OPHTHALMIC PATHOLOGY

An Atlas and Textbook

SECOND EDITION

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FOREWORD

THE FIRST EDITION of this book was received with such appreciation that it was soon sold out. The publishers were confronted with the problem of reprinting or production of a revised edition. The matter was referred to the Academy and to the Academy Committee on Ophthalmic Pathology. As in any new work of the kind portrayed in the Atlas-Textbook of Ophthalmic Pathology, some portions were not acceptable in the light of present day concepts and subjects of great importance conceived since the preparation of the text were, of course, not included. Suggestions were received from teachers of pathology concerning the organization of the text and it was the opinion of the Committee on Pathology that a revision was necessary and could conceivably be done in approximately three years.

The Committee graciously accepted the assignment and early in 1956 work on revision was started. It soon became evident that besides some reorganization of the text, several parts had to be rewritten and new chapters added. It meant an increase in pagination of the text and the addition of a number of illustrations. An estimate of the cost to the Academy for underwriting the revision was submitted to the Council together with the contract terms of the publishers. The necessary funds were appropriated to cover the actual out of pocket expenses incurred by the Committee in preparation of the manuscript for the printer and the authors gave generously of their time without compensation. Thus, a second edition of Ophthalmic Pathology, An Atlas and Textbook was made possible.

Some of the illustrations and legends prepared for the first edition have been used in this new edition and many new ones added. It has been the aim of the Committee to preserve the form of the earlier edition, in order to indicate lineage and to acknowledge the debt owed to Dr. Jonas Friedenwald and his co-authors in producing a new textbook in ophthalmic pathology, and to Mrs. Helenor C. Foerster, who assembled the most remarkable Atlas of ophthalmic histopathologic reproductions ever produced. This heritage is a most valuable possession of the Academy and reflects the objectives proclaimed by the founders that, "The object of the Academy shall be to promote and advance the science and art of medicine appertaining to the eye, ear, nose and throat; and to encourage the study of the relationship of these specialties to surgery, general medicine, and hygiene" (Constitution. Art. II).

W. L. BENEDICT, M.D., LL.D.

FOREWORD

THIS SECOND EDITION of Ophthalmic Pathology, An Atlas and Textbook represents the continued close collaboration and cooperation of the American Academy of Ophthalmology and Otolaryngology and the Armed Forces Institute of Pathology. The remarkably complementary relationship of the Academy and the AFIP goes back almost four decades, having had its origin in the organization of the Museum of Ophthalmic Pathology at the old Army Medical Museum in 1921. This Registry, the pioneer component of the American Registry of Pathology, is unequaled and can justly claim to be the largest and most active registry of ophthalmic pathology in the world today.

The popularity of the first edition of this book (like that of the earlier Atlases of DeCoursey and Ash) and the preparation of the second edition are signal tributes to the many ophthalmologists and pathologists working in harmony to advance the field of ophthalmology and ophthalmic pathology.

In this edition the Atlas component has been integrated with the text as closely as possible so as to achieve maximum teaching value and continuity. A majority of the excellent plates prepared for the first edition have been retained while many new illustrations have been added. Many of the inevitable advances that have taken place in the understanding of specific etiology, pathogenetic mechanisms and natural course