## Laboratory Test Handbook

4<sup>th</sup> Edition

with Key Word Index

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# Laboratory Test

4th Edition . with **Key Word Index** 

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#### NOTICE

This handbook is intended to serve as a useful reference and not as a complete laboratory testing resource. The explosion of information in many directions, in multiple scientific disciplines, with advances in laboratory techniques, and continuing evolution of knowledge requires constant scholarship. The publication covers common, as well as many esoteric testing procedures. The authors, editors, reviewers, contributors, and publishers cannot be responsible for the continued currency of the information or for any errors or omissions in this book or for any consequences arising therefrom. Because of the dynamic nature of laboratory medicine as a discipline, readers are advised that decisions regarding diagnosis and treatment must be based on the independent judgment of the clinician. The editors are not responsible for any inaccuracy of quotation or for any false or misleading implication that may arise due to the text.

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## Laboratory Test Handbook

— 4<sup>th</sup> Edition with Key Word Index



#### IN MEMORY OF - PAUL R. FINLEY, MD

The University of Arizona was in need of a pathologist to head up clinical chemistry when Dr Paul Finley dropped in one day. He was interested in relocating to the southwest because his wife, Cici, an accomplished potter, wanted to be near the well-springs of southwestern pottery. With his roots in private practice, Paul was deeply suspicious of academic medicine. We emphasized that our department was indeed clinically oriented, but I still remember, after a recruitment outing, a colleague whispering "I'm pretty sure she's bought the farm, but I still don't know about him." Paul did join us in 1972 and remained on the job until his death in 1994.

A native of St Paul, Minnesota, Paul graduated in medicine from the University of Minnesota, interned in Seattle, and did his pathology residency at the University of Minnesota. After advanced work in clinical chemistry in London, England, Paul returned to Minnesota as Director of Clinical Laboratories for the Fairview Hospital system. Twelve years later, he came to us, already well known on the national scene in clinical chemistry, as well as in the brand new applications of computers to clinical pathology. He was a great and ingenious methodologist. Once persuaded that he should let the world know about his innovations, he produced over a hundred scientific papers. The Chemistry chapter of the 3rd edition of the *Laboratory Test Handbook*, 1994, is among his many accomplishments. Paul was particularly active in therapeutic drug monitoring, polymerase chain reaction technology, and DNA fingerprinting. In the last 10 years, he took up music again (he had led a dance band in college) and played clarinet in various jazz, swing, and symphonic groups in Tucson.

Always the best of colleagues and friends, Paul was a keen observer of humanity, with a puckish sense of humor and an irreverent attitude that enlivened many faculty meetings. He was always ready to help with someone else's project, no matter how busy he was. God knows, we miss him.

Douglas W. Huestis, MD

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#### **FOREWORD**

The first version of this publication, released in 1984, was an effort by four community-based pathologists to include in a single volume all the routine and many of the more specialized analyses available in a modern clinical laboratory. The next edition represented the efforts of additional authors. The number of contributors to this edition has been considerably expanded. All are respected authorities in their fields of expertise. It is hoped that this enlarged edition is at once current and more comprehensive.

As in the previous edition, information about each laboratory procedure is presented in a standardized format, including test name and synonyms, patient care recommendations, specimen requirements, reference ranges, interpretive information, footnotes, and references. Each entry is complete in itself, but the whole work is extensively cross-referenced and indexed. The handbook is intended as a convenient reference resource for clinicians, pathologists, residents, medical and nursing students, medical technologists, ancillary medical personnel, and medical records staff.

We have devoted a great deal of effort to **clinical relevance**. We have been fortunate to have available to us the Lexi-Comp Pathfinder<sup>TM</sup> system, the Medline® system, and the computer publishing expertise of Lexi-Comp Inc. These assets have made possible extensive internal cross-referencing of entries, the inclusion, even late in the publishing process, of the most current references, and the Key Word Index.

The new edition has greatly expanded coverage of laboratory assays directly and indirectly related to molecular pathology; other additions include expanded treatments of clinical virology and therapeutic drug monitoring, and many new entries in the realm of clinical immunology and other subspecialties of clinical laboratory medicine. A new addition, Cytogenetic test listings, reflects exciting contemporary advances in laboratory medicine.

