that very small changes in free T_4 result in large changes in TSH. Thus, TSH is the most sensitive first-line screening test for suspected thyroid abnormalities. If the TSH is within the normal reference range, no further testing is performed. If the TSH is outside of the reference range, a free T_4 is obtained.

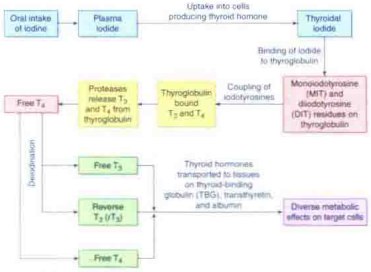


FIGURE 22–3 The formation, secretion, and transport of thyroid hormones.

200 tables and full-color algorithms encapsulate important information

TABLE 22–1 Laboratory Evaluation of Patients for Thyroid Disease

Disorder	Laboratory Test Results Suggestive of Diagnosis in the Appropriate Clinical Setting
Hyperthyroidism	
Graves disease	TSH low; free T_4 high; in some cases, T_3 is elevated and free T_4 is normal; TRAbs or TSI elevated
Toxic multinodular goiter	TSH low; free T_4 and T_3 normal or high; normal or increased radioactive iodine uptake; thyroid scan with multiple areas of increased uptake surrounded by suppressed uptake
Toxic adenoma	TSH low; free T_4 and T_3 normal or high; normal or increased radioactive iodine uptake; thyroid scan with focal increased uptake in tumor surrounded by suppressed uptake in nontumor tissue
Subacute thyroiditis	TSH low; free T_4 and T_3 high; increased/decreased radioactive iodine uptake
Painless thyroiditis	TSH low; free T_4 and T_3 high; erythrocyte sedimentation rate normal; decreased radioactive iodine uptake
Hypothyroidism	
Hashimoto thyroiditis	TSH high; T_4 normal and then low, preceding a decline in T_3; anti-TPO and/or antithyroglobulin antibody positive
Ablative hypothyroidism	TSH high; free T_4 and T_3 low following procedure that ablates thyroid
Infantile hypothyroidism	TSH high; free T_4 low in a newborn or infant
Euthyroid sick syndrome	TSH normal to high; free T_4 normal, T_3 low; rT_3 high; concentrations of TSH and thyroid hormones vary throughout disease course

rT_3, reverse triiodothyronine; T_3, triiodothyronine; free T_4, free thyroxine; TSH, thyroid-stimulating hormone; TRAbs, TSH-receptor autoantibodies; TSI, thyroid-stimulating immunoglobulins

may have exophthalmos, emotional changes, menstrual changes, and a fine tremor of the hands. In the presence of a clinical history and physical examination consistent with hyperthyroidism, a diagnosis of hyperthyroidism (but not necessarily its cause) can be established by the demonstration of a low TSH level and a high free T_4. In uncommon situations, only the total T_3 level is elevated and the serum free T_4 is normal (T_3 thyrotoxicosis). To determine the etiology of the hyperthyroidism, additional testing is usually necessary. Graves disease, toxic multinodular goiter (TMNG), and toxic adenoma account for the vast majority (>95%) of cases of hyperthyroidism. It should be noted that diffuse or focal enlargement of the thyroid gland, also known as goiter, can be associated with hyperfunction, normal function, and hypofunction of the gland.

Graves disease is a relatively common hyperthyroid disorder occurring more frequently in women. It is an autoimmune disease caused by TSH receptor autoantibodies that bind to and stimulate TSH receptors resulting in autonomous production of thyroid hormone.

Thyroid Storm

Thyroid storm is a relatively uncommon, but life-threatening manifestation of hyperthyroidism caused by excess circulation of thyroid hormones. Symptoms of thyroid storm are similar, but much more severe than traditional hyperthyroidism, including a markedly high fever of 105°F to 106°F, tachycardia, hypertension, and neurological and gastrointestinal abnormalities. Thyroid storm is precipitated by acute illnesses such as sepsis, diabetic ketoacidosis, and preeclampsia, as well as surgical or other diagnostic or therapeutic actions such as radioactive iodine use, anesthesia, excessive thyroid hormone ingestion, or thyroid palpation. Thyroid storm is associated with a high fatality rate if not identified early. The diagnosis is based on the presence of clinical signs and symptoms of severe hyperthyroidism in the context of a precipitating cause. In addition, marked elevations in free and total T_4 are common in thyroid storm. Total T_3 is unreliable in this setting because concomitant nonthyroidal illness (NTI) may cause T_3 to decrease significantly.

Graves Disease

Graves disease is a relatively common hyperthyroid disorder occurring more frequently in women. It has a familial predisposition. It is an autoimmune disease caused by TSH receptor

CHAPTER

21

Breast

Karin E. Finberg

LEARNING OBJECTIVES

1. Learn the tissue- and serum-based biomarkers in breast cancer.
2. Understand how the individual biomarkers are used clinically.

CHAPTER OUTLINE

INTRODUCTION

This chapter focuses on laboratory testing relevant to breast cancer. Infections of the breast are included in Chapter 3.

