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Preface to the Second Edition

Preparing a text in pediatric immunology is much like explaining what has happened so far to the latecomer attending a thriller play: by the time the plot is reviewed, the play has advanced so much that another explanation is needed. Since 1973, when the first edition was published, new characters (B and T lymphocytes, killer cells) have been introduced, new detectives (methods) have been added, new complications (diseases) have arisen, and new solutions (treatments) have emerged. Accordingly, this second edition will be a review and update for the reader, constructed so as to condense the past, interpret the present, and prepare for the future.

New material has enlarged the text to some degree, but in view of the growth of the field this is inevitable. We have tried to consider each subject in the same degree of depth as before, assuming a minimal initial knowledge of basic immunology, but, realizing that most of our readers are pediatricians, we have also advanced our coverage to a level appropriate for sophisticated patient care. We have retained many of the past contributors, but in order to infuse new insights, we have added 12 new authors and 6 new chapters.

Throughout the first section, Development and Function of the Immune System, new information on lymphocyte subpopulations, cellular interactions, IgE immunoglobulin, and biochemical events associated with immunologic processes has been added. Particularly noteworthy is the chapter on The Mononuclear Phagocytic System (Chapter 7), which is emerging as a crucial system for antigen processing, effector function, and inflammation.

The second section, Immunodeficiency Disorders, contains expanded coverage of enzyme deficiencies, suppressor defects, and methods of immunologic reconstitution. This section has also been strengthened by the addition of chapters on disorders of the IgE system (Chapter 15) and the mononuclear phagocytic system (Chapter 18), both relatively new areas of clinical immunology. Perhaps the best measure of the enlarged scope of this section is a comparison of Table 11-3 (page 186), "Immunodeficiencies Discussed in this Section", with the corresponding table from the first volume. The table from the first edition lists 53 immunodeficiency disorders, while the present edition has 110 disorders, an increase of more than 100 per cent.

The third section, Immunologic Aspects of Pediatric Illness, has new chapters

on Pulmonary Disorders (Chapter 22), Infection in the Compromised Host (Chapter 32), and Disorders of the Serum Proteins (Chapter 33). The enlargement of this section reflects the impact that immunology has had on many aspects of pediatric practice, ranging from endocrinology to neurology.

Several subjects are covered in different contexts. For example, IgE is discussed in The B-Lymphocyte System (Chapter 4), Disorders of the IgE System (Chapter 15), and Allergic Disorders (Chapter 21). The HLA system is discussed in Biology of the Immune System (Chapter 2), Disorders of the T-Cell System (Chapter 16), Rheumatic Disorders (Chapter 24), and Transplantation (Chapter 35).

In addition to the growth of this edition, the growth of pediatric immunology can be measured in yet another way. A majority of academic pediatric departments now have divisions of pediatric immunology. In most cases, these are amalgamated with allergy, but some stand alone and others are associated with infectious or rheumatic diseases. The increasing number of pediatricians with an interest in immunology is also reflected by the proliferation of articles, meetings, abstracts, and discussions on pediatric immunology, and by the enthusiastic acceptance of the first edition of this book.

We thus return to the next portion of the play; intrigue and complexity have increased, yet the investigators and audience have grown concomitantly. We look forward to another half-decade of challenge and excitement.

We wish to extend special gratitude to our contributors, all of whom have spent many hours writing and rewriting their chapters. The editorial guidance of Mr. Albert Meier of the W. B. Saunders Company and the secretarial assistance of Ms. Winifred Cole are gratefully acknowledged.

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Preface to the First Edition

Twenty-five years ago, the thymus was a mystery organ that was irradiated for respiratory stridor, organ transplantation was science fiction, a gamma globulin determination was a sophisticated research effort, the function of the lymphocyte was not known, and the immunodeficiencies were not yet discovered. Since then a bountiful harvest of immunologic information has been gathered by the combined efforts of physicians, biochemists, microbiologists, pathologists, and other scientists. A significant portion has relevance to human health and disease and has been collected under the heading of clinical immunology. This book is concerned with the clinical immunology of infancy and childhood.

Like other specialty fields, clinical pediatric immunology is primarily concerned with a specific group of related illnesses necessitating special investigative procedures—the primary immunodeficiency diseases. Unlike most other specialties, pediatric immunology widens its horizon to include such related areas as collagen diseases, infectious diseases, allergies, transplantation, and immunization procedures. Further, the field encompasses many aspects of endocrine, hematologic, renal, neurologic, gastrointestinal, and malignant diseases, and thus it is especially attractive to the physician who enjoys the entire scope of pediatric medicine. In sum, pediatric immunology has some relevance and contribution to the whole of pediatrics.

