CRC Handbook Series in Clinical Laboratory Science

David Seligson, Editor-In-Chief

Section C: Pathology

Volume I – Immunopathology

Raymond Yesner, Section Editor

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PUBLISHER'S PREFACE

In 1913, when the First Edition of the *Handbook of Chemistry and Physics* appeared, scientific progress, particularly in chemistry and physics, had produced an extensive literature but its utility was seriously handicapped because it was fragmented and unorganized. The simple but invaluable contribution of the *Handbook of Chemistry and Physics* was to provide a systematic compilation of the most useful and reliable scientific data within the covers of a single volume. Referred to as the "bible," the Handbook soon became a universal and essential reference source for the scientific community. The 57th Edition, published in the bicentennial year of 1976, represents more than 63 years of continuous service to millions of professional scientists and students throughout the world.

In the years following World War II, scientific information expanded at an explosive rate due to the tremendous growth of research facilities and sophisticated analytical instrumentation. The single-volume Handbook concept, although providing a high level of convenience, was not adequate for the reference requirements of many of the newer scientific disciplines. Due to the sheer quantity of useful and reliable data being generated, it was no longer feasible or desirable to select only that information which could be contained in a single volume and arbitrarily to reject the remainder. **Comprehensiveness** had become as essential as **convenience.**

By the late 1960's, it was apparent that the solution to the problem was the development of the multi-volume Handbook. This answer arose out of necessity during the editorial processing of the *Handbook of Environmental Control.* A hybrid discipline or, to be more precise, an interdisciplinary field such as Environmental Science could be logically structured into major subject areas. This permitted individual volumes to be developed for each major subject. The individual volumes, published either simultaneously or by some predetermined sequence, collectively became a multi-volume Handbook series.

The logic of this new approach was irrefutable and the concept was promptly accepted by both the scientist and science librarian. It became the format of a growing number of CRC Handbook Series in fields such as Materials Science, Laboratory Animal Science, and Marine Science.

Within a few years, however, it was clear that even the multi-volume Handbook concept was not sufficient. It was necessary to create an information structure more compatible with the dynamic character of scientific information, and flexible enough to accommodate continuous but unpredictable growth, regardless of quantity or direction. This became the objective of a "third generation" Handbook concept.

This latest concept utilizes each major subject within an information field as a "Section" rather than the equivalent of a single volume. Each Section, therefore, may include as many volumes as the quantity and quality of available information will justify. The structure achieves permanent flexibility because it can, in effect, expand "vertically" and "horizontally." Any section can continue to grow (vertically) in number of volumes, and new sections can be added (horizontally) as and when required by the information field itself. A key innovation which makes this massive and complex information base almost as convenient to use as a single-volume Handbook is the utilization of computer technology to produce up-dated, cumulative index volumes.

The *Handbook Series in Clinical Laboratory Science* has the distinction of being the prototype for the "sectionalized, multi-volume Handbook series." Currently underway are additional information programs based on the same organizational design. These include information fields such as Nutrition, Energy, and Agricultural Science which are of critical importance not only to scientific progress but to the advancement of the total quality of life.

We are confident that the "third generation" CRC Handbook comprises a worthy contribution to both information science and the scientific community. We are equally certain that it does not represent the ultimate reference source. We predict that the most dramatic progress in the management of scientific information remains to be achieved.

B. J. Starkoff
President
CRC Press, Inc.

PREFACE
CRC HANDBOOK SERIES IN CLINICAL LABORATORY SCIENCE

According to the *Webster – Merriam Dictionary,* 3rd ed., a handbook is

1a. a book capable of being conveniently carried as a ready reference,
1b. a concise reference book covering a particular field of knowledge,
2a. a bookmaker's book of bets.

In order to accommodate the information in the field of clinical laboratory science we shall need more than 20 volumes. A series of volumes such as these, that will weigh in the order of 24 kg (53 pounds), will not fit the meaning of 1a; nor will 2a fit, although we are gambling that we can get the appropriate information together in a reasonable time. Definition 1b is more appropriate to our goal which is to accumulate, arrange, and present the qualitative and quantitative clinical laboratory data related to men and women (of all ages), so that anyone who needs to extract some information from the vast amount available will have it at his or her fingertips, provided he or she is within arm's length of these volumes.

