THE EYE AND IMMUNOLOGY

MATHEA R. ALLANSMITH, M.D.

THE EYE AND IMMUNOLOGY

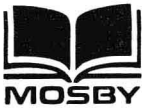
MATHEA R. ALLANSMITH, M.D.

Associate Professor of Ophthalmology, Harvard Medical School;
Senior Scientist, Eye Research Institute of Retina Foundation,
Boston, Massachusetts

with **162** *illustrations*

The C. V. Mosby Company

ST. LOUIS • TORONTO • LONDON 1982



A TRADITION OF PUBLISHING EXCELLENCE

Editor: Eugenia A. Klein
Manuscript editor: Rebecca A. Reece
Design: Susan Trail
Production: Debbie Wedemeier

Cover:

Transmission electron micrograph of degranulating conjunctival mast cell of rat.

Micrograph prepared by **Laila A. Hanninen,**
Eye Research Institute, Boston, Massachusetts

Printed in the United States of America

The C.V. Mosby Company
11830 Westline Industrial Drive, St. Louis, Missouri 63141

Library of Congress Cataloging in Publication Data

Allansmith, Mathea R., 1930-
The eye and immunology.

Bibliography: p.
Includes index.
1. Eye—Diseases and defects—Immunological aspects. 2. Immunology. I. Title. [DNLM: 1. Eye—Immunology. 2. Eye diseases—Immunology. WW 140 A418e]
RE68.A37 617.7'1 81-14163
ISBN 0-8016-0117-7 AACR2

C/CB/CB 9 8 7 6 5 4 3 2 1 01/B/049

Preface

Soon after I wrote a brief syllabus to go with my Stanford Basic Science Course lectures on ocular immunology in 1970, requests for the syllabus started coming in from people not taking the course. Embarrassed by the ever more apparent incompleteness of the syllabus, I added one article, then another and another, to fill the gaps. The appendix became larger than the original syllabus. Attractive texts on basic immunology continued to appear (I counted 29 on the shelves of a Boston medical bookstore). Books on ocular immunology began to appear. Still the syllabus was requested, although some readers complained that it was becoming unwieldy.

People seemed to be looking for a short, readable, and not-too-costly introduction to the relationship of immunology to the eye. This book is intended to fill that need; it is especially for resident ophthalmologists wanting to learn the basic science of ocular immunology, for practitioners interested in the state of the field, and for the growing number of interested scientists in other fields.

Immunology books fall into two general categories. The first is the collection of papers, often from a symposium, in which many contributors present their own narrowly framed research experiences. Books of this type represent the leading edge of the field. Ideas often conflict, and details outweigh concepts. Such books, which typically have long, detailed bibliographies, are only slightly less immediate than journal articles. They are quickly outdated by new findings and are most useful to experienced workers looking for a summary of recent research. Books of the second type summarize the principles established by those of the first type and contain only enough detail to back up the concepts. Their bibliographies list only a few crucial detailed reports and refer to previous publications on concepts. Immunology is a fast-moving science to which new concepts are added rapidly, but books of the second type are not quickly outdated; concepts, once established by many detailed reports, generally survive.

This is a book of the second type, concerned with the *principles* of ocular immunology. The seven chapters approach the subject according to the following scheme.

Chapter 1 discusses the basic aspects of immunology that are most pertinent to the eye. Although much is excluded—genetics and phylogeny are barely touched—this is offset by the concentration on the exciting details of antibodies, mediators, and cells.

Chapter 2 describes how the immunologic process can injure tissue. The four types of hypersensitivity reactions—anaphylactic, antibody-dependent cytotoxic, complex-mediated, and cell-mediated—are detailed. This chapter covers transplantation immunology, autoimmunity, and immunodeficiency.

Chapter 3 describes the immunology of the normal eye and how an eye remains normal in an environment full of antigens and microbes.

Chapters 4 to 7 discuss disease entities that have immunologic properties in relation to the eye. Chapter 4 covers the lids and the conjunctiva; Chapter 5 the cornea and the sclera; Chapter 6 the uvea, the retina, the optic nerves, and tumors; and Chapter 7 the ocular aspects of systemic immune disease.