To survive in today's atmosphere of change in healthcare, clinicians must order the **needed** test, obtain reliable and accurate results, and have access to current clinical laboratory information. This book, we hope, will assist with ordering and such access. To attain accurate and reliable test results will depend in large measure upon quality attributes of the laboratory performing the analyses.

It is the authors' desire that this newest edition serve as a guide for the clinician and laboratorian, assist in obtaining the appropriate specimen for analysis, and provide avenues toward interpretation and relevance in the interest of optimal patient care.

#### **ACKNOWLEDGMENTS**

The Laboratory Test Handbook with Key Word Index exists in its present form as the result of the concerted efforts of many individuals. The publisher and president of Lexi-Comp Inc, Mr Robert D. Kerscher, deserves much credit for bringing the concept of such a book to fruition. His dedication to the project and his support and development of the many unique and innovative features included in the book (eg, format, internal cross-references, comprehensive indexing and Key Word Index) contribute substantially to the content and usefulness of the book.

Diane M. Harbart, MT (ASCP), medical editor, provided invaluable contributions, and her patience with the author's enumerable drafts, revisions, deletions, additions, and enhancements deserves special commendation.

Other members of the Lexi-Comp staff whose contributions were invaluable and whose efforts are especially appreciated include Barbara F. Kerscher, production manager; Lynn D. Coppinger, managing editor; Alexandra J. Hart, composition specialist; Leonard L. Lance, pharmacist; John Janosik, PharmD; Jacqueline L. Mizer, Jil R. Neuman, Jeanne E. Wilson, Tracey Reinecke, Leslie Ruggles, Beth Daulbaugh, and Julie Weekes, production assistants; Jeff J. Zaccagnini, Jerry M. Reeves, and Brian B. Vossler, sales managers; Edmund A. Harbart, vice-president, custom publishing division; Jack L. Stones, vice-president, reference publishing division; and Jay L. Katzen, product manager. The complex computer programming required for the production of this book was provided by Dennis P. Smithers, David C. Marcus, Kenneth Hughes, and Sean Conrad, system analysts, under the direction of Thury L. O'Connor, vice-president.

Lowell L. Tilzer, MD, PhD deserves special commendation and expression of appreciation. Dr Tilzer provided insight in a number of his areas of expertise, orchestrated many portions of the *Laboratory Test Handbook*, and provided valuable author recommendations. Unanticipated professional obligations prevented him from providing all the contributions he had intended.

The editors express appreciation to Charles W. Gorodetzky, MD, PhD for his review and contributions to the Therapeutic Drug Monitoring entries.

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After completing his undergraduate work at MIT (BS, 1958), Dr Gorodetzky earned his MD degree at Boston University School of Medicine (1962), followed by an Internal Medicine internship at Boston City Hospital, and a PhD in Pharmacology at the University of Kentucky (1975).

Dr Gorodetzky spent 21 years in intramural NIH research in substance abuse at the National Institute on Drug Abuse, Addiction Research Center in Lexington, Kentucky (1963-1984). His major research interests were the human pharmacology and metabolism of drugs of abuse. He served as the director of the Lexington Center from 1979 to 1984. In 1984, Dr Gorodetzky joined the pharmaceutical industry and is currently Vice President of Global Therapeutic Area, CNS in the Drug Development Department at Hoechst Marion Roussel Inc in Kansas City, Missouri.

Dr Gorodetzky has authored or co-authored over 100 papers, book chapters, and books and has served on numerous government committees, including an FDA advisory committee and grant review committees. He holds or has held adjunct full professorships at the medical schools of the University of Kentucky, University of Louisville, and University of North Carolina. He served as an advisor and consultant to the Special Action Office on Drug Abuse Prevention, CDC and NIDA in the development and implementation of the Proficiency Testing Program for Drugs of Abuse.

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Dr Grady received his PhD from St Louis University. He joined the staff of the University of Kansas Medical Center in 1950 as Assistant Professor and Director of Clinical Chemistry. He became Full Professor of Pathology in 1965. During this period he was a consultant in Clinical Chemistry to several area hospitals.

He left the Medical Center in 1970 to become Director of Clinical Chemistry for Baptist Medical Center. He retired from this position in 1988.