This book has been written by men and women from 18 universities in North America and Europe whose own careers have been devoted to some aspect of clinical immunology. Writing with both the specialist and the generalist in mind, the contributors have combined the basic knowledge of the immunologic system with clinical descriptions of immunologic disorders.

The book begins with the development and biology of the immune response and the components of the immunologic system (Part One), continues with a detailed exposition of the immunodeficiencies (Part Two), and concludes with a group of chapters detailing the immunologic aspects of various pediatric disorders (Part Three). Included in Part One is a review by Dr. Robert Good of the major experiments in nature which have served as the impetus for the advances in clinical immunology.

The terminology employed for the immunoglobulin classes, complement components, and immunodeficiencies is that recommended by the World Health Organization. The terminology for the primary immunodeficiencies has only recently been codified, and since many eponyms are well established in the literature (e.g., Wiskott-Aldrich syndrome), we have added these to avoid ambiguity. Except in the section on immunodeficiencies (Part Two), no attempt has been made to present complete bibliographies. In the other sections, key references to summary and review articles are often used.

A suitable subtitle for a primarily American work on pediatric immunology might be "A Tale of Two Cities." The cities are not London and Paris in the 1780's but Minneapolis and Boston in the 1960's. The pediatric departments of the University of Minnesota and Harvard, under the leadership of Good, Janeway, and Gitlin, have provided much of the information in this volume and served as the training grounds for many of the contributors. Others, including the editors, have indirectly benefited by the stimulation from these centers. In 1859 Dickens stated about the 1780's that "It was the best of times, it was the worst of times." In 1973, it is the best of times for physicians concerned with the exciting and challenging aspects of immunologic disorders; for most patients, it is still the worst of times, because, with rare exceptions, therapy is unrewarding. The outlook should be bright; one large cloud is the diminution of support for the further exposition of this subject.

The skilled secretarial assistance of Mrs. Paulette Stroehnis and Mrs. Donna Keller is acknowledged. The editorial guidance of Mr. Albert Meier and Mr. Michael Jackson of the W. B. Saunders Company is greatly appreciated.

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PART ONE

**Development and Function of
the Immune System**

PART ONE

Development and Function of
the Immune System

CHAPTER ONE

Crucial Experiments of Nature That Have Guided Analysis of the Immunologic Apparatus

Robert A. Good

Real contributions toward understanding the nature of immunity and the relations of structure to function in the lymphoid system have been derived from analysis of a series of experiments of nature. For example, the science of immunology was dramatically launched when Jenner (1798, 1806) attempted to apply, generally, the observation that milkmaids who had experienced cowpox could not contract smallpox. His attempts to interpret this natural experiment introduced the principles of vaccination and active immunization and provided the first evidence that hypersensitivity may be associated with immunity. They represented the first use of an attenuated virus vaccine and even presented the first glimpse at viral interference. This legacy has proved a truly remarkable contribution, derived from the interpretation of a single experiment of nature.

Pasteur's discovery that cholera organisms grown at room temperature as an aged culture yielded the starting material for an effective vaccine based on a culture of an attenuated organism also can be viewed as an interpretation of a natural experiment — a chance conjunction of a natural event and a uniquely prepared and concerned mind. The principles that derive from this discovery, coupled with the introduction of tissue culture for virus propagation by Alexis Carrel

(1926) and the extraordinary contributions, especially of John Enders and his colleagues (1954) and many others, have given us the powerful attenuated virus vaccines, including vaccines against rabies, polio, rubeola, mumps, and rubella. They promise many more.

At the turn of this century, von Pirquet (1905) taught us that not all immune reactions function for the benefit of man, when he discovered and developed the concept of allergy from the interpretation of two natural experiments. He recognized that the incubation period of infections and the expression of the symptoms and origins of infectious disease are reflections of immunologic functions just as much as is resistance to recurrence of infection following an initial attack of disease (1911). His study of serum sickness, an illness which he clearly related to the immune reaction of the body against the foreign serum that had been injected earlier, launched studies of the nature of immunologic injury which have culminated in our understanding of certain forms of immunologic damage. These concepts have been resolved at the molecular level through signal contributions by Ishizaka and Campbell (1958), Germuth (1957), Dixon et al. (1958), and Dixon (1962).

Prausnitz and Küstner (1921), studying Küstner's own allergy to boiled fish protein, interpreted another major experiment of nature and provided evidence of the passive transfer of reaginic allergy and the persistent fixation of reaginic antibody in tissues. The potential value of desensitization or immunization, perhaps the first form of immunodeviation or immunization against immunity, was also a legacy of this early interpretation. Of course, we now have IgE and a molecular definition of reaginic antibody. Here, once again, crucial experiments of nature — two

From the Memorial Sloan-Kettering Cancer Center, New York, New York 10021.

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