IMMUNOLOGY

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PREFACE

Immunology is the study of those processes with which the host maintains constancy of his internal environment when confronted with substances which are recognized as foreign—whether generated from within the host or introduced from the external environment. A knowledge of these processes is essential for the student of medicine and for the practitioner since they form the basis for the prevention, diagnosis and treatment of many disease processes.

Immunology has been traditionally taught in the medical school curriculum as a part of microbiology. This has occurred primarily because of the basic emphasis of immunologic processes in the protection of the host from pathogenic microorganisms. Over the past 10 years, immunology has undergone a great renaissance, and it has become apparent that the defense function of the immunologic system is but a part of a much broader reactivity concerned with the recognition of foreignness. Thus, the present text deals with such diverse aspects of the immune system as man's pollution of his external environment, altered states of nutrition, the genesis and prevention of malignancy, the inflammatory diseases of connective tissue, as well as the basic functions of defense against invasion by infectious agents. With this broader scope has come the problem of providing a proper place for immunology in the undergraduate curriculum, a problem which is as yet incompletely solved in most medical schools. In this connection, the recommendations of the World Health Organization concerning the teaching of immunology in the medical curriculum* have been most helpful in the organization of the material for this book.

It is our purpose to present the new immunology with its innumerable clinical implications. The book is organized into three sections: (1) the principles, (2) the mechanisms of response and (3) the clinical applications. The principles section sets forth the scientific bases upon which current concepts of immunology rest. Next, the section dealing with mechanisms of response describes the interactions of these principles in the context of immunobiology. Finally, the clinical applications section is concerned with the clinical meaning of immunology and em-

*World Health Organization: Teaching of immunology in the medical curriculum. WHO Techn. Rep. Ser., No. 358, 1967.

ploys certain diseases as illustrative models. The suggestions for further reading at the end of each chapter serve only as a selected core of information to which the reader can refer.

Many persons have contributed to the preparation of this text and I wish to express my indebtedness to them. I wish first to thank Dr. Philip L. Calcagno who has been most generous in his encouragement and support of the total effort. He has permitted a rearrangement of the functions of the Department to allow the time necessary for the writing of this text. Those others who have read sections of the manuscript and have contributed substantive comments include the following: Dr. Robert J. Clayton, Dr. Robert I. Krasner, Dr. Frederick G. Burke, Dr. Raja Hawit, Dr. Malcolm M. Martin, Dr. William McFarland, Dr. Theodore I. Malinin, Dr. F. Paul Alepa, Dr. Joseph J. Biundo, Dr. Heinz Bauer, Dr. S. Gerald Sandler, Dr. Robert D. Meyers, Dr. Val Abbassi, Dr. Rita Colwell, Dr. John L. Nemes, Dr. Donald E. Kayhoe, Dr. Lloyd W. Law, Dr. John B. Robbins, Dr. Norman Conant, Dr. David T. Smith, Dr. William D. Terry, Dr. Leroy E. Hood, Dr. Fred S. Rosen, Dr. Elliott F. Ellis, Dr. George Santos, Dr. Ronald B. Herberman, Dr. D. Carleton Gajdusek, Dr. Arthur M. Silverstein, Dr. N. R. Shulman, Dr. Charles H. Kirkpatrick, Dr. Malcolm S. Artenstein, Dr. Kenneth J. Sell and Dr. John J. Miller, III.

My appreciation is also extended to my clinical and research fellows and house staff who contributed their comments and criticisms. I owe a special debt of gratitude to the medical students. It is the questions they ask of their patients at the bedside and in the clinic that have provided the incentive with which to write this textbook. In particular, I would like to acknowledge the help of Mr. Mark A. Filippone and Mr. Lewis Kanter who made many helpful criticisms during the preparation of the manuscript and to Dr. Vincent J. Capostagno who helped in correcting the galley proofs. While many individuals have contributed to information in this text, I alone assume responsibility for any errors found within these pages.

I am deeply indebted to the entire staff of the Department of Medical and Dental Communications for their assistance in the preparation of the illustrations and to the Department of Pathology who submitted many of the illustrations. I wish to thank Miss Diane Hargrave and Mrs. Vincent W. Hollis for their diligent typing of the entire manuscript.