BREAST CANCER

Description

Cancers of the breast constitute a major cause of mortality in women of Western countries. In the United States, the lifetime probability that a woman will develop breast cancer is 1 in 8. Breast cancer accounts for 29% of new cancer cases and 14% of cancer deaths in American women. About 1% of breast cancers occur in males. The risk of developing breast cancer is influenced by several factors. These factors include increased age, family history of breast cancer (especially in a first-degree relative), hormonal factors (early age at menarche, older age of menopause, older age at first full-term pregnancy, fewer number of pregnancies, and use of hormone replacement therapy), clinical factors (high breast tissue density and benign breast diseases associated with atypical hyperplasia), obesity, and alcohol consumption. Since 1990, the mortality rate associated with female breast cancer has decreased in the United States, a decline that has been attributed to both therapeutic advances and early detection.

For localized breast cancer, primary treatment typically consists of either breast-conserving surgery and radiation or mastectomy. Most patients with invasive breast cancer subsequently receive systemic adjuvant chemotherapy and/or hormone therapy, both of which have been shown to reduce systemic recurrence and breast cancer–related mortality. However, the fact that some patients who lack lymph node involvement are cured by the combination of surgery and radiotherapy suggests that adjuvant treatment may not be necessary in all cases.

Valuable learning aids are included in each chapter

Authors

Yash P. Agrawal, MD, PhD
Professor of Clinical Pathology and Laboratory Medicine, Department of Pathology and Laboratory Medicine; Director of Central Laboratory; Director of Point of Care Testing Services, New York Presbyterian Hospital-Cornell Campus, New York, New York

Samir L. Aleryani, PhD, C(ASCP), CLS (NCA), FACB
Formerly Assistant Professor in Clinical Pathology, Director Clinical Research Center Laboratory, Vanderbilt Institute of Clinical and Translational Research (VICTR), Department of Pathology, Microbiology, and Immunology School of Medicine, Vanderbilt University, Nashville, Tennessee

David N. Alter, MD
Clinical/Chemical Pathologist, Spectrum Health/ Michigan Pathology Specialists, Grand Rapids, Michigan

Fred S. Apple, PhD
Medical Director, Clinical Laboratories, Hennepin County Medical Center; Professor, Laboratory Medicine and Pathology, University of Minnesota School of Medicine, Minneapolis, Minnesota

Sheila P. Dawling, PhD
Vice President of Laboratories, Aegis Sciences Corporation, Nashville, Tennessee

D. Robert Dufour, MD, FCAP, FACB
Consultant, Emeritus Professor of Pathology, Department of Pathology and Hepatology, Veterans Affairs Medical Center, The George Washington University Medical, Washington, District of Columbia

Karin E. Finberg, MD, PhD
Assistant Professor of Pathology, Yale School of Medicine, New Haven, Connecticut

Ann M. Gronowski, PhD
Professor, Department of Pathology & Immunology and Obstetrics & Gynecology, Washington University School of Medicine, St. Louis, Missouri

Jacqueline J. Haas, MD
Staff Pathologist, Laboratory Medical Director, Department of Pathology, Clinical Pathology Associates, St. David's Medical Center, Austin, Texas

Vipul Lakhani, MD
Assistant Professor of Medicine, Department of Medicine, Division of Endocrinology, Vanderbilt University Medical Center, Nashville, Tennessee

Michael Laposata, MD, PhD
Chairman, Department of Pathology, University of Texas Medical Branch, Galveston, Texas

Daniel D. Mais, MD
Clinical Pathology Associates, Department of Pathology, Baptist Health System, San Antonio, Texas

Stacy E.F. Melanson, MD, PhD
Assistant Professor, Associate Medical Director, Clinical Chemistry, Clinical Laboratories, Harvard Medical School Brigham and Women's Hospital, Boston, Massachusetts

Charles H. Muller, PhD, HCLD (AAB)
Director, Male Fertility Laboratory and Lecturer, Full-Time, Department of Urology and Biological Structure, University of Washington School of Medicine, Seattle, Washington

Mandakolathur R. Murali, MD
Director, Assistant Professor, Department of Clinical Immunology Laboratory, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts

James H. Nichols, PhD
Professor of Pathology, Microbiology and Immunology; Medical Director of Clinical Chemistry, Vanderbilt University School of Medicine, Nashville, Tennessee

Daniel E. Sabath, MD, PhD
Associate Professor, Department of Laboratory Medicine; Adjunct Associate Professor, Department of Medicine (Medical Genetics); Head, Hematology Division, Department of Laboratory Medicine; Director of Hematology Laboratories, University of Washington Medical Center and Harborview Medical Center, Seattle, Washington

Susan L. Saidman, PhD
Associate Professor of Pathology, Harvard Medical School; Director, Histocompatibility Laboratory, Massachusetts General Hospital, Boston, Massachusetts

Eric D. Spitzer, MD, PhD
Associate Professor, Department of Pathology, Stony Brook University Medical Center, Stony Brook, New York

