IMMUNOLOGY:
Basic Processes

JOSEPH A. BELLANTI, M.D.

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CONCERNING THE COVER

The illustration on the cover is an enlargement of a figure that appears in Chapter 11—"A Unifying Model for Immunologic Processes." The intent is to indicate the complexity of the environment and its interaction with the human immunologic system.

In the design are representations of the various categories of environmental substances that are disposed of by the immunologic system and that, on occasion, may have an adverse effect on the host, resulting in disease. These include the foods that we ingest, the microorganisms that cause infection, the plant and animal products and insects that contribute to allergic disease, the drugs used in therapy, and the myriad chemical substances that have resulted from our industrialized society and that continue to multiply as a consequence of our ever-expanding technology. The design is appropriate in the late 20th century when many federal agencies, professional and voluntary societies, and concerned citizens are focusing greater interest on the interaction between humans and their environment.

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Drawings for this book were made with skill and insight by JANE A. HURD.

PREFACE

Immunology is the study of those processes used by the host to maintain constancy in his internal environment when confronted with foreign substances. Implicit in this broad definition is the fact that immunology embraces both the basic and the clinical sciences. In turn, significant advances in immunology have resulted from the interaction of these disciplines. *Immunology* and *Immunology II*, its second edition, have emanated from an interdisciplinary center whose mission of research, education, and patient care is based upon the symbiotic relationship among individuals engaged in this multitude of scholarly disciplines. Both texts were organized into the same three basic sections—Principles, Mechanisms, and Clinical Applications.

The present "minitext" introduces the principles of immunology and is directed primarily at the undergraduate, predoctoral, nursing, or medical technology student who may not require the extensive clinical correlations found in *Immunology II*. Such a text seems timely in light of the increasing number of courses at the undergraduate level that include immunology.

The chapters of the "minitext" have been extensively revised and updated. They culminate in a complete and concise overview of the immunologic system (Chapter 11), which has been imaginatively illustrated with two-color drawings by Ms. Jane Hurd.

My appreciation is extended to the many colleagues, both at Georgetown and elsewhere, who have read and commented upon the manuscript. They have added immeasurably to my own intellectual life and to the life of the Immunology Center. I also owe a special debt of gratitude to students of all ages for whom the book is written and with whom I share the joy of discovery. It is the questions they ask in the lecture hall, in the laboratory and clinic, and at the bedside that have provided me with the incentive to write. Although many individuals have contributed information to this text, I alone assume responsibility for any errors found within these pages.

I am deeply indebted to the staff of the Department of Medical and Dental Communications at Georgetown for their assistance in the preparation of the charts and drawings. I wish also to thank Miss Diane Hargrave for her diligent typing of the entire manuscript.

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JOSEPH A. BELLANTI

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Chapter 1

INTRODUCTION TO IMMUNOLOGY

Joseph A. Bellanti, M.D.

HISTORICAL BACKGROUND

The concepts of immunology are ancient and pragmatic and are derived primarily from the study of resistance to infection. It was known for centuries before the discovery of the germ theory of infectious disease that recovery from illness was accompanied by the ability to resist reinfection. Thus, the elements of classical immunology preceded bacteriology and contributed to it. Similarly, contributions were made to immunology 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 some major milestones important in the development of immunology.

Preceding modern medicine, Chinese physicians in the eleventh century observed that the inhalation of smallpox crusts prevented the subsequent occurrence of the disease. Later, 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 Mary Wortley 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 finding resulted from Jenner's observation that milkmaids who had contracted 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" (from *vacca*: L., cow) 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 that could be used for