The glossary is a comprehensive list of relevant immunologic terms.

I would like to thank Diane L. Hubisz, Paul Bethge, and Dorothy Scott for the enormous amount of time and effort they devoted to the making of this book and Ivan Roitt for his excellent book, *Essential Immunology*, which makes a complex subject simple.

Mathea R. Allansmith

Contents

THE EYE AND IMMUNOLOGY

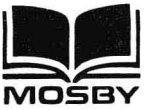
MATHEA R. ALLANSMITH, M.D.

Associate Professor of Ophthalmology, Harvard Medical School;
Senior Scientist, Eye Research Institute of Retina Foundation,
Boston, Massachusetts

with **162** *illustrations*

The C. V. Mosby Company

ST. LOUIS • TORONTO • LONDON 1982



A TRADITION OF PUBLISHING EXCELLENCE

Editor: Eugenia A. Klein
Manuscript editor: Rebecca A. Reece
Design: Susan Trail
Production: Debbie Wedemeier

Cover:

Transmission electron micrograph of degranulating conjunctival mast cell of rat.

Micrograph prepared by **Laila A. Hanninen,**
Eye Research Institute, Boston, Massachusetts

Printed in the United States of America

The C.V. Mosby Company
11830 Westline Industrial Drive, St. Louis, Missouri 63141

Library of Congress Cataloging in Publication Data

Allansmith, Mathea R., 1930-
The eye and immunology.

Bibliography: p.
Includes index.
1. Eye—Diseases and defects—Immunological aspects. 2. Immunology. I. Title. [DNLM: 1. Eye—Immunology. 2. Eye diseases—Immunology. WW 140 A418e]
RE68.A37 617.7'1 81-14163
ISBN 0-8016-0117-7 AACR2

C/CB/CB 9 8 7 6 5 4 3 2 1 01/B/049

1
Immunologic principles

"Immunity" is defined, abstractly, as exemption from hazard. As Ivan Roitt stated, the main features of *biologic* immunity are memory, specificity, and the recognition of "nonself." Biologic immunity can be divided into the native and acquired types.

MEMORY

Seldom does anyone suffer from smallpox, measles, chickenpox, or mumps a second time. The initial encounter with an infectious organism imparts some information so that the body remembers to call up its defenses to resist any later attack by the same organism. In a first encounter protection is provided by antibodies and/or lymphocytes evoked in response to the infectious agent behaving as an antigen (Fig. 1-1). Interaction with antibodies or lymphocytes leads to elimination of the antigen. Several days after the first contact with an antigen, antibodies appear in the blood (the *primary response*). These antibodies subside after reaching a certain level. If the subject rests and then is exposed again to the same antigen, the course of events is much different. In the *secondary response* the antibody in the blood rises in 2 to 3 days to a level much higher than that attained in the primary response. Secondary antibody production is faster and more profuse because the antibody-forming system has been primed by the first encounter with the antigen.

Vaccination creates immunologic memory by provoking a primary response to a relatively innocuous form of an antigen. Any later contact with the virulent form of that antigen stimulates a secondary response, in which intense production of antibody or sensitized cells battles the invader.

SPECIFICITY

Early on, investigators noticed that immunologic defense is based on engagement of the invading antigen by a *specific* defender. It became evi-