Finally, I wish to express my thanks and appreciation to Mr. John L. Dusseau and to his colleagues at W. B. Saunders Company for their patience, support and understanding in the lengthy preparation of this text.

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Chapter 1

INTRODUCTION: DEVELOPMENT OF THE IDEA OF IMMUNITY

The concept of immunity is an ancient and pragmatic one and is properly termed the study of resistance to infection. It was known for centuries before the discovery of the germ theory of infectious disease that recovery from illnesses was accompanied by the ability to resist reinfection. Thus, the elements of classical immunology preceded bacteriology and contributed to it. Similarly, contributions to immunology were made by anthropologists, anatomists, biologists, chemists and geneticists. These fields in turn have been enhanced by the application of immunologic phenomena. Shown in Figure 1-1 is a schematic representation of the major milestones important in the development of immunology.

Preceding modern medicine, in the eleventh century, the Chinese physicians observed that the inhalation of smallpox crusts prevented the subsequent occurrence of the disease. Subsequently the technique of variolation, the intradermal application of powdered scabs, was used in the Middle East where its primary intent was "preserving the beauty of their daughters." This primitive immunization reached England in the eighteenth century through Pylarini and Timoni and was later popularized by Lady Montagu (Fig. 1-2). Wide variations in vaccination procedures, however, occasionally led to death. In addition, the widespread acceptance of herb medicine prevented the full acceptance of this form of therapy.

The future of modern immunobiology was assured when Edward Jenner (Fig. 1-3), as a medical student, made the surprisingly sophisticated discovery that inoculation with cowpox crusts protected man from smallpox. This important discovery resulted from Jenner's observation that milkmaids who had contacted cowpox were resistant to infection with smallpox.

The enhancement and further development of preventive immunization was made possible by Louis Pasteur (Fig. 1-4) who coined the term "vaccine" (*vacca*: cow, L.) in honor of Jenner's contribution. Pasteur's researches led to the development of the germ theory of disease from which he developed techniques for the *in vitro* culture of microorganisms. This work produced material which could be used for vac-

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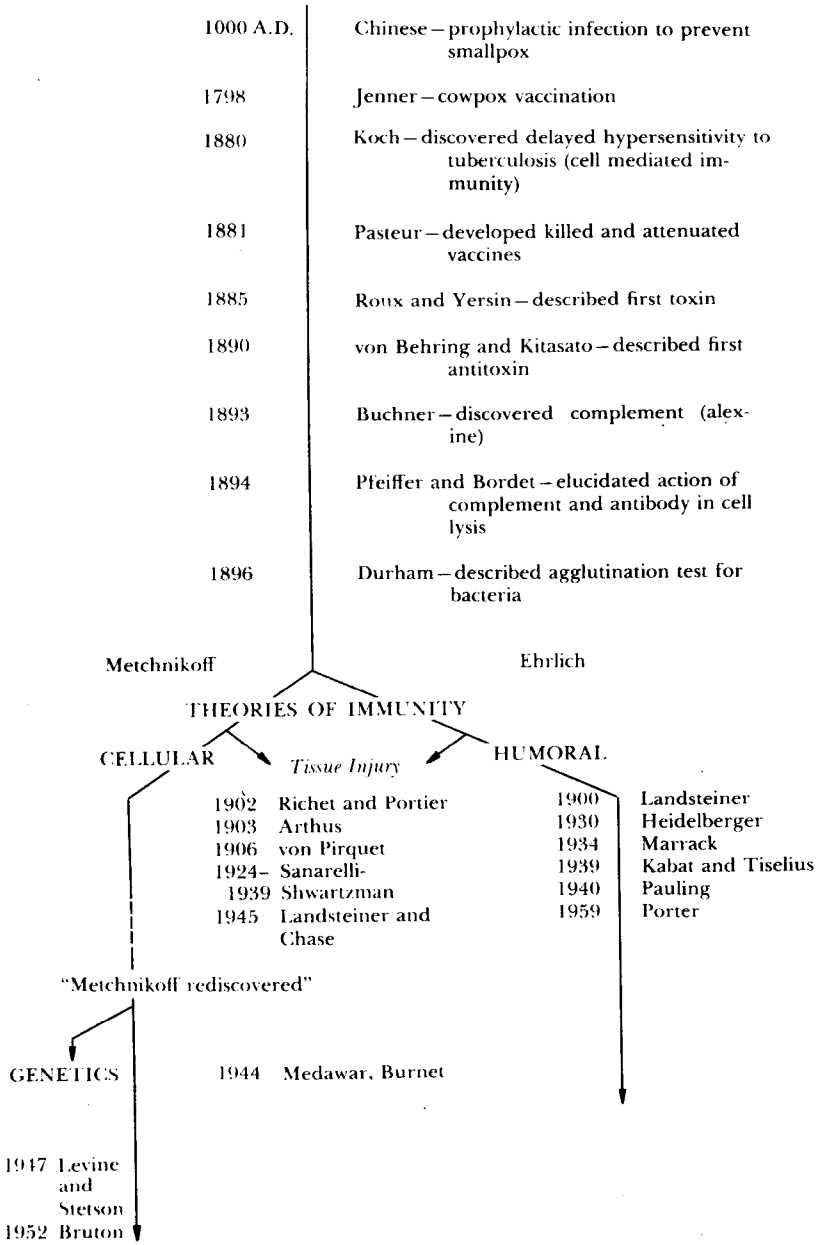