He is currently Full Professor of Pathology at the University of Missouri Kansas City School of Medicine and Co-Director of Clinical Chemistry at Truman Medical Center.

Dr Grady is a member of the American Association for Clinical Chemistry and has been on the Board of Directors of that organization. He is a member of the American Chemical Society. He is on the Board of Directors of the American Board of Clinical Chemistry and is certified by that body in Clinical Chemistry and Toxicological Chemistry.

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Dr Gray received his bachelor's degree from the University of North Carolina at Chapel Hill and his master's and doctorate degrees from Wake Forest University (Bowman Gray School of Medicine). He received his postdoctoral training in Clinical Microbiology and Infectious Diseases at the Mayo Clinic.

Dr Gray has been the Director of Microbiology at Bethesda Hospitals in Cincinnati, Ohio for the last 5 years. He is a Volunteer Associate Professor of Pathology and Laboratory Medicine at the University of Cincinnati College of Medicine, is a Diplomate of the American Board of Medical Microbiology, and is on the editorial board of the Journal of Clinical Microbiology. In addition, he is an active member of the American Society for Microbiology, the American Board of Medical Microbiology, and the South Central Association for Clinical Microbiology.

Dr Gray's background includes 12 years of research in the pathogenesis of infectious diseases (ocular and pulmonary bacterial infections, electron microscopy) and the publication of many research, review, chapter, and book publications.

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Dr Hinrichs is an Associate Professor in the Department of Pathology and Microbiology at the University of Nebraska Medical Center (UNMC) in Omaha, Nebraska. He also holds joint appointments in the Department of Orthopedics and the Eppley Cancer Research Institute for Cancer and Allied Diseases. Dr Hinrichs is Director of Clinical Microbiology and Virology at UNMC and is also Director of the Molecular Diagnostics Group which coordinates development of molecular diagnostic assays and establishes validation criteria. His clinical research involves the role of viruses in the immune-compromised host with particular emphasis on bone marrow transplant and solid organ recipients.

Dr Hinrichs' research interests focus on the role of viruses in oncogenesis, specifically how viruses disrupt cellular control of transcription. Current funded studies investigate the structural interaction between transcription factors and their DNA-binding motifs.

#### Rebecca T. Horvat, PhD

Dr Horvat received her doctorate from the University of Kansas Medical Center, Department of Microbiology. After completing her doctorate, Dr Horvat was awarded a postdoctoral fellowship from the American Cancer Society. Subsequent to her postdoctoral fellowship she worked as a Technical Director in the Clinical Laboratories at the University of Kansas Medical Center. In this capacity, she worked with Virology, Microbiology, and Hematology in developing new diagnostic tests based on nucleic acid analysis. Currently, Dr Horvat is an Assistant Professor in the Department of Pathology and Laboratory Medicine at the University of Kansas Medical Center in Kansas City, Kansas.

Dr Horvat's research interest involves the investigation of human herpes viruses in the development of leukemias and lymphomas. She is also interested in the diagnostic potential of nucleic acid detection, especially in immunocompromised patients. In her current position, she assists in the administration of the Microbiology and Virology sections of the clinical laboratories. This involves the education and teaching of residents and medical students, developing and instituting new diagnostic technology, and coordinating quality assurance in the Microbiology and Virology sections. In addition, Dr Horvat is the Clinical Microbiology consultant at the Dwight D. Eisenhower Veterans Administration Medical Center in Leavenworth, Kansas.

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#### Douglas W. Huestis, MD

Dr Huestis received his MD degree from McGill University, Montreal, Canada, in 1948 and did postgraduate training in pathology and related fields in Canada, Sweden, England, and the U.S.A. After a few years of general hospital pathology, he began concentrating on the field of blood transfusion and immunohematology in Chicago in 1960 then moved to Tucson to the then new medical school at the University of Arizona in 1969.