To understand the biology of man, to know man, sick and well, requires knowledge of the body constituents and their interrelationships; the dynamic relationships of these constituents; and information about tools, chemicals and techniques used to get these data. Notation of the source of the data is important to scholars. It is our purpose to present this information in tabular and graphic form in a systematic way in order to help readers retrieve it.

If we are successful, we will make it possible for a user to find any information related to constituents of blood, body fluids, body tissues, and so on, whether they be organic or inorganic molecules, viruses, bacteria, or parasites. Users of these volumes should be able to find easily the composition of a buffer, the half-life of an isotope, or the life cycle of a parasite if that information has been used to study man or if the chemicals or particles are found in man.

We shall consider this *Handbook Series in Clinical Laboratory Science* successful if it meets most of our goals and if it provides the nidus for continuing growth. The editor of the series, the executive editor of each volume, the advisory boards, contributors, and publisher will make every effort to improve subsequent editions of this *Handbook*. The user will undoubtedly find errors of omission and commission or will have new information (all of which we hope will be called to our attention). All of us should strive to improve these volumes so that users and contributors the world over will find them useful in knowing more about man.

David Seligson
Editor-in-Chief

DAVID SELIGSON, EDITOR-IN-CHIEF
CRC HANDBOOK SERIES IN CLINICAL LABORATORY SCIENCE

Dr. David Seligson is Professor and Chairman of the Department of Laboratory Medicine (Clinical Pathology) and Professor of Pathology in the School of Medicine at Yale University. He is the Director of the Department of Clinical Laboratories of the Yale-New Haven Hospital. He has an Sc.D. in Biochemistry from Johns Hopkins University (1942) and an M.D. from the University of Utah (1946). He has been a President of the American Association of Clinical Chemists and the Academy of Clinical Laboratory Physicians and Scientists. He is a Fellow of the American Society of Clinical Pathologists, College of American Pathologists, American College of Physicians, and American Board of Clinical Chemistry.

He has been editor of *Standard Methods of the American Association of Clinical Chemists* (Volumes 2, 3, and 4) and he is a member of other editorial boards.

Dr. Seligson has an honorary Masters degree from Yale University and has received the following awards:

John G. Reinhold Award, Philadelphia Section of the American Association of Clinical Chemists, 1966

Fellowship of Medici Publici, University of Utah College of Medicine and Medical Alumni Association, 1966

Donald D. Van Slyke Award, American Association of Clinical Chemists

1971 Ames Award, American Association of Clinical Chemists, National Meeting, Seattle, Washington, August 1971

Gerald T. Evans Award, Academy of Clinical Laboratory Physicians and Scientists, June 1974

Honorary Member Association of Clinical Biochemists, London, April 1976

PREFACE
SECTION C: PATHOLOGY
VOLUME I

In the disciplines of anatomic pathology there are encyclopedias of descriptive material and color atlases with little text, but no general reference work for data. The Pathology section of the *CRC Handbook Series in Clinical Laboratory Science* attempts to fill the gap. This first volume, edited by Dr. Byron Waksman, deals with immunopathology. Dr. Waksman's great efforts, host of accommodating friends in this field, and organizing ability, as well as the great interest in this burgeoning subject in the field of Pathology all contribute to making this volume a valuable source. Although new knowledge is being added with such rapidity that the "facts" of yesterday are submerged beneath the flood of accumulating information, a source book of good data is a valuable resource at any given point in time. The other volumes being planned deal largely with systemic pathology and include a Pulmonary Pathology section edited by Dr. Oscar Auerbach and a Cardiovascular Pathology section edited by Dr. S. Evans Downing. The evolution of these volumes will depend on their usefulness and feedback from the users.