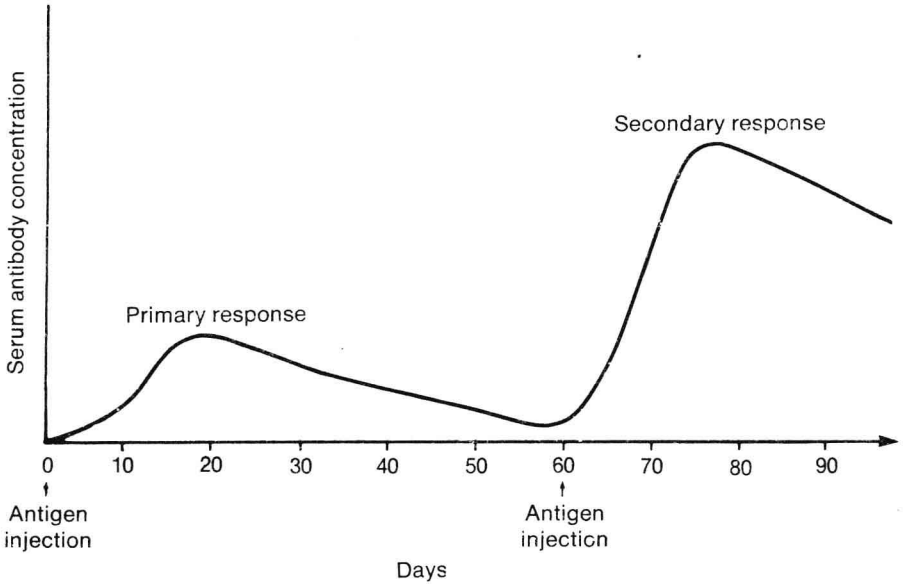


Fig. 1-1. Primary and secondary response. Animal is injected with antigen on day 0 and day 60. Antibody response to second injection is more rapid and more intense than response to first injection.

dent that when a bacterium or a bacterial toxin enters the body, something reacts to its presence by producing a substance (soluble protein) that carries a pattern enabling it to attach specifically to the invader's surface. The soluble proteins were named *antibodies*. Their importance was obvious; so was the ease with which they could be studied.

The establishment of memory (immunity) against one organism does not confer protection against unrelated organisms. After an attack of chickenpox one is immune to further infection with chickenpox but still susceptible to other agents, such as measles or polio viruses. The complete specificity of antibodies was the central theme in the early immunologists' understanding of defense against infection and the nature of postinfection immunity.

RECOGNITION OF NONSELF

The body's ability to recognize one antigen and distinguish it from another has other functions in addition to repelling invaders. The individual must also distinguish between what is "nonself" (not a component of the individual's own body) and what potential antigens are part of the self. Failure to do so leads to the synthesis of antibodies directed against com-

ponents of the self (autoantibodies). Self and nonself recognition mechanisms develop early in gestation. A permanent unresponsiveness (tolerance) is then created so that at immunologic maturity the body is unable to respond to "self" components. As we shall see later, the ability to distinguish self from nonself breaks down as aging proceeds, and this results in autohypersensitivity.

NATIVE IMMUNITY

Native immunity is immunity expressed toward a primary infection before acquired immunity (discussed below) has developed, and does not require experience with antigen to be activated (Fig. 1-2). Anatomic barriers, macrophage activity, high vascularity, and flushing of fluids over surfaces all represent native immunity.

Native immunity is important in the defense of the eye. The globe is recessed into a bony cavern, which protects it on all sides except the one through which it peeps at the world. Overhanging ledges protect the globe from direct blows. The lids defend the front of the globe and resurface the cornea with tears. The flushing action of the tears in removing foreign particles is an important aspect of native defense, as are the nonspecific antibacterial substances within the tears (such as lysozymes and other antibacterial substances). Even the degree of vascularity around the eye must be considered a part of native defense. In general, areas with much vascularity have strong native immunity; areas with little or no vascularity have weak native immunity.

ACQUIRED IMMUNITY

Acquired immunity is immunity activated by contact with an antigen. The production of specific antibody or specifically sensitized cells is the essence of acquired immunity. The acquired immune response that has evolved in higher animals provides more effective defense by directing the action of the appropriate defense cells against whatever agents are infecting the body at the time. The specific antibodies synthesized by the defending cells greatly speed up disposal of the infecting organisms by facilitating their adherence to the already present phagocytic cells. That is, increasing the efficiency of the nonspecific or native immunologic systems is a major function of the specific acquired immune response.