His major work while in Chicago was on erythrocyte antigens and antibodies and their relationship to difficulties and complications of blood transfusion. He also did some early work on the development of frozen blood systems, including the use of a unique vaporphase liquid nitrogen storage freezer and a simplified thawing-deglycerolizing system utilizing invert sugar. In Arizona, he developed a procedure for the collection of granulocytes by intermittent flow centrifugation and applied this to the special transfusion support of patients with cancer and leukemia. He has had much to do with the development of technical procedures with blood cell separators for the collection of white blood cells and platelets for transfusion, and for the treatment of leukemic patients with a dangerous excess of white blood cells or platelets. Most recently, he has been increasingly involved in transplantation immunology and in the rapidly developing field of plasma exchange. These various activities have resulted in over 90 scientific articles.

Dr Huestis has served as a director and vice-president of the American Association of Blood Banks and on many of its committees and was editor of two editions of its Technical Manual. He received the John Elliott award of that association for such activities. He has been an associate editor of the journal Transfusion since 1968. He has served on several advisory committees for the National Institutes of Health, has been a consultant to the U.S. Army and Air Force, and took part in two scientific exchange visits to the Soviet Union under the Soviet-American Health Exchange.

He considers one of his most important achievements to be the textbook Practical Blood Transfusion, coauthored with Joseph R. Bove and John Case and published by Little, Brown & Co. The 4th edition of this book appeared in 1988.

#### Daniel H. Jacobs, MD

Dr Daniel H. Jacobs is Assistant Professor of Neurology at Tufts University in Boston, Massachusetts. Dr Jacobs is specialized in behavioral neurology and higher cortical function and has published original research in the fields of aphasia, attention and neglect, and higher cortical function problems of patients with epilepsy.

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#### David S. Jacobs, MD, FACP

Dr Jacobs was Director of Laboratories at Providence Medical Center for 29 years, leaving that position in 1994. He served as a member of the institutional Credentials Committee for 20 years. During Dr Jacobs' tenure as Director, then Medical Director of the School of Medical Technology, 173 medical technologists graduated from 1965 to 1990.

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Dr Jacobs' special interests include general pathology, particularly surgical pathology, interpretation of clinical laboratory tests, and transfusion medicine. His publications address topics in surgical pathology and the clinical relevance of laboratory testing.

He received his premedical education at the University of Michigan. Entering the UM Medical School in the "Letters and Medicine" program, Dr Jacobs remained at Michigan as a general rotating intern, then did his residency in Anatomic and Clinical Pathology at the same institution. Following service in the U.S. Army Medical Corps as a pathologist with 13 months residency, he returned to Ann Arbor and completed the pathology program under Drs A. J. French and M. R. Abell. He then spent an additional year in Chicago in clinical pathology with Drs Israel Davidsohn and Douglas Huestis. Dr Jacobs is certified in both Anatomic and Clinical Pathology by the American Board of Pathology.

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Dr Kasten was a principal author of the first edition of the *Laboratory Test Handbook* and the author of the *Physicians DRG Handbook* and a principal author of the *Infectious Diseases Handbook*. His writings include articles on the use of bar codes in the clinical laboratory, optical storage of laboratory data and the computerized medical record. He has presented numerous lectures and seminars on the subjects of improving workflow in the laboratory, and total quality management. He is a member of the editorial board for Lexi-Comp Inc's medical publishing.

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Dr Tilzer received his medical degree and PhD in a combined medical science program from the Kansas University Medical Center in Kansas City, Kansas and did his residency in Anatomic and Clinical Pathology there. Certified in both Anatomic and Clinical Pathology, Dr Tilzer served at Kansas University Medical Center as associate Medical Director for 14 years and became full Professor, in charge of Hematology, Blood Bank, Clinical Chemistry, and Lab Computer. His research interests included laboratory computing (especially use of bar codes in specimen management, which he pioneered in the United States) and diagnostic Molecular Biology. He has extensive teaching experience with medical technology students, medical students, graduate students, and pathology residents. He holds several patents in the molecular biology field.

In 1992, Dr Tilzer moved to the Community Blood Center of Greater Kansas City in Kansas City, Missouri. He is Associate Medical Director. He is working on stem cell collection and bone marrow processing.

Dr Tilzer is a member of the American Association of Blood Banks, College of American Pathologists, American Association of Clinical Chemists, American Association for the Advancement of Science, and the Metropolitan Medical Society of Kansas City.