Paul Steele, MD
Medical Director, Clinical Associate Professor, Department of Pathology and Laboratory Medicine, Clinical Laboratories, Cincinnati Children's Hospital Medical Center, University of Cincinnati, Cincinnati, Ohio

Christopher P. Stowell, MD, PhD
Director, Blood Transfusion Service; Associate Professor of Pathology, Department of Pathology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts

Thomas P. Stricker, MD, PhD
Assistant Professor, Department of Pathology, Microbiology, and Immunology, Vanderbilt University School of Medicine, Nashville, Tennessee

Elizabeth M. Van Cott, MD
Director, Coagulation Laboratory; Medical Director, Core Laboratory, Massachusetts General Hospital; Associate Professor, Harvard Medical School, Boston, Massachusetts

Mark H. Wener, MD, ABIM, ABAI (CLI/DLI)
Professor, Departments of Laboratory Medicine & Medicine, University of Washington, Seattle, Washington

William E. Winter, MD
Professor, Department of Pathology, Immunology, and Laboratory Medicinem, University of Florida College of Medicine, Gainesville, Florida

Alison Woodworth, PhD
Assistant Professor, Medical Director of Esoteric Chemistry, Department of Pathology, Microbiology, and Immunology, Vanderbilt University Medical Center, Nashville, Tennessee

Preface

In the early 1990s when I was at the Massachusetts General Hospital as director of clinical laboratories, I was invited by Ramzi Cotran to join him and Stan Robbins at the Brigham and Women's Hospital for a meeting. In that meeting, they indicated to me that the *Robbins Pathologic Basis of Disease*, primarily an anatomic pathology book, would greatly benefit from a parallel book in clinical pathology (laboratory medicine). At that time, areas such as coagulation and toxicology were expanding rapidly with new disorders and new tests to diagnose them. Because there was little anatomic pathology in these fields, the discussions of these major areas of diagnostic medicine in the Robbins book were limited. In addition, as the test menu in the clinical laboratory was growing in complexity and cost, many important clinical laboratory tests for common disorders, such as the troponin test for myocardial infarction, were also discussed only briefly in the Robbins book. Both Robbins and Cotran understood that a discussion regarding the threshold for diagnosis of myocardial infarction, as troponin testing rapidly evolved and improved, was necessary to fully discuss the topic. There were many twists and turns from that meeting about 20 years ago to the development of this second edition of *Laboratory Medicine: The Diagnosis of Disease in the Clinical Laboratory* in the prestigious Lange series by McGraw-Hill. With this second edition, I believe we truly have a book that is essential for education of medical students and residents studying clinical pathology, and importantly, for practitioners in a clinical setting. By selecting the correct tests and interpreting the results correctly, physicians using this book should be able to optimize patient outcomes and reduce the cost to achieve a diagnosis.

This second edition is a great step forward from the first edition. It contains information about genetic tests now in common use. Additional descriptions of test methods with simply illustrated figures have been added to this edition. The authors of the individual chapters have all taken significant steps to make the tables that indicate the diagnostic tests for different clinical conditions more concise and easy to understand. It is now clear that significant morbidity and mortality occur on a daily basis, affecting thousands of patients, because incorrect tests are ordered, important tests for the diagnosis are omitted, and/or the interpretation of test results by the physicians who ordered the tests is incorrect. A survey of medical schools currently underway has shown that the teaching of laboratory medicine over the full 4 years of medical school includes (as a mean value across the US medical schools) only about 10 hours of formal training in laboratory medicine. This study also shows that, unlike virtually every other medical discipline, laboratory medicine is commonly *not* taught by experts in the field, even if they are present in the institution. As a result, medical schools graduate physicians who have had almost no training in something they do virtually every day—order laboratory tests and interpret the test results. Surprisingly, the patients and the medical institutions suffer cost and care disadvantages quietly and unknowingly. There are surely hundreds of patients every month in the United States who present to an emergency room with shortness of breath, for whom a diagnosis of pulmonary embolism is overlooked, and an appropriate test (the D-dimer test for pulmonary embolism) is not ordered. Such patients are discharged from the emergency room without ever being anticoagulated, and for some, to die shortly thereafter, from an expansion of the pulmonary embolism. Like surgical errors or medication errors, the error of the healthcare provider who did not order a necessary test results in a preventable death—but unlike surgical and medication errors, the fact that such a case represents a preventable death is rarely recognized by the patient, the patient's family, fellow physicians, and often even the physician who failed to order the correct test.

There are several groups of healthcare providers who would benefit significantly by using this book to correctly order laboratory tests and correctly interpret the test results. Certainly, there is every reason to believe that medical students can learn the histopathologic changes associated with a disease using a textbook such as the *Robbins Pathologic Basis of Disease*, and learn laboratory tests associated with that disorder, using this book, at the same time.