Raymond Yesner
Section Editor

RAYMOND YESNER
SECTION EDITOR
SECTION C: PATHOLOGY

Raymond Yesner, M.D., is Professor of Pathology at the Yale University School of Medicine and Director of Pathologic Anatomy at the Veterans Administration Hospital of West Haven, Connecticut, where he is also Director of Electron Microscope Laboratories. He received an A.B. degree from Harvard (1934) and an M.D. from Tufts University School of Medicine (1941). He is a Fellow, Past Chairman of the Government Section, and Alternate Delegate to the House of Delegates of the College of American Pathology and a member of the American Association of Pathology and Bacteriology, the International Academy of Pathologists, and other professional societies. Dr. Yesner is Chairman of the Pathology panel of the Veterans Administration Lung Cancer Group, a member of the Board of Governors of the Connecticut Chapter of the American Cancer Society, and has served on many pathology and oncology study committees.

BYRON H. WAKSMAN
VOLUME EDITOR
SECTION C: PATHOLOGY
VOLUME I

Byron H. Waksman, M.D., received his A.B. degree from Swarthmore College (1940) and his M.D. from the University of Pennsylvania (1943). He did immunologic research and graduate work in chemistry at the Mayo Foundation and postdoctoral work in immunochemistry at Columbia University. From 1949 to 1963, Dr. Waksman was a member of the faculty of the Departments of Bacteriology and Immunology of the Harvard Medical School and Massachusetts General Hospital. From 1964 to 1970 and 1972 to 1974, he served as Chairman of the Department of Microbiology at Yale University, where he is currently Professor of Pathology (Immunology). He was President of the American Association of Immunologists and is a member of numerous other professional societies. As well as serving as American Editor of *Progress in Allergy* and on the Advisory and/or Editorial Boards of several journals, Dr. Waksman has over 200 publications in the field of immunopathology, especially dealing with autoimmune reactions, reactions of "cellular" hypersensitivity, the role of the thymus, specific acquired tolerance, and suppressor T cells.

ADVISORY BOARD MEMBERS
SECTION C: PATHOLOGY
VOLUME I

TABLE OF CONTENTS
SECTION C: PATHOLOGY
VOLUME I

Introductory 1

I. Diseases for which Immunologic Study is Relevant 13

II. Morphologic Study 27

III. Morphologic Techniques 41

IV. Purpose of Morphologic Study 95

V. Functional Studies of Lymphocytes 97

VI. Morphologic Techniques 107

VII. Functional Techniques 119

VIII. Purpose of Tests of Lymphocytic Functions 169

IX. Functional Studies of Other Cells 187

X. Antigen-Antibody Reactions 217

XI. Complement 265

XII. Other Serum Mediators of Immunologic Disease 277

XIII. Proteins of Body Fluids 283

XIV. Tests in Intact Subjects 301

Index 329

INTRODUCTORY

A much wider variety of immunologic techniques is used in pathologic and clinical diagnosis today than 20 years ago. Most of these should be available in hospital laboratories, and all should be familiar to the modern physician. These are illustrated below in a wide variety of clinical settings, both normal and pathologic.

TABLE OF CONTENTS

Introductory

I. Diseases for which Immunologic Study is Relevant

Infection: Bacteria, Fungi, Viruses and Rickettsiae, Protozoan and Metazoan Parasites
Allergy: Atopy, Contact Allergy, Serum Disease, Drug Allergy
Autoimmune Disease
Granulomatous Disease
Transplanted Tissues or Organs
Tumor
Immunologic Deficiency Disease
Lymphoproliferative Disease
Development of Immune Competence
Endocrine Diseases

II. Morphologic Study of

A. Sections of Non-lymphoid Tissues
   1. Known Conditions
   2. Diseases of Unknown Origin
B. Sections of Lymphoid Organs
   (Spleen, Lymph Nodes, Tonsils, Peyer's Patches, Appendix, Thymus, Bone Marrow)
   1. Known Conditions
   2. Disease of Unknown Origin
C. Cells Isolated from Lesions
D. Cells Isolated from Lymphoid Organs
E. Cells of Blood, Lymph, Cerebral Spinal Fluid, Urine
F. Cells of Pus, Inflammatory Exudates