LYMPHOCYTES

Development of the lymph system

The ability to make a specific immune response to potentially harmful agents is confined to vertebrates (Fig. 1-3). Lampreys, primitive elasmo-

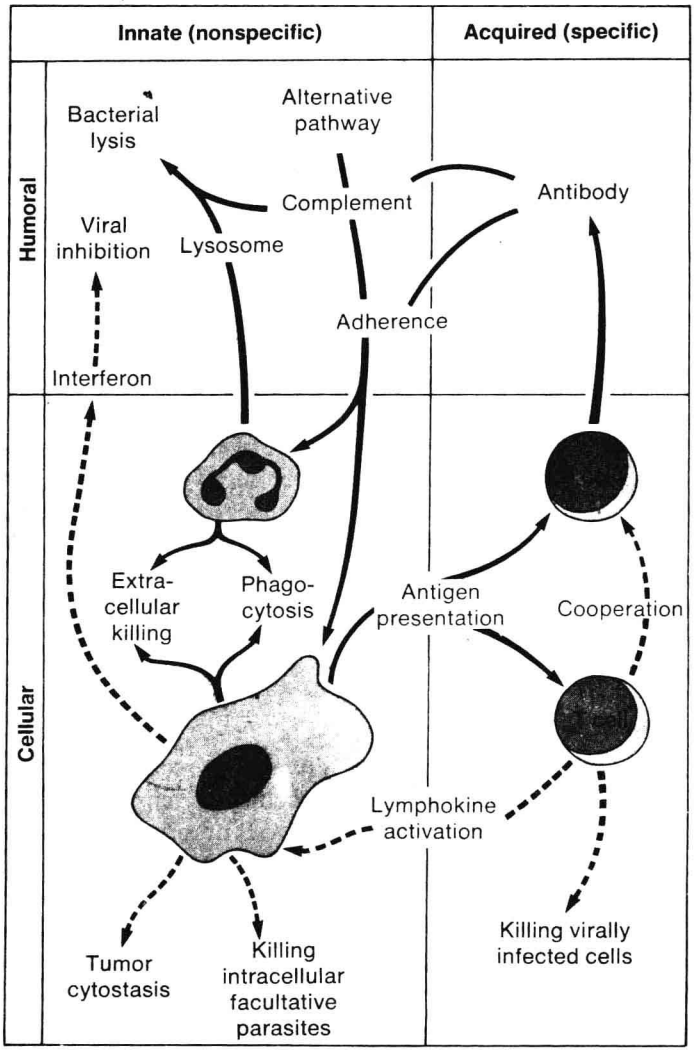


Fig. 1-2. Simplified scheme to emphasize interactions between natural and acquired (specific) immunity mechanisms. *Broken line,* reactions influenced by T cells. (Modified, with permission, from Roitt, I.M.: Essential immunology, ed. 4, Oxford, England, 1980, Blackwell Scientific Publications, Ltd.)