Medical technology students would greatly benefit by a thorough understanding of the methods that are illustrated in Chapter 2 of this book. In addition, it would be of immense benefit for medical technology students to more fully understand the clinical significance of the test results that they generate so that they can more knowledgeably interact with

physicians who are confused about laboratory test results. Interactions between medical technologists and physicians ordering tests that result in improved performance in test selection and result interpretation would greatly increase the respect for the medical technologist (also known as clinical laboratory scientist) from physicians who use the clinical laboratory.

In conversations with primary care physicians attempting to select the correct laboratory tests, they often indicate that one of their first inquiries about which laboratory tests to select is to search *Wikipedia*. It is most likely that there is a table in this textbook, written by a prominent expert in the field, that will tell a practicing physician exactly what test to order, and importantly, how to interpret the result as well by describing common interpretation mistakes – with a much higher reliability than virtually all of what is available on the Internet.

It is my greatest hope that the use of this textbook, which presents the entire field of laboratory medicine to a large audience of future physicians, medical technologists, and healthcare providers ordering laboratory tests, will result in better clinical outcomes for patients at a greatly reduced cost.

Michael Laposata
Galveston, Texas

Acknowledgments

I would first like to acknowledge all the expert chapter authors associated with this textbook. Many of them have been close professional friends for many years, and I am deeply honored to be a colleague of theirs. I also worked closely with Mr. Robert Pancotti at McGraw-Hill in the production of the first edition of the book, and Ms. Cindy Yoo in production of the second edition. They are both effective editors. I would also like to extend my deepest thanks to the others at McGraw-Hill who have been involved in the production of this book. I am delighted that this book has been included in the Lange series of medical books, which has such a proud tradition in medical education.

Clinical Laboratory Reference Values

The conventional units in this table are the ones most commonly used in the United States. Outside the United States, SI units are the predominant nomenclature for laboratory test results. The base units in the SI system related to laboratory testing that are found in this table include the mole (amount of substance), meter (length), kilogram (mass), second (time), and Celsius (temperature).

Reference ranges vary depending on the instrument and the reagents used to perform the test. Therefore, the reference ranges shown in this table are only close approximations to the adult reference ranges found in an individual clinical laboratory. It is also important to understand that reference ranges can be significantly affected by age and sex.

Conversion factors are provided in the table to allow the reader to convert conventional units to SI units and vice versa. The conversion of the conventional unit to SI unit requires a multiplication with the conversion factor, and conversion of the SI unit to the conventional unit requires division by the conversion factor.

The sample fluid is sometimes highly restrictive. For example, coagulation tests must be performed using plasma samples and serum samples are unacceptable. For other compounds, both plasma samples and serum samples may be acceptable. However, there may be differences, often minor, in the results obtained using plasma versus serum. Potassium is 1 such compound in which reference ranges may be different for plasma and serum. There is a significant movement away from the use of serum in favor of plasma. The principal reason for this is that extra time is required for samples to clot so that serum may be generated. A sample collected into a tube with anticoagulant results in the generation of plasma rather than serum after the tube is centrifuged. The clotting step is omitted when plasma samples are prepared, and therefore the turnaround time for the performance of the test is shortened. In some circumstances, whole blood is used for analysis, but the number of tests performed using whole blood is very limited. Urine and other body fluids, such as pleural fluid and cerebrospinal fluid, are also used for testing. Some of the entries in the table are associated with a fluid other than plasma, serum, or whole blood.