III. Morphologic Techniques

A. Light Microscopy, Phase and Nomarski Optics
   1. Identification of Lesion
   2. Classification as Anaphylactic, Immune Complex, Cell Mediated, Lymphoproliferative, Immunologic Deficiency
B. Immunofluorescence
   1. Analysis of Immune Complex Lesions
   2. Counts of Immunoglobulin-bearing Cells
   3. Localization of Antigens (Microbial, Tissue)
C. Autoradiography
   1. Localization of Injected Materials
   2. Assessment of Cell Proliferation, Macromolecular Synthesis
   3. Counts of Immunoglobulin-bearing or Antigen-binding Cells

D. Histochemistry
E. Electron Microscopy
F. Scanning Electron Microscopy
G. Electron Microscopy and Peroxidase, Ferritin, Other
H. Electron Microscopy and Autoradiography

IV. Purpose of Morphologic Study

V. Functional Studies of Lymphocytes

A. Cells
(See List in Section II. C to F)
B. Separation Techniques
1. Velocity Sedimentation
2. Density Gradients
3. Column Techniques
4. Adherence, Phagocytic Properties, etc.
5. Selective Lysis
6. Rosetting Techniques

VI. Morphologic Techniques

A. "Classical"
(Techniques Listed in Section III. A to H)
B. Markers
(Identification, Quantitation, Topography)
1. Specific Antigens Characteristic of T or B Lymphocytes
2. HL-A (See Separate Section on Tissue Typing)
3. Rosette Formation
4. Fc Receptors
5. Complement Receptors
6. Lectin Binding (Fluorescent, Radiolabelled)
C. Membrane-bound Immunoglobulin
1. Presence
2. Molecular Class
3. Specific Antigen Binding

VII. Functional Techniques

A. Responsiveness
(Blast Transformation; DNA, RNA, Protein Synthesis; Capping)
1. Specific Antigen (See Section on Testing CMI)
2. Mitogens (PHA, Con A, PWM, LPS, SLO, Staphylococcal Filtrate, Other)
3. Mixed Lymphocyte Culture
4. Antibody Against Immunoglobulin, Viral Antigens, Other
5. Blocking Factors
B. Lymphokine Production
1. Migration Inhibitory Factor
2. Macrophage Activation Factor
3. Lymphotoxin
4. Blastogenic Factors
5. Chemotactic Factors
6. Others

C. Lymphocytotoxicity
   1. Direct Cytotoxicity (Microorganisms, Virus-infected Cells, or Target Cells of Graft Donor, Tumor, Organ)
   2. Antibody-mediated Lymphocytotoxicity
      a. Opsonic Antibody + Cells (Monocytes, "K Cells", B Cells, Other)
      b. Cytophilic Antibody + Macrophages
   3. Blocking Factors
D. Helper or Suppressor Activity
E. Migratory Properties

VIII. Purpose of Tests of Lymphocytic Functions
   1. Presence and Degree of Sensitivity to Antigens of Microorganisms, Graft, Tumor, Organ
   2. Enumeration (e.g., of Monocytes, T Cells, B Cells, Blasts, Etc.)
   3. Presence of Immunologic Competence (e.g., T Cell)
   4. Level of Competence
   5. Characterization of Cells in Lymphoproliferative Disease
   6. Enumeration of Gene Frequencies in Human Populations

IX. Functional Studies of Other Cells
A. Macrophages
   1. Counts, Morphology, Receptors, Etc.
      a. In Tissues: Histiocytes, Macrophages, Epithelioid and Giant Cells
      b. Blood Monocytes
   2. Clearance Function In Vivo
   3. In Vitro Functions: Motility, Phagocytosis, Enzyme Levels, Microbial Inhibition or Killing
B. Neutrophilic Granulocytes
   1. Counts, Morphology, Receptors
   2. In Vitro Functions: Motility, Phagocytosis, Enzyme Levels, Microbial Inhibition or Killing
   3. Inclusions
C. Eosinophils
D. Basophils
E. Plasmacytes