#### Patricia G. Tweeddale, Ed D, CT(ASCP)

Dr Tweeddale is the general supervisor of cytology at Hays Pathology Laboratories, Hays, Kansas. She received her cytology training at Muhlenberg Hospital, Plainfield, New Jersey in 1973, and her doctorate in Educational Administration from East Texas State University in 1991. She has served as President of the New Jersey State Society of Cytotechnology, established the first Cytology Department in Saudia Arabia, and was a founding member of the American Society for Cytotechnology.

#### Glen R. Willie, MD

Dr Willie earned his Masters in Biochemistry and Doctor of Medicine at the University of Minnesota in 1976 with research studying the receptor on the bacterial ribosome binding the antibiotic fusidic acid. He then completed his residency in Internal Medicine at Sinai Hospital of Detroit and a Nephrology Fellowship at Henry Ford Hospital in Detroit.

Since then, he has held teaching positions at Texas A&M University School of Medicine in Nephrology and Nutrition, currently as Assistant Professor of Medicine. Special areas of interest include nutrition, trace metals, metabolic bone disease, and applications of computers to the practice of medicine.

Dr Willie is a member of the American College of Physicians, Texas Medical Association, Renal Physicians Association, and the International Society of Nephrology.

#### HOW TO USE THIS HANDBOOK

The Laboratory Test Handbook with Key Word Index is arranged alphabetically by major clinical laboratory disciplines: Anatomic Pathology, Chemistry, Coagulation, Cytogenetics, Cytopathology, Hematology, Immunology and Serology, Microbiology, Molecular Pathology, Therapeutic Drug Monitoring/Toxicology/Drugs of Abuse, Trace Elements, Transfusion Service (Blood Bank), Urinalysis and Clinical Microscopy, and Virology. A general section, Specimen Collection, precedes the individual laboratory monographs. A section providing overviews of selected topics, including statistics, is entitled "Statistics, the Normal Range and the Ulysses Syndrome". The laboratory tests are listed alphabetically within each section and cross-referenced with synonyms referring the user to the actual test name. A brief introduction before each section provides general information about each major discipline.

Each individual test listing is arranged in a consistent format providing specific types of information. The fields of information include the following. The test name; the current procedural terminology (CPT) code is listed for most testsrelated information which lists other tests that may be of interest and the page number where these tests can be found; synonyms or other common names for a test are noted; topics or procedures which are not exact synonyms but have similar instructions or require similar consideration are referred to under the applies to heading; tests replaced by a current procedure are noted; a definition of procedures included within the named test is given under test includes; an abstract or overview of the test is often provided; patient preparation includes patient care considerations prior to the collection of specimen or performance of a test; aftercare includes patient care considerations following the collection of a specimen or performance of a procedure; the specific specimen required, the container, sampling time, specific collection instructions, specimen storage instructions, causes for rejection of the specimen by the laboratory, turnaround time when relevant, and special instructions indicating additional pertinent considerations relating to the specimen are all listed; a discussion of basic information relevant to the clinical application of the test, including reference (or normal) range, critical values, and possible panic ranges, specific use of the test, limitations of the test method, specific test methodology where appropriate, contraindications to the test, and additional information which may contribute to the interpretation or utilization of a the test are given.

#### **Footnotes and References**

The bibliographic information provided with test listings may include footnotes referring to specific literature quotations, specific points of information, or opinions. Selected general references are provided as sources of information concerning the individual test listings. Footnotes and references are intended, as well, to expedite access to useful literature. Many are current, but the alert reader will find an important reference from 1785.

#### **Acronyms and Abbreviations Glossary**

This glossary provides a useful listing of many acronyms and abbreviations commonly associated with laboratory medicine. We offer this glossary not as an exhaustive authoritative list, but more as a guide to assist in interpreting frequently used terminology.

#### **Key Word Index**

The Key Word Index is not intended in any way to suggest patterns of physicians' orders, nor is it complete. Rather, it is the intent of the authors and editors to make information easier to find and utilize in order to support better patient care.

The Key Word Index provides a reference to test names based on a diagnostic property, disease entity, organ system, or syndrome for which the test may be useful. It provides lists of specific tests. Some may support possible clinical diagnoses or help to rule out other diagnostic possibilities.