	Specimen	Traditional Reference Interval	Traditional Units	Conversion Factor, Multiply →, ← Divide	SI Reference Interval	SI Units
Acetaminophen (therapeutic)	Serum, plasma	10-30	µg/mL	6.62	70-200	µmol/L
Acetoacetic acid	Serum, plasma	<1	mg/dL	0.098	<0.1	mmol/L
Acetone	Serum, plasma	<2.0	mg/dL	0.172	<0.34	mmol/L
Acetylcholinesterase	Red blood cells	5-10	U/mL	1	5-10	U/L
Activated partial thromboplastin time (APTT)	Whole blood	25-40	s	1	25-40	s
Adenosine deaminase[a]	Serum	11.5-25.0	U/L	0.017	0.20-0.43	µKat/L
Adrenocorticotropic hormone (ACTH) (see corticotropin)						
Alanine[b] (adult)	Plasma	1.87-5.88	mg/dL	112.2	210-661	µmol/day
Alanine aminotransferase (ALT, SGPT)[b]	Serum	10-40	U/L	1	10-40	U/L
Albumin[b]	Serum	3.5-5.0	g/dL	10	35-50	g/L
Alcohol (see ethanol, isopropanol, methanol)						
Alcohol dehydrogenase[a]	Serum	<2.8	U/L	0.017	<0.05	µKat/L
Aldolase[a,b]	Serum	1.0-7.5	U/L	0.017	0.02-0.13	µKat/L
Aldosterone[b] (upright)	Plasma	7-30	ng/dL	0.0277	0.19-0.83	nmol/L
Aldosterone	Urine, 24 h	3-20	µg/24 h	2.77	8-55	nmol/day
Alkaline phosphatase[b]	Serum	50-120	U/L	1	50-120	U/L
α_1-Acid glycoprotein	Serum	50-120	mg/dL	0.01	0.5-1.2	g/L
α_2-Macroglobulin	Serum	130-300	mg/dL	0.01	1.3-3.0	g/L
Alprazolam (therapeutic)	Serum, plasma	10-50	ng/mL	3.24	32-162	nmol/L
Aluminum	Serum, plasma	<6	ng/mL	37.06	0.0-222.4	nmol/L
Amikacin (therapeutic, peak)	Serum, plasma	20-30	µg/mL	1.71	34-52	µmol/L
Amino acid fractionation						
Alanine[b]	Plasma	1.87-5.89	mg/dL	112.2	210-661	µmol/L
α-Aminobutyric acid[b]	Plasma	0.08-0.36	mg/dL	97	8-35	µmol/L
Arginine[b]	Plasma	0.37-2.40	mg/dL	57.4	21-138	µmol/L
Asparagine[b]	Plasma	0.40-0.91	mg/dL	75.7	30-69	µmol/L
Aspartic acid[b]	Plasma	<0.3	mg/dL	75.1	<25	µmol/L
Citrulline[b]	Plasma	0.2-1.0	mg/dL	57.1	12-55	µmol/L
Cystine[b]	Plasma	0.40-1.40	mg/dL	83.3	33-117	µmol/L
Glutamic acid[b]	Plasma	0.2-2.8	mg/dL	67.97	15-190	µmol/L
Glutamine[b]	Plasma	6.1-10.2	mg/dL	68.42	420-700	µmol/L
Glycine[b]	Plasma	0.9-4.2	mg/dL	133.3	120-560	µmol/L
Histidine[b]	Plasma	0.5-1.7	mg/dL	64.5	32-110	µmol/L
Hydroxyproline[b]	Plasma	<0.55	mg/dL	76.3	<42	µmol/L
Isoleucine[b]	Plasma	0.5-1.3	mg/dL	76.24	40-100	µmol/L
Leucine[b]	Plasma	1.0-2.3	mg/dL	76.3	75-175	µmol/L
Lysine[b]	Plasma	1.2-3.5	mg/dL	68.5	80-240	µmol/L
Methionine[b]	Plasma	0.1-0.6	mg/dL	67.1	6-40	µmol/L
Ornithine[b]	Plasma	0.4-1.4	mg/dL	75.8	30-106	µmol/L
Phenylalanine[b]	Plasma	0.6-1.5	mg/dL	60.5	35-90	µmol/L
Proline[b]	Plasma	1.2-3.9	mg/dL	86.9	104-340	µmol/L
Serine[b]	Plasma	0.7-2.0	mg/dL	95.2	65-193	µmol/L
Taurine[b]	Plasma	0.3-2.1	mg/dL	80	24-168	µmol/L
Threonine[b]	Plasma	0.9-2.5	mg/dL	84	75-210	µmol/L
Tryptophan[b]	Plasma	0.5-1.5	mg/dL	48.97	25-73	µmol/L
Tyrosine[b]	Plasma	0.4-1.6	mg/dL	55.19	20-90	µmol/L
Valine[b]	Plasma	1.7-3.7	mg/dL	85.5	145-315	µmol/L