X. Antigen-Antibody Reactions
(To Identify Antigen, to Demonstrate or Titer Antibody, to Follow Epidemics)
   1. Neutralization
   2. Complement Fixation
   3. Precipitation
      a. Tube Methods
      b. Gel Diffusion
      c. Immunoelectrophoresis and Related Methods
   4. Agglutination
      a. Classical Agglutination Methods
      b. Passive Hemagglutination
      c. Latex Agglutination
      d. Bentonite and Other Particles
   5. Lysis Tests
   6. Opsonization

7. Radioimmunoassay
8. Immunofluorescence

XI. Complement

1. Levels and Metabolism of Individual Components
2. Complement Component Split Products
3. Properdin; Alternate Pathway

XII. Other Serum Mediators of Immunologic Disease

1. Histamine, 5-Hydroxytryptamine, SRS
2. The Kinin System
3. Lymphokines

XIII. Proteins of Body Fluids

1. Immunoglobulin Levels
2. Other Proteins

XIV. Tests in Intact Subjects

A. Skin Tests
   1. Wheal and Flare
   2. Arthus
   3. Delayed (Intradermal)
   4. Delayed (Patch Test)

B. Response to Immunization
   1. Antibody Formation
      a. Primary
      b. Anamnestic
   2. Delayed Sensitivity
   3. Antigen Clearance
   4. Morphology of Lymphoid Organs

C. Response to Transfer Factor

D. Response to Drugs or "Immunotherapy"
   1. Drugs
   2. Immunotherapy

E. Response to Grafts of Lymphoid Tissue

REPORT OF THE COMMITTEE ON CLINICAL IMMUNOLOGY OF THE INTERNATIONAL UNION OF IMMUNOLOGICAL SOCIETIES (IUIS)*

Background and Aims

Development and Significance of Clinical Immunology

The decision to establish the Clinical Immunology Committee was influenced by the tremendous growth of immunology from a discipline involving primarily immunity to infectious diseases into a science concerned with all the characteristics and effects of the immune response in health and disease. Applied immunology has had a significant impact on all aspects of medical practice. This impact has taken several forms: modern immunology has defined entire areas of new medical practice (such as in the immunodeficiency diseases), has lent major strength to the development of other areas (such as transplantation), has provided new understanding of the etiology and pathogenesis of certain diseases or manifestations of diseases, has provided new investigative approaches and laboratory methods for the study of diseases, and may play a major role in diagnosis and treatment of cancer. In some instances, immunology has helped to reshape other established disciplines. For example, radioimmunoassay, which depends on the exquisite sensitivity and specificity of antibodies, has contributed greatly to the development of allergology and endocrinology. Other immunological techniques have had a major role in the diagnosis of rheumatic diseases and in histocompatibility typing.

Despite the rapid growth of the science of immunology and its recognized impact on other disciplines, many universities and medical schools have not accorded formal recognition to these developments through the creation of departments of immunology. The lack of departmental organization at the basic science level hampers the definition and organization of clinical immunology at the clinical level.

Aims for a Committee on Clinical Immunology

Against the background outlined above, it was decided to establish a Committee on Clinical Immunology to work together with national societies for immunology, other IUIS Committees, and the WHO Immunology Unit to help

a. To establish and organize departments and centers for clinical immunology, including immunology of tropical diseases

b. To provide training opportunities in clinical immunology

c. To provide criteria by which national agencies may recognize clinical immunology as a speciality

d. To evaluate and standardize the immunological tests, and develop guidelines for immunological treatments necessary for the management of patients with immunological disorders.

It was fundamentally accepted that the work of the Committee should be guided by the WHO technical report on clinical immunology (No. 496, 1972), which outlines the basis for the application of immunology for the benefit of patients

a. By applying the expert knowledge of the immunologist to the various clinical specialties

b. By providing tests for diagnosis and for assessing disease activity in patients with immunological disorders

* From Report of the Committee on Clinical Immunology of the International Union of Immunological Societies, *J. Immunol. Methods*, 11, 87, 1976. With permission.