Each laboratory test which may be relevant to the indexed diagnosis is listed and weighted. Two symbols (••) indicate that the test strongly supports a diagnosis or entity, that is, it significantly contributes to documentation of the diagnosis if the expected result is found. A single symbol (•) indicates a test frequently used in the diagnosis or management of the particular disease. The other listed tests may be useful on a selective basis with consideration of clinical factors and specific aspects of the case. A negative laboratory test result can be, and frequently is, highly relevant in the practice of medicine

Clinical diagnosis is determined following history, physical examination, and usual laboratory investigation with selected additional tests. Complete blood count (CBC) with differential, urinalysis, and a basic chemistry profile are not only good medicine, they are in fact cost effective. Thus, these basic tests are excluded from much of the Key Word Index.

Diagnoses with International Classification of Disease—Ninth Revision—Clinical Modification (ICD-9-CM) codes are indicated within the [] symbol.

#### **CPT Index**

CPT codes are provided with each test for reference, as a basis for documentation of diagnostic procedures performed and to facilitate financial and patient record keeping. The codes are current. Applications of codes may vary by region of the country and in some instances the application of a specific code to a given procedure is a matter of individual interpretation.

Any five-digit numeric Physicians' Current Procedural Terminology, (CPT) codes service descriptions, instructions and/or guidelines are Copyright 1995 American Medical Association. All rights reserved.

CPT is a listing of descriptive terms and five-digit numeric identifying codes and modifiers for reporting medical services performed by physicians. This presentation includes only CPT descriptive terms, numeric identifying codes and modifiers for reporting medical services, and procedures that were selected by Lexi-Comp Inc for inclusion in this publication.

The most current CPT is available from the American Medical Association.

No fee schedules, basic unit values, relative value guides, conversion factors or scales or components thereof are included in CPT.

Lexi-Comp has selected certain CPT codes and service/procedure descriptions and assigned them to various specialty groups. The listing of a CPT service or procedure description and its code number in this publication does not restrict its

use to a particular specialty group. Any procedure or service in this publication may be used to designate the services rendered by any qualified physician.

The AMA assumes no responsibility for the consequences attributable to or related to any use or interpretation of any information or views contained in or not contained in this publication.

#### **Alphabetical Index**

The most expedient method for locating a given test is the Alphabetical Index in the last section of this handbook. Test names and synonyms are listed and the page number on which the test description may be found is indicated.

### STATISTICS, THE NORMAL RANGE, AND THE ULYSSES SYNDROME

or

#### A TEST IN SEARCH OF A DISEASE

David S. Jacobs, MD

#### Eugene S. Olsowka, MD, PhD

During and after the Trojan War, Ulysses was away from home 20 years. While traveling, he was involved in a series of frequently dangerous and sometimes needless adventures. The syndrome<sup>1</sup> was named for Ulysses because patients with it, although healthy at the beginning, journey through clinical investigations and undergo a number of experiences new to them before they once again reach the safe harbor of being considered healthy.

The bottom line of complex clinical, technical, and statistical data leads to a decision – whether or not a given laboratory report is normal for a particular patient.

The College of American Pathologists, in setting standards for their Inspection and Accreditation Program for Clinical Laboratories, advocates that reference values (normal values) for each test should be provided when possible. Two modern laboratory realities must be recognized:

- 1. A reference range is required for the interpretation of most laboratory tests, and
- 2. It may not be possible to provide an appropriate reference range in all cases.

It is important to recognize that laboratory methods and types of equipment greatly influence the outcome of any given test. The most relevant reference ranges are those generated by the laboratory performing the assay. Ability of a laboratory to provide meaningful reference ranges is limited by many factors.

Purely statistical approaches are unsatisfactory. For instance, since coronary arterial disease is rampant in present day America, we cannot base "normal" ranges for serum lipids on a Gaussian distribution.

Most tests do not have sharp cutoff points between normal and abnormal. "Normal" curves can be bell shaped, but they are often skewed.

Nominally, "normal" findings may have diagnostic significance in an appropriate setting. Thus, efforts to increase our knowledge of the significance of normal range, and thus narrow the normal range for a given patient, can add value to "normal" results.

The effects of drugs on clinical laboratory tests have been exhaustively reviewed<sup>3</sup> and are therefore not emphasized in this book.

With computers, laboratories can stratify normal ranges by age and sex. We would no more expect a college varsity athlete and a great-grandmother to have the same normal ranges for clinical laboratory examinations, than we would expect them to have the same hat or shoe size. Such stratification remains at the fringe of clinical documentation, and relatively few published studies are available which are pertinent to normal ranges for all of the tests done by most laboratories. Clinical input is continually needed to improve available normal ranges.

Special situations in which computer generated normal ranges may be inappropriate, misleading, or nonexistent include the following.

- 1. **Glucose:** A computer may only be provided with normal ranges for fasting plasma glucose. Blood sugar levels have not been done in laboratories in years; serum and plasma are used.
- 2. Pregnancy: The well known increases in alkaline phosphatase, plasma volume, glomerular filtration rate, and hepatic protein synthesis, decreases in urea nitrogen, sodium, osmolality, albumin, and other changes accompanying pregnancy are not always taken into consideration when normal ranges are reported in pregnant individuals. (The laboratory is commonly not aware if an individual is pregnant, and if so, the length of gestation. Many laboratories do not have normal ranges for pregnancy available.) Cortisol, alpha<sub>1</sub>-fetoprotein, alpha<sub>1</sub>-antitrypsin, amylase, cholesterol, and triglycerides may increase.
- 3. Athletes and Exercise: Athletes are apt to have slight elevations of urea nitrogen and LD, as well as depressions of pulse rate. After physical exercise, significant elevations of total CK are commonplace and creatinine, potassium, uric acid, bilirubin, leukocyte count, haptoglobin, transferrin, and BUN may increase. Exercise increases HDLC, lactate, and may increase aldolase.
- 4. The First Month of Life: Tremendous shifts in normal ranges occur during the first month of life. Some tests ideally should be stratified depending on whether the patient is premature or term, and others (hemoglobin, bilirubin) change significantly during the first month. Many computers cannot stratify in so many intervals. For such tests, a number of normal ranges exist depending upon the age in days in the first month of life, prematurity or term, and other factors.
- 5. Posture: Posture is reported to change the normal range for a number of tests total protein, albumin, calcium, hemoglobin and hematocrit, plasma renin activity, urinary catecholamines, and perhaps alkaline phosphatase, cholesterol,<sup>5</sup> ALT (SGPT), and iron. Levels of such substances have been described as being higher in an upright position than in a reclining position. Consider that in the reclining individual, interstitial fluid enters the vascular compartment, diluting constituents which the clinical laboratory measures. On standing, the venous pressure in the lower part of the body increases, capillary pressure increases, and some plasma is ultrafiltered into the interstitial space. Cells and constituents such as protein, which do not readily pass the capillary

endothelium, increase. So do substances wholly or partly bound to protein (eg, calcium). Urea nitrogen, on the other hand, is so diffusible that patient posture makes no difference.

- 6. Body Weight: Some laboratory computer software makes no allowance for body weight. Creatinine clearance and blood volumes require this data. Positive weight dependencies are described for uric acid, glucose, and cholesterol; many subjects with high concentrations of such analytes are prone to be found in the high-weight group. Males, but not females, have such body weight associations for creatinine, protein, hemoglobin, and AST (SGOT). Inverse relationships are reported for phosphate and, in females, for calcium.<sup>6</sup>
- 7. **Topics Requiring Medical Judgment:** The significance of a few red cells in urine depends upon the clinical setting (voided versus catheterized urine, sex, menstruation or not); therefore, some tests cannot be classified as "normal" or "abnormal" by computer, but only by the physician caring for that particular patient.

Tests having no normals - because positivity in any quantity is itself abnormal - include:

Serum acetone
Porphobilinogen
Alcohol and certain other toxins
Urine glucose, ketones, blood, bile, nitrite
ART, VDRL, and other serologic tests for syphilis
Nucleated RBC/100 WBC, blasts, promyelocytes, myelocytes in diff
LE slide test
Test for sickling
Malaria smear

Laboratory data must always be considered in light of the physician's clinical impression. If the clinician considers acute infarct of myocardium likely, and the early laboratory data do not support his initial impression, the patient should be treated as if he indeed had an infarct. (Laboratory data may be normal or inconclusive early in myocardial infarct; this is a particularly good example of the importance of the physician's clinical diagnosis.) When laboratory results are abnormal but not supported by clinical findings, the physician should thoroughly consider the laboratory reports before dismissing them as inconsequential.