Continued next page—

	Specimen	Traditional Reference Interval	Traditional Units	Conversion Factor, Multiply →, ← Divide	SI Reference Interval	SI Units
α-Aminobutyric acid[b]	Plasma	0.08-0.36	mg/dL	97	8-35	μmol/L
Amiodarone (therapeutic)	Serum, plasma	0.5-2.5	μg/mL	1.55	0.8-3.9	μmol/L
δ-Aminolevulinic acid	Urine	1.0-7.0	mg/24 h	7.626	8-53	μmol/day
Amitriptyline (therapeutic)	Serum, plasma	80-250	ng/mL	3.61	289-903	nmol/L
Ammonia (as NH_3)[b]	Plasma	15-50	μg/dL	0.714	11-35	μmol/L
Amobarbital (therapeutic)	Serum	1-5	μg/mL	4.42	4-22	μmol/L
Amoxapine (therapeutic)	Plasma	200-600	ng/mL	1	200-600	μg/L
Amylase[a,b]	Serum	27-130	U/L	0.017	0.46-2.21	μKat/L
Androstenedione,[b] male	Serum	75-205	ng/dL	0.0349	2.6-7.2	nmol/L
Androstenedione,[b] female	Serum	85-275	ng/dL	0.0349	3.0-9.6	nmol/L
Angiotensin I	Plasma	<25	pg/mL	1	<25	ng/L
Angiotensin II	Plasma	10-60	pg/mL	1	10-60	ng/L
Angiotensin-converting enzyme (ACE)[a,b]	Serum	8-52	U/L	0.017	0.14-0.88	μKat/L
Anion gap (Na^+)–($Cl^- + HCO_3^-$)	Serum, plasma	8-16	mEq/L	1	8-16	nmol/L
Antidiuretic hormone (ADH, vasopressin) (varies with osmolality: 285-290 mOsm/kg)	Plasma	1-5	pg/mL	0.926	0.9-4.6	pmol/L
α_2-Antiplasmin	Plasma	80-130	%	0.01	0.8-1.3	Fraction of 1.0
Antithrombin III	Plasma	21-30	mg/dL	10	210-300	mg/L
Antithrombin III activity	Plasma	80-130	%	0.01	0.8-1.3	Fraction of 1.0
α_1-Antitrypsin	Serum	80-200	mg/dL	0.01	0.8-2.0	g/L
Apolipoprotein A[b]						
Male	Serum	80-151	mg/dL	0.01	0.8-1.5	g/L
Female	Serum	80-170	mg/dL	0.01	0.8-1.7	g/L
Apolipoprotein B[b]						
Male	Serum, plasma	50-123	mg/dL	0.01	0.5-1.2	g/L
Female	Serum, plasma	25-120	mg/dL	0.01	0.25-1.20	g/L
Arginine[b]	Plasma	0.37-2.40	mg/dL	57.4	21-138	μmol/L
Arsenic (As)	Whole blood	<23	μg/L	0.0133	<0.31	μmol/L
Arsenic (As), chronic poisoning	Whole blood	100-500	μg/L	0.0133	1.33-6.65	μmol/L
Arsenic (As), acute poisoning	Whole blood	600-9300	μg/L	0.0133	7.9-123.7	μmol/L
Ascorbate, ascorbic acid (see vitamin C)						
Asparagine[b]	Plasma	0.40-0.91	mg/dL	75.7	30-69	μmol/L
Aspartate aminotransferase (AST, SGOT)[a,b]	Serum	20-48	U/L	0.017	0.34-0.82	μKat/L
Aspartic acid[b]	Plasma	<0.3	mg/dL	75.1	<25	μmol/L
Atrial natriuretic hormone	Plasma	20-77	pg/mL	1	20-77	ng/L
Barbiturates (see individual drugs; pentobarbital, phenobarbital, thiopental)						
Basophils (see complete blood count, white blood cell count)						
Benzodiazepines (see individual drugs; alprazolam, chlordiazepoxide, diazepam, lorazepam)						

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	Specimen	Traditional Reference Interval	Traditional Units	Conversion Factor, Multiply →, ← Divide	SI Reference Interval	SI Units
Beryllium, toxic	Urine	>20	µg/L	0.111	>2.22	µmol/L
Bicarbonate	Plasma	21-28	mEq/L	1	21-28	mmol/L
Bile acids (total)	Serum	0.3-2.3	µg/mL	2.448	0.73-5.63	µmol/L
Bilirubin						
Total[b]	Serum	0.3-1.2	mg/dL	17.1	2-18	µmol/L
Direct (conjugated)	Serum	<0.2	mg/dL	17.1	<3.4	µmol/L
Biotin	Whole blood, serum	200-500	pg/mL	0.0041	0.82-2.05	nmol/L
Bismuth	Whole blood	1-12	µg/L	4.785	4.8-57.4	nmol/L
Blood gases						
P_{CO_2}	Arterial blood	35-45	mm Hg	1	35-45	mm Hg
pH	Arterial blood	7.35-7.45	—	1	7.35-7.45	—
P_{O_2}	Arterial blood	80-100	mm Hg	1	80-100	mm Hg
Blood urea nitrogen (BUN, see urea nitrogen)						
BNP	Plasma	<100	pg/mL	1	<100	pg/mL
Bupropion (Wellbutrin, Zyban)	Serum, plasma	25-100	ng/mL	3.62	91-362	nmol/L
C1 esterase inhibitor	Serum	12-30	mg/dL	0.01	0.12-0.30	g/L
C3 complement[b]	Serum	1200-1500	µg/mL	0.001	1.2-1.5	g/L
C4 complement[b]	Serum	350-600	µg/mL	0.001	0.35-0.60	g/L
CA125	Serum	<35	U/mL	1.0	<35	kU/L
CA19-9	Serum	<37	U/mL	1.0	<37	kU/L
CA15-3	Serum	<30	U/mL	1.0	<30	kU/L
CA27.29	Serum	<37.7	U/mL	1.0	<37.7	kU/L
Cadmium (nonsmoker)	Whole blood	0.3-1.2	µg/L	8.897	2.7-10.7	nmol/L
Caffeine (therapeutic, infants)	Serum, plasma	8-20	µg/mL	5.15	41-103	µmol/L
Calciferol (see vitamin D)						
Calcitonin	Serum, plasma	<19	pg/mL	1	<19	ng/L
Calcium, ionized	Serum	4.60-5.08	mg/dL	0.25	1.15-1.27	mmol/L
Calcium, total	Serum	8.2-10.2	mg/dL	0.25	2.05-2.55	mmol/L
Calcium, normal diet	Urine	<250	mg/24 h	0.025	<6.2	mmol/day
Carbamazepine (therapeutic)	Serum, plasma	8-12	µg/mL	4.23	34-51	µmol/L
Carbon dioxide	Serum, plasma, venous blood	22-28	mEq/L	1	22-28	mmol/L
Carboxyhemoglobin (carbon monoxide), as fraction of hemoglobin saturation						
Nonsmoker	Whole blood	<2.0	%	0.01	<0.02	Fraction of 1.0
Toxic	Whole blood	>20	%	0.01	>0.2	Fraction of 1.0
β-Carotene	Serum	10-85	µg/dL	0.0186	0.2-1.6	µmol/L
Catecholamines, total (see norepinephrine)						
CEA, nonsmoker	Serum	<3	ng/mL	1.0	<3	µg/L
CEA, smoker	Serum	<5	ng/mL	1.0	<5	µg/L
Ceruloplasmin[b]	Serum	20-40	mg/dL	10	200-400	mg/L
Chloramphenicol (therapeutic)	Serum	10-25	µg/mL	3.1	31-77	µmol/L