Figure 1-1. Schematic representation of some major milestones in immunology.

Figure 1–2. Lady Mary Wortley Montagu. (Courtesy of National Library of Medicine.)

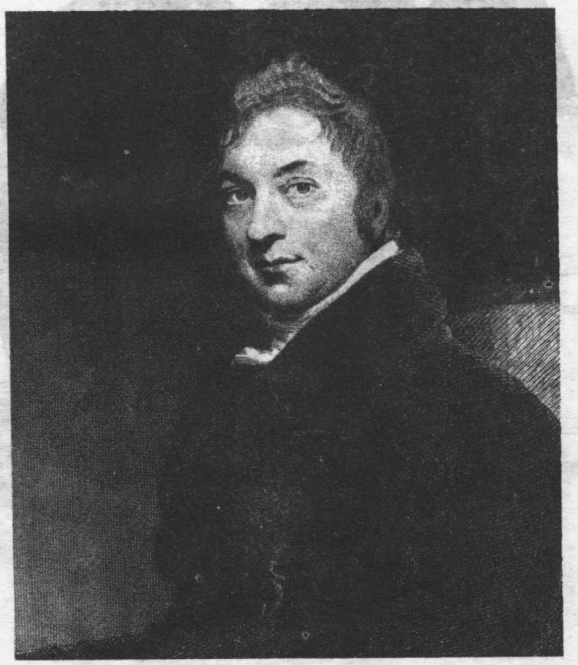

Figure 1–3. Edward Jenner (1749–1823). (Courtesy of National Library of Medicine.)

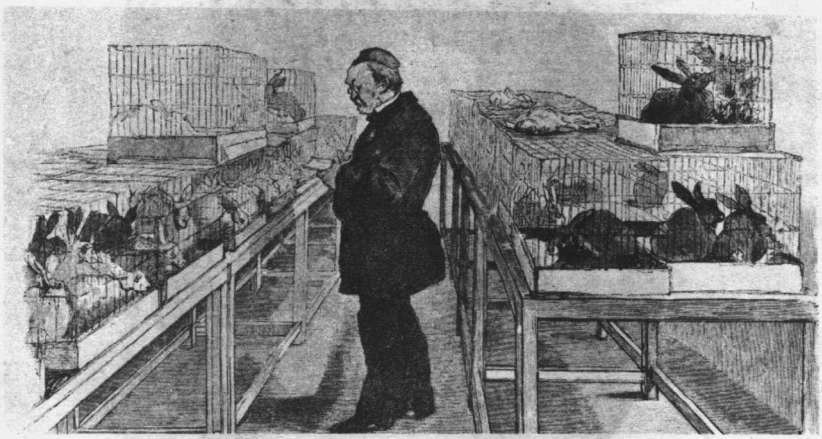

Figure 1–4. Louis Pasteur (1822–1895). (Courtesy of National Library of Medicine.)

Figure 1–5. Louis Pasteur, to left, watches as an assistant inoculates a boy for "hydrophobia" (rabies). (Wood engraving in "L'Illustration" from Harper's Weekly *29*:836, 1885; courtesy of National Library of Medicine.)

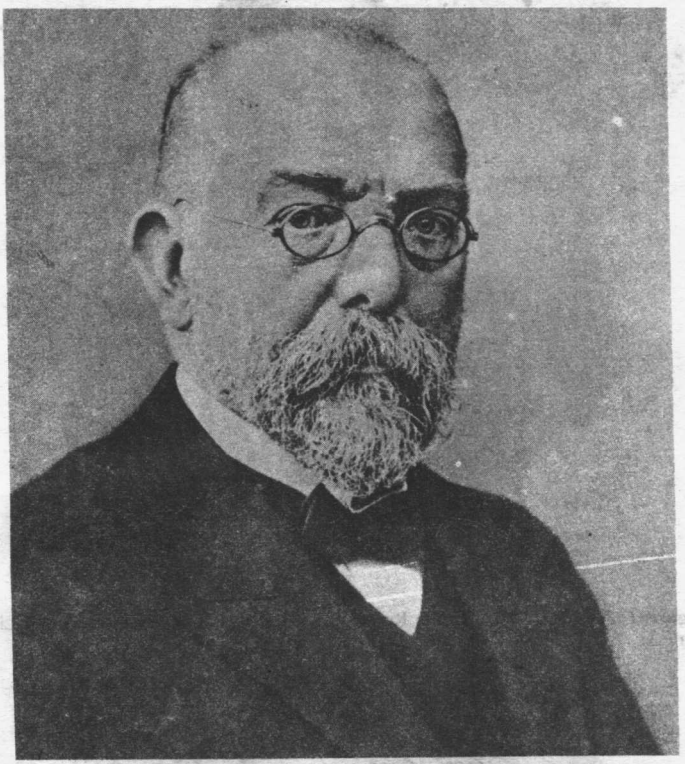

Figure 1–6. Robert Koch (1843-1910). (Courtesy of National Library of Medicine.)

cines: living, heat-killed and attenuated (living but with reduced virulence). During these investigations, Pasteur observed that old cultures (attenuated) of fowl cholera organisms when inoculated into fowl produced no disease. Surprisingly, these fowl were resistant to subsequent infection with the organism and were solidly immune. This early use of living attenuated cultures for active immunization is still our therapy of choice in the prophylaxis of many infectious diseases (Fig. 1-5).

Later, Robert Koch, during his studies of the bacterial etiology of infectious diseases, discovered the tubercle bacillus (Fig. 1-6). During attempts at developing a vaccine for tuberculosis, he observed the phenomenon known today as delayed hypersensitivity or cell-mediated immunity.

Following the isolation of the diphtheria bacillus, Roux and Yersin demonstrated the existence of a potent soluble exotoxin elaborated by this organism (Fig. 1–7). This toxin was used by von Behring (Fig. 1–8) and Kitasato to inoculate animals who produced in their serum a toxin-neutralizing substance called *antitoxin.* This neutralizing cap-

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Figure 1–7. Pierre Paul Emile Roux (1853–1933). (Courtesy of National Library of Medicine.)

Figure 1–8. Emil Adolf von Behring (1854–1917). (Courtesy of National Library of Medicine.)

Figure 1–9. Paul Ehrlich (1854–1915). (Courtesy of National Library of Medicine.)

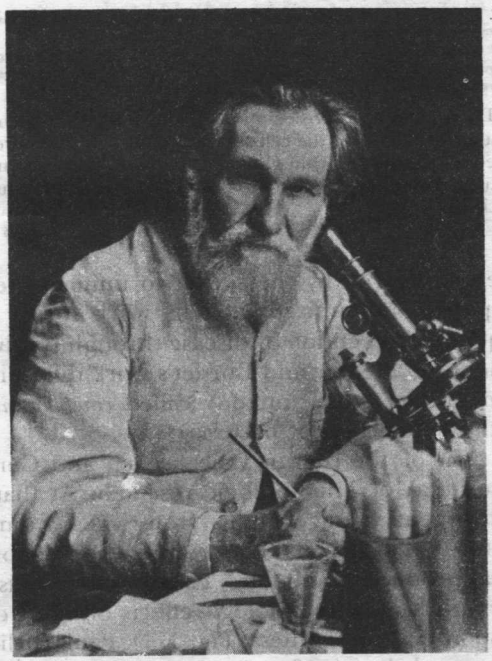

Figure 1–10. Elie Metchnikoff (1845–1916). (Courtesy of National Library of Medicine.)

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