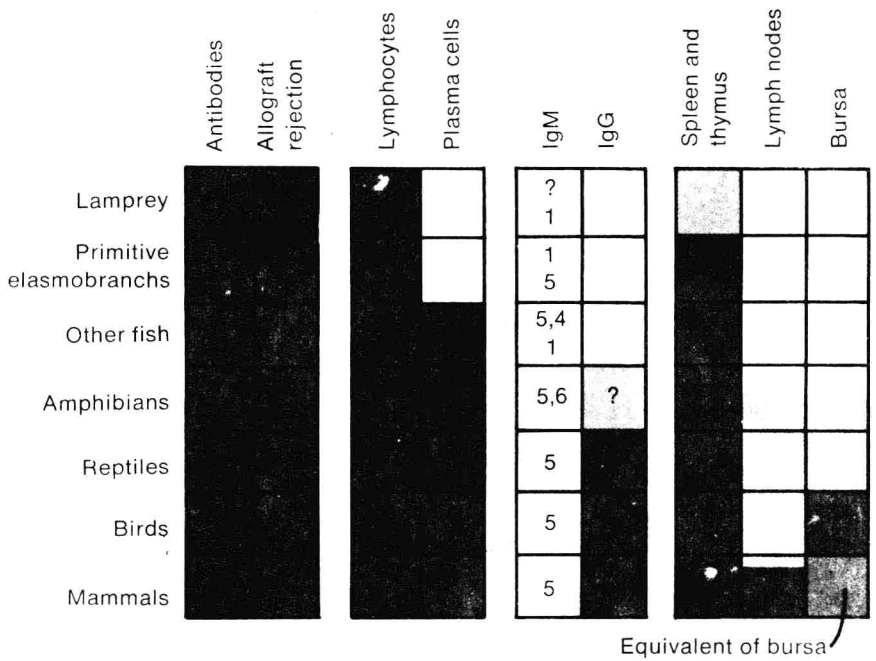


Fig. 1-3. Overall view of development of vertebrate immunity. Columns are separated into four categories *(from left):* immune functions, morphologic cell types associated with immunity, immunoglobulins, and presence or absence of immunologically significant organs. All vertebrates from lamprey onward have circulating cells with qualities of lymphocytes and capacity to produce antibodies and reject grafts from other individuals of same species. Immunoglobulin G (IgG) appears relatively late but is preceded by monomeric IgM of similar molecular size. In IgM column number of subunits in macromolecule in various species is shown for various animal groups. Note that birds are only vertebrates that have unequivocal bursa of Fabricius, though any animal with plasma cells can be said to have equivalent. Light gray areas show weak or doubtful findings. Where two shadings are shown in a square, differences are present within an order. (Reproduced, with permission, from Immunology, readings from Scientific American with introductions and additional material by J.M. Burnet. Copyright © 1976 by Scientific American, Inc. All rights reserved. Diagram prepared from data in Marchalonis, J.J.: Immunity in evolution, Cambridge, Mass., 1975, Harvard University Press.)

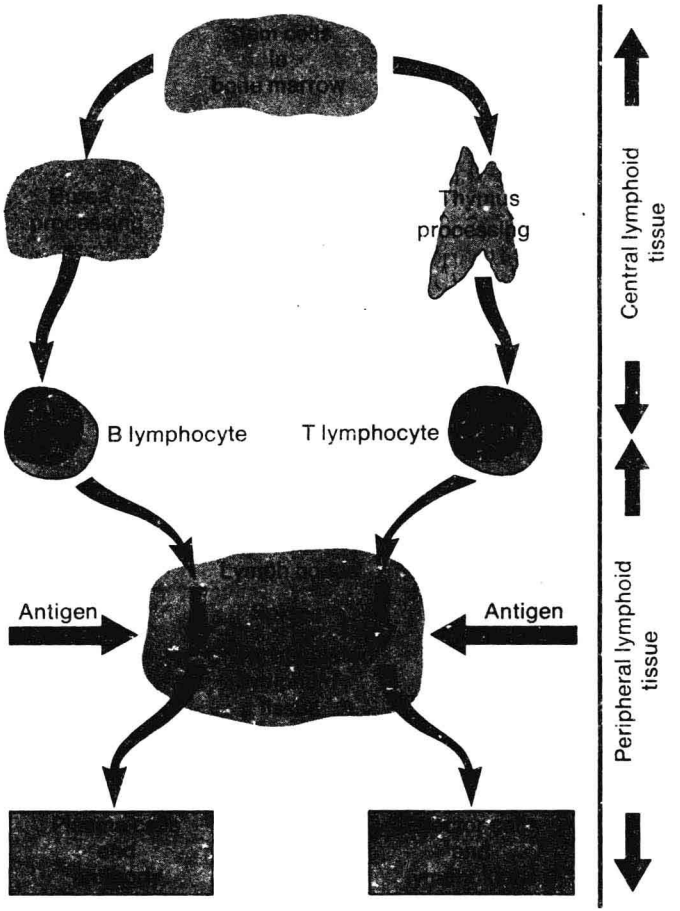


Fig. 1-4. Processing of bone marrow cells by thymus to yield immunocompetent T cells and by gut-associated central lymphoid tissue to yield immunocompetent B cells. On antigenic stimulation, proliferation and transformation to cells of lymphoblast and plasma cell series occur.

branchs, other fishes, and amphibians have antibodies, lymphocytes, and immunoglobulin M (IgM), and can reject allografts, but they lack immunoglobulin G (IgG), organized lymph nodes, and the equivalent of a bursa. Reptiles, birds, and mammals have antibodies, lymphocytes, and IgM, plus IgG and a bursa system or its equivalent. Only mammals are known to have all of the above plus a highly organized lymph node system.

When an antigen enters the body, two different types of immunologic reaction may occur: (1) the synthesis and release of free antibody into the