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	Specimen	Traditional Reference Interval	Traditional Units	Conversion Factor, Multiply →, ← Divide	SI Reference Interval	SI Units
Chlordiazepoxide (therapeutic)	Serum, plasma	0.7-1.0	µg/mL	3.34	2.3-3.3	µmol/L
Chloride	Serum, plasma	96-106	mEq/L	1	96-106	mmol/L
Chloride	CSF	118-132	mEq/L	1	118-132	mmol/L
Chlorpromazine (therapeutic, adult)	Plasma	50-300	ng/mL	3.14	157-942	nmol/L
Chlorpromazine (therapeutic, child)	Plasma	40-80	ng/mL	3.14	126-251	nmol/L
Chlorpropamide (therapeutic)	Plasma	75-250	mg/L	3.61	270-900	µmol/L
Cholesterol, high-density lipoproteins (HDL)	Plasma	40-60	mg/dL	0.02586	1.03-1.55	mmol/L
Cholesterol, low-density lipoproteins (LDL)[b]						
Optimal	Plasma	<100	mg/dL	0.02586	<2.59	mmol/L
Near optimal	Plasma	100-129	mg/dL	0.02586	2.59-3.34	mmol/L
Borderline high	Plasma	130-159	mg/dL	0.02586	3.37-4.12	mmol/L
High	Plasma	160-189	mg/dL	0.02586	4.15-4.90	mmol/L
Very high	Plasma	>190	mg/dL	0.02586	>4.90	mmol/L
Cholesterol (total), adult						
Desirable	Serum	<200	mg/dL	0.02586	<5.17	mmol/L
Borderline high	Serum	200-239	mg/dL	0.02586	5.17-6.18	mmol/L
High	Serum	>240	mg/dL	0.02586	>6.21	mmol/L
Cholesterol (total), children						
Desirable	Serum	<170	mg/dL	0.02586	4.40	mmol/L
Borderline high	Serum	170-199	mg/dL	0.02586	4.40-5.15	mmol/L
High	Serum	>200	mg/dL	0.02586	>5.18	mmol/L
Chromium	Whole blood	0.7-28.0	µg/L	19.2	13.4-538.6	nmol/L
Citrate	Serum	1.2-3.0	mg/dL	52.05	60-160	µmol/L
Citrulline[b]	Plasma	0.4-2.4	mg/dL	57.1	20-135	µmol/L
Clonazepam (therapeutic)	Serum	15-60	ng/mL	3.17	48-190	nmol/L
Coagulation factor I (fibrinogen)	Plasma	150-400	mg/dL	0.01	1.5-4.0	g/L
Coagulation factor II (prothrombin)	Plasma	60-140	%	0.01	0.60-1.40	Fraction of 1.0
Coagulation factor V	Plasma	60-140	%	0.01	0.60-1.40	Fraction of 1.0
Coagulation factor VII	Plasma	60-140	%	0.01	0.60-1.40	Fraction of 1.0
Coagulation factor VIII	Plasma	50-200	%	0.01	0.50-2.00	Fraction of 1.0
Coagulation factor IX	Plasma	60-140	%	0.01	0.60-1.40	Fraction of 1.0
Coagulation factor X	Plasma	60-140	%	0.01	0.60-1.40	Fraction of 1.0
Coagulation factor XI	Plasma	60-140	%	0.01	0.60-1.40	Fraction of 1.0
Coagulation factor XII	Plasma	60-140	%	0.01	0.60-1.40	Fraction of 1.0
Cobalt	Serum	<1.0	µg/L	16.97	<17	nmol/L
Codeine (therapeutic)	Serum	10-100	ng/mL	3.34	33-334	nmol/L
Complete blood count (CBC)						
Hematocrit[b]						
Male	Whole blood	41-50	%	0.01	0.41-0.50	Fraction of 1.0
Female	Whole blood	35-45	%	0.01	0.35-0.45	Fraction of 1.0
Hemoglobin (mass concentration)[b]						
Male	Whole blood	13.5-17.5	g/dL	10	135-175	g/L
Female	Whole blood	12.0-15.5	g/dL	10	120-155	g/L

