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EDITION

CLINICAL &
DIAGNOSIS
MANAGEMENT

BY LABORATORY
METHODS

JOHN BERNARD HENRY, M.D.

CLINICAL & DIAGNOSIS & MANAGEMENT

BY LABORATORY METHODS

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To
Georgette,
my wife of 37 years
and mother of our six children,
Maureen Henry Mayer, Julie Patricia Henry, M.D.,
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John Bernard Henry, Jr., and Thomas David Henry;
our sons-in-law Thom A. Mayer, M.D., and Peter J. Paganussi, M.D.;
and our grandchildren,
Caroline Paganussi, Joshua Mayer, and Kevin Mayer,
all of whom accepted patiently the inconvenience
and separation associated with my preoccupation
with this work, which, without their sustained
support and understanding,
could not have been completed.

TODD-SANFORD-DAVIDSOHN:

A Tribute

Todd and Sanford is a legend among medical textbooks. It has spanned 83 years and has served as a resource for thousands of physicians, scientists, students, and medical technologists. This textbook has its roots in the first edition, published in 1908 as **A Manual of Clinical Diagnosis** by James C. Todd, M.D. Dr. Todd was the author of the first six editions, though he was in ill health in his final years; he died in 1928 at the age of 54.

The sixth edition was edited by Dr. Todd and Arthur H. Sanford, M.D. Dr. Sanford continued with four more editions on his own. He had the assistance of George G. Stilwell, M.D., as a collaborator on the eleventh edition, and Benjamin B. Wells, M.D., as co-editor on the twelfth edition. Dr. Sanford died in 1959 at age 77.

The thirteenth edition, **Clinical Diagnosis by Laboratory Methods**, was edited by Israel Davidsohn, M.D., and Dr. Wells. I joined Dr. Davidsohn with the fourteenth edition, published in 1969. We shared the fifteenth edition, published in 1974. Israel Davidsohn, M.D., died in 1979, at the age of 84. I have continued as editor for the subsequent editions. The title of the sixteenth edition, **Clinical Diagnosis and Management by Laboratory Methods**, was augmented to reflect major current use of laboratory measurements and examinations in patient care management as well as diagnostic applications. The eighteenth edition represents my fifth edition.

Although the names of Todd, Sanford, and Davidsohn are no longer visible on the cover, their presence will always be with this textbook. We stand on the shoulders of giants and can account for whatever contributions we have made as individuals because of the tremendous effort and commitment of those who have preceded us.

It is with deep humility and respect that I pause to reflect and point out to the reader the history of this remarkable text. After more than 80 years, it can take its place among the most significant textbook contributions in modern medicine as attested by the durability of its readership for these many years.

Personally, I have greatly missed working with Dr. Davidsohn over the past three editions, and can only encourage the reader who has an interest in history to read "The History of a Book and of a Medical Specialty, Todd and Sanford (1908–1969)," written by Israel Davidsohn, M.D., in the fourteenth edition of **Clinical Diagnosis by Laboratory Methods**, edited by Davidsohn and Henry, published in 1969.

The memory and contribution of Todd, Sanford, and Davidsohn should never be forgotten. I am and always will be indebted to each of them. May you share my feelings of respect and gratitude for these leaders in medicine and pathology.

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PREFACE

It is a privilege and an honor to serve as editor of a textbook that has for over 80 years served generations of primary care physicians, specialists, and scientists in laboratory medicine/clinical pathology as well as medical laboratory personnel. I doubt if there is a single medical textbook that has so many diverse users, including medical technologists and medical technicians, medical students, family physicians, internists, surgeons, pediatricians, physiatrists, obstetricians/gynecologists, neurologists, and dermatologists, among others; and, of course, pathologists, both in practice and in training.

The goals of this eighteenth edition, in addition to providing an information resource base in virtually all aspects of clinical pathology and laboratory medicine with sufficient emphasis to promote understanding and facilitate learning with critical analysis, include the following:

1. Identification of appropriate measurements and examinations for diagnosis, for confirmation of a clinical impression, for guiding therapy or patient management, and for prognosis
2. Delineation of the order or sequence or grouping when appropriate in which such measurements and examinations should be requested
3. Interpretation and translation of laboratory measurements and examinations in light of a patient's particular medical problem(s)
4. Promotion of the understanding and clarification of pathophysiology or natural history of disease as reflected by clinical pathology data
5. Recognition of pitfalls, problems, and limitations of laboratory data, including quality control (sensitivity, precision, accuracy, specificity), drug interaction, and predictive values; as well as relative merits of an assay in terms of methodology, turnabout time, patient preparation, communication, and cost-effectiveness
6. Appreciation and understanding of the importance of laboratory organization and management for efficient and cost-effective medical and health care delivery