Laboratory data suggest clues to unsuspected disease in about 12% of patients studied in a university hospital series.<sup>7</sup>

8. Food and Nutrition: Tests requiring the fasting state include fasting blood sugar, lipid profile, iron, iron binding capacity, B<sub>12</sub>/folate levels, carotene, d-xylose, lactose, and glucose tolerance tests, Schilling test, most insulins, serum bile acids, and gastrin. Serum bile acids are sometimes measured before and after a meal. Prolonged fasting may increase serum bilirubin (up to 240% after a 48-hour fast) and cause decreases of plasma glucose and proteins (albumin, transferrin, and complement C3). Samples for PKU (chemical test), FTA-ABS, and antibodies for virus, fungal, and Mycoplasma agents should be clear serum, fasting if necessary.

Blood drawn immediately after a meal is apt to have elevated potassium and depressed phosphorus and later elevated triglycerides. Alkaline phosphatase may be elevated 2-4 hours after a fatty meal, especially in people who are Lewis-positive secretors of blood type O or B. Increased turbidity in postprandial blood can interfere with certain other tests, including bilirubin, LD (LDH), and total protein. Increased turbidity might depress uric acid and BUN, depending on methodology.

High protein diet can elevate BUN, ammonia, and urate. Purines increase uric acid. High intake of bananas, pineapples, tomatoes, and avocados may elevate 5-HIAA. Caffeine elevates catecholamines, as does theophylline.

9. Drugs: Ethanol causes immediate increases of uric acid, lactate, and acetone. Intermediate effects include increases of GGT (GGTP) and to a lesser degree ALT (SGPT). Actually, a short-chain carbohydrate, ethanol may induce increases in triglycerides. More chronic alcoholism may be manifested by increases of bilirubin, AST (SGOT), alkaline phosphatase, as well as GGT, and a decrease of folate. Although considerable information is available, a great deal more is needed.

**Oral contraceptives** increase  $T_4$  (RIA) and decrease  $T_3$  uptake. They are reported to increase alpha<sub>1</sub>-antitrypsin (half of alpha<sub>1</sub> in serum protein electrophoresis), iron, triglycerides, ALT (SGPT), and GGT; to decrease albumin; and to affect as many as 100 laboratory tests.

- 10. Hemolysis from hemolytic anemia or venipuncture causes increases in LD, bilirubin, AST (SGOT), CK, potassium, ALT (SGPT), magnesium, and acid phosphatase. Hemolysis from traumatic venipuncture may be associated with release of thromboplastins and may invalidate the results of coagulation tests in some cases. Hemolysis has a less marked effect on total protein, alkaline phosphatase, iron, and phosphorus. Hemolysis will mask hemolyzing antibodies in the antibody screen and crossmatch.
- 11. Circadian Rhythms: Circadian (approximately 24-hour) rhythms have implications for physiology, measurement of many laboratory tests, drug excretion (eg, salicylates, sulfonamides), and responses to therapy. Levels fluctuating very significantly during the 24-hour cycle include cortisol (which has different normals for 8 AM and 8 PM), growth hormone, serum acid phosphatase, aldosterone (high 6 AM to 3 PM), transferrin (maximum 4 PM to 8 PM), ACTH, serum iron, serum creatinine (7 PM values 130% of 7 AM concentration), eosinophils (low in afternoon), lymphocytes (maximum early AM), WBC (maximum in early AM), leukocyte function and urine urobilinogen (maximum excretion in afternoon). Urinary excretion of potassium, LH, FSH, TSH, testosterone, and some less commonly ordered hormones have some diurnal variation. Parathyroid hormone is best drawn at 8 AM.

Triglyceride is higher in the afternoon, as is phosphate, BUN, and the hematocrit. Bilirubin falls in the PM, but overnight fasting itself causes bilirubin to increase.<sup>8</sup>

The waves which characterize circadian rhythms may be square shaped or may occur as a series of pulses. The latter pattern is seen with plasma cortisol concentration, which begins to increase during sleep. A large