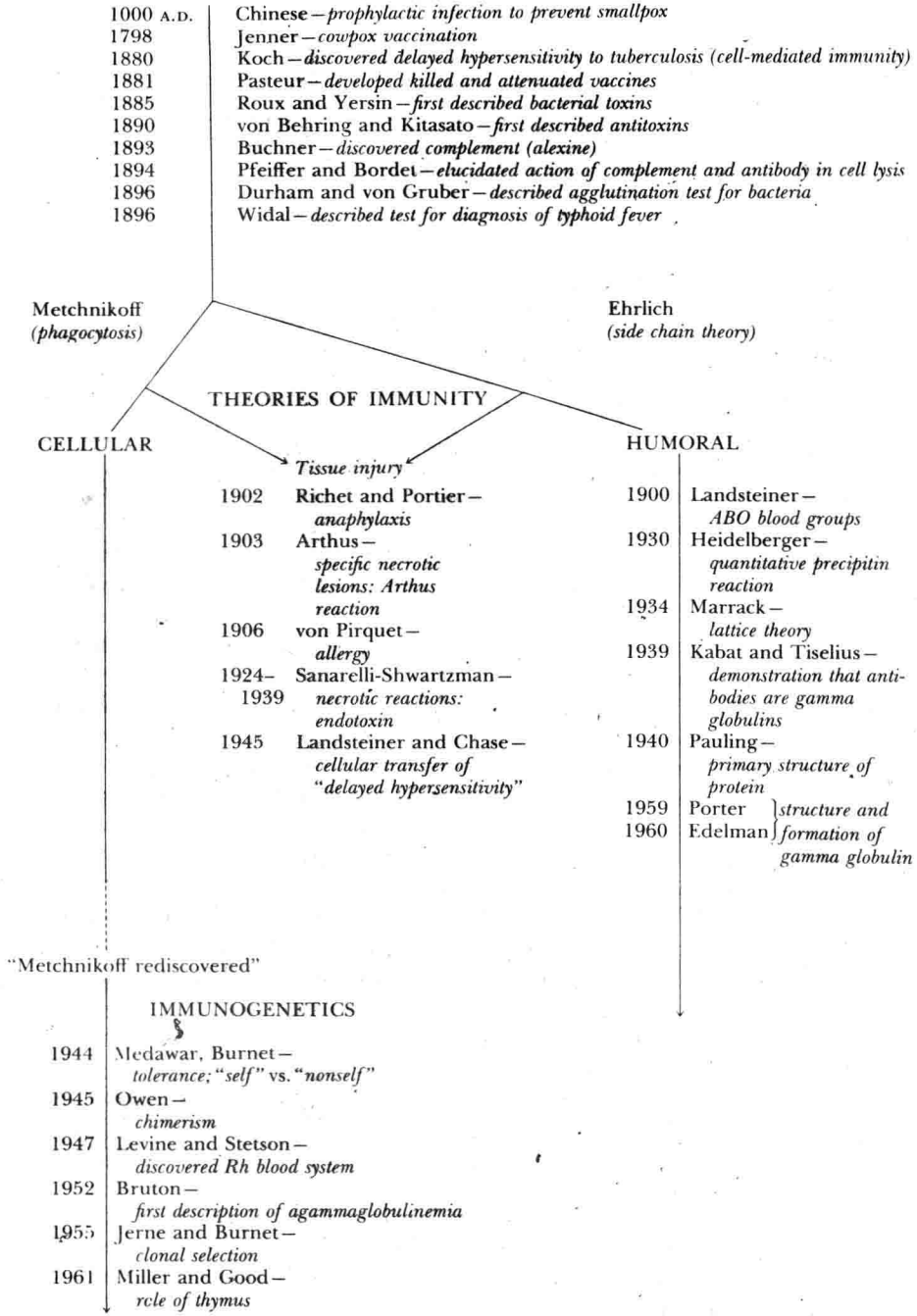

Figure 1–1. Schematic representation of some major milestones in immunology.

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.)

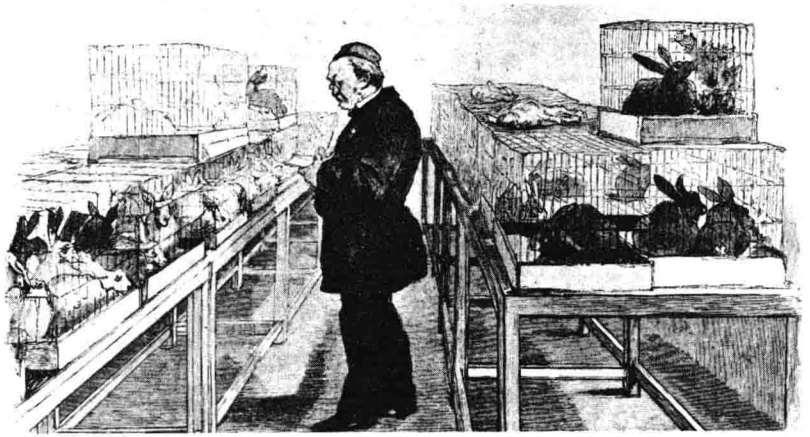

Figure 1–4. Louis Pasteur (1822–1895). (Courtesy of National Library of Medicine.)