Clinicians sometimes take for granted the quality of laboratory measurements and examinations. The art and science of laboratory medicine have clearly established the validity of laboratory data in terms of accuracy, precision, and reliable scientific data. Over the past 20 years, a major thrust has been made in the achievement of rapid turnabout time, reflected in the prompt reporting of measurements and examinations to the physician at the bedside or in the office. Technologic advances in instrumentation and information processing have accomplished this where there is appropriate laboratory organization and management. Currently, there is a major emphasis on the cost of laboratory measurements and examinations and indeed cost of health care delivery. Regulations, reimbursement, and competition prompt this concentration on costs/charges with the assumption that quality and turnabout time are ensured. Reimbursement based on diagnosis-related groups brings cost-effectiveness into sharp focus and undoubtedly promotes laboratory diagnosis-related groups (LDRG) that will reflect both diagnostic and management applications. At the same time, new technology continues unabated with the marriage of the computer chip to chemistry and immunology, including the emergence of biosensors. Furthermore, the new biology of medicine includes molecular and cell pathology, which provides sophisticated diagnostic applications—e.g., DNA probes and polymerase chain reaction (PCR).

The seven parts of this text reflect the organization of the laboratory by function and according to medical problems: (I) The Clinical Laboratory, (II) Clinical Chemistry, (III) Medical Microscopy, (IV) Hematology and Coagulation, (V) Immunology and Immunopathology, (VI) Medical Microbiology, and (VII) Administration of the Clinical Laboratory.

The chapters emphasize topics that have compelling practical application to the patient. The new technology of medicine included in clinical pathology is reviewed, as is the important

role of the physician in laboratory medicine. Virtually all of the material has been updated, thoroughly revised, or newly introduced to reflect current thrusts. This is especially prominent in Part V, Immunology and Immunopathology. New chapters on the serodiagnosis of HIV and HBV infections, problems in host defenses, and paternity testing round out Part V and bring it into focus on current applications of molecular pathology.

This eighteenth edition begins with the introduction to the clinical laboratory, the purpose and practice of laboratory medicine, and follows through with instrumentation, interpretation of laboratory results, sources of variations of measurements in examinations, and rule-based decision analysis (artificial intelligence). It concludes with management, which is so important in laboratory medicine today as part of quality control and quality assurance in medical practice. Statistics is incorporated into existing chapters with the recognition that computer software packages have altered statistical applications in the clinical laboratory.

Among other topics in Part II, Clinical Chemistry, lipids have been thoroughly addressed to reflect their expansion in application and significance as well as current interest, emphasizing not only cholesterol and lipoproteins but also their importance in patient assessment in health and wellness promotion and risk factor identification. Likewise, Toxicology and Therapeutic Drug Monitoring was written by two new authors, who cover not only the vast array of drugs in TDM but also environmental carcinogenesis and the expanded interest in drugs of abuse. A brand new chapter, Molecular Markers of Malignant Neoplasms, pulls together the increasingly important subject of tissue genes and their expression in tissues, cells, and body fluids of various diseases. This chapter underscores the interest in incorporation of tumor markers in the diagnosis and treatment of cancer, the third leading cause of death in the United States.

In Part III, Medical Microscopy, three chapters have been consolidated into one, incorporating gastrointestinal and pancreatic disorders. There is a new chapter entitled Clinical Application of Human Chorionic Gonadotropin, which, with the chapter on analysis of amniotic fluid, emphasizes laboratory implications of reproductive biology.

Molecular pathology is widely incorporated into Part IV, Hematology and Coagulation, which continues to be most comprehensive as well as current in content and laboratory utilization. Part VII has new first authors for each chapter and embraces not only the organization and management of the laboratory but also fiscal management and information management.

Finally, a new chapter entitled Physician Office Laboratories (POL) has been incorporated because of the expansion of laboratory medicine in physician offices, most notably in internal medicine, family medicine, and pediatrics. It combines many current considerations in establishing and operating, both effectively and legally, such a POL, including accreditation. Finally, the four appendices, including SI Units, have been thoroughly updated.

In this edition, more medical technologists are included as coauthors: for example, urinalysis, basic examination of the blood, immunohematology, paternity testing, and organizational and fiscal management. With authors representing pathologists, other scientists in laboratory medicine, and also medical technologists, the relevancy and usefulness of this text become even greater.

In summary, this comprehensive text portrays concisely current knowledge of molecular and clinical pathology to assist physicians and other health professionals in their roles as benefactors of the patient.

While individual authors deserve full credit for their contributions, I accept full responsibility for any errors of omission or commission and enthusiastically welcome any comments, reactions, or suggestions regarding this edition.

JOHN BERNARD HENRY, M.D.

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JOHN BERNARD HENRY, M.D.

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