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	Specimen	Traditional Reference Interval	Traditional Units	Conversion Factor, Multiply →, ← Divide	SI Reference Interval	SI Units
Hemoglobin (substance concentration, Hb [Fe])						
Male	Whole blood	13.6-17.2	g/dL	0.6206	8.44-10.65	mmol/L
Female	Whole blood	12.0-15.0	g/dL	0.6206	7.45-9.30	mmol/L
Mean corpuscular hemoglobin (MCH), mass concentration[b]	Whole blood	27-33	pg/cell	1	27-33	pg/cell
MCH, substance concentration, Hb [Fe]	Whole blood	27-33	pg/cell	0.06206	1.70-2.05	fmol
Mean corpuscular hemoglobin concentration (MCHC), mass concentration	Whole blood	33-37	g Hb/dL	10	330-370	g Hb/L
MCHC, substance concentration, Hb [Fe]	Whole blood	33-37	g Hb/dL	0.6206	20-23	mmol/L
Mean cell volume (MCV)[b]	Whole blood	80-100	μm^3	1	80-100	fL
Platelet count	Whole blood	150-450	$10^3\ \mu L^{-1}$	1	150-450	$10^9\ L^{-1}$
Red blood cell count						
Female	Whole blood	3.9-5.5	$10^6\ \mu L^{-1}$	1	3.9-5.5	$10^{12}\ L^{-1}$
Male	Whole blood	4.6-6.0	$10^6\ \mu L^{-1}$	1	4.6-6.0	$10^{12}\ L^{-1}$
Reticulocyte count[b]	Whole blood	25-75	$10^3\ \mu L^{-1}$	1	25-75	$10^9\ L^{-1}$
Reticulocyte count[b] (fraction)	Whole blood	0.5-1.5	% of RBCs	0.01	0.005-0.015	Fraction of RBCs
White blood cell count[b]	Whole blood	4.5-11.0	$10^3\ \mu L^{-1}$	1	4.5-11.0	$10^9\ L^{-1}$
Differential count[b] (absolute)						
Neutrophils	Whole blood	1800-7800	μL^{-1}	1	1.8-7.8	$10^9\ L^{-1}$
Bands	Whole blood	0-700	μL^{-1}	1	0.00-0.70	$10^9\ L^{-1}$
Lymphocytes	Whole blood	1000-4800	μL^{-1}	1	1.0-4.8	$10^9\ L^{-1}$
Monocytes	Whole blood	0-800	μL^{-1}	1	0.00-0.80	$10^9\ L^{-1}$
Eosinophils	Whole blood	0-450	μL^{-1}	1	0.00-0.45	$10^9\ L^{-1}$
Basophils	Whole blood	0-200	μL^{-1}	1	0.00-0.20	$10^9\ L^{-1}$
Differential count[b] (number fraction)						
Neutrophils	Whole blood	56	%	0.01	0.56	Fraction of 1.0
Bands	Whole blood	3	%	0.01	0.03	Fraction of 1.0
Lymphocytes	Whole blood	34	%	0.01	0.34	Fraction of 1.0
Monocytes	Whole blood	4	%	0.01	0.04	Fraction of 1.0
Eosinophils	Whole blood	2.7	%	0.01	0.027	Fraction of 1.0
Basophils	Whole blood	0.3	%	0.01	0.003	Fraction of 1.0
Copper[b]	Serum	70-140	µg/dL	0.1574	11.0-22.0	µmol/L
Coproporphyrin	Urine	<200	µg/24 h	1.527	<300	nmol/day
Corticotropin[b] (08:00)	Plasma	<120	pg/mL	0.22	<26	pmol/L
Cortisol, total[b]						
08:00	Plasma	5-25	µg/dL	27.6	138-690	nmol/L
16:00	Plasma	3-16	µg/dL	27.6	83-442	nmol/L
20:00	Plasma	<50% of 08:00	µg/dL	1	<50% of 08:00	nmol/L
Cortisol, free[b]	Urine	30-100	µg/24 h	2.76	80-280	nmol/day
Cotinine (smoker)	Plasma	16-145	ng/mL	5.68	91-823	nmol/L
C-peptide	Serum	0.5-3.5	ng/mL	0.333	0.17-1.17	nmol/L
Creatine, male	Serum	0.2-0.7	mg/dL	76.3	15.3-53.3	µmol/L
Creatine, female	Serum	0.3-0.9	mg/dL	76.3	22.9-68.6	µmol/L
Creatine kinase (CK)[a]	Serum	50-200	U/L	0.017	0.85-3.40	µKat/L
CK-MB fraction	Serum	<6	%	0.01	<0.06	Fraction of 1.0
Creatinine[b]	Serum, plasma	0.6-1.2	mg/dL	88.4	53-106	µmol/L
Creatinine	Urine	1-2	g/24 h	8.84	8.8-17.7	mmol/day
Creatinine clearance, glomerular filtration rate	Serum, urine	75-125	mL/min/1.73 m^2	0.00963	0.72-1.2	mL/s/m^2

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