vaccines: 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 (Fig. 1–6), discovered the tubercle bacillus during his studies of the bacterial etiology of infectious diseases. While attempting to develop 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 capability could be transferred by the serum to uninoculated animals, a process called passive immunization. Their work forms a model for the modern techniques of preventing disease through passive immunization (immunotherapy). Pfeiffer and Bordet's work differentiated a substance in serum, distinct from antibody, called *complement* that also participates in the destruction of bacteria. The observations of Durham and von Gruber that serum could clump or agglutinate bacteria formed the basis for tests for the diagnosis of infectious specific agglutination reactions, such as the test described by Widal for the diagnosis of typhoid fever (Widal test).

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.)

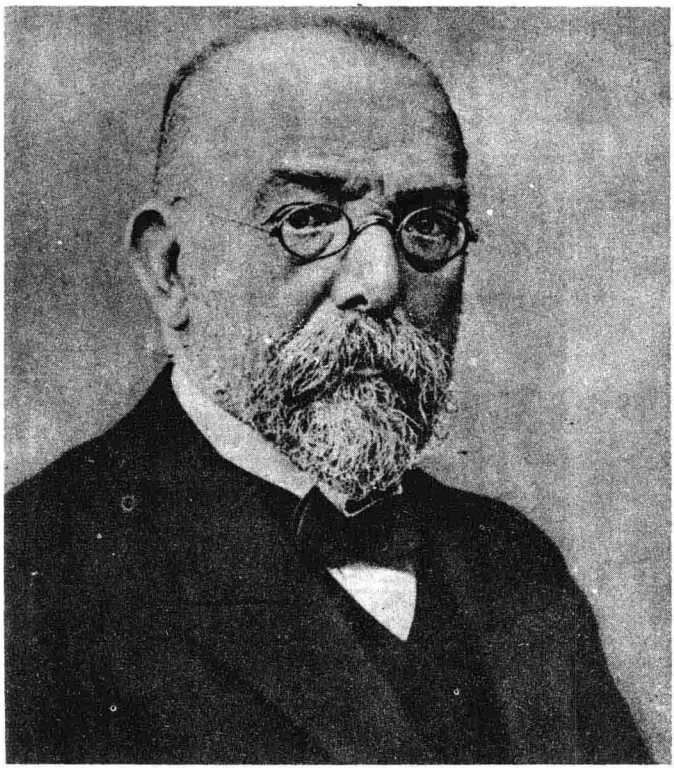

Figure 1–6. Robert Koch (1843–1910). (Courtesy of National Library of Medicine.)

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

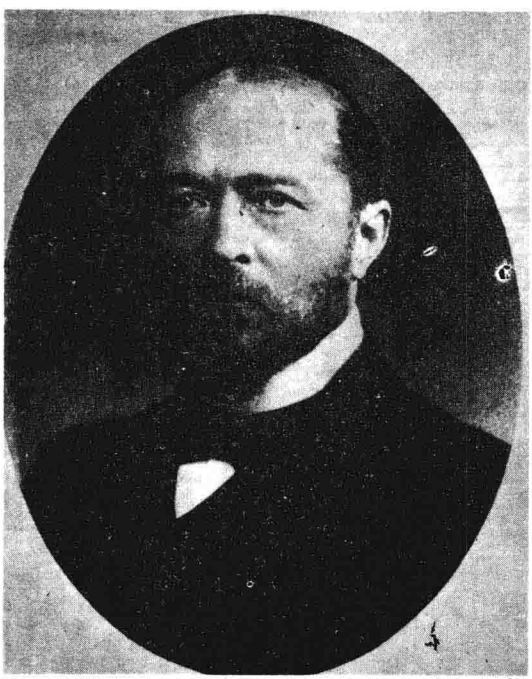

Figure 1–8. Emil Adolf von Behring (1854–1917). (Courtesy of National Library of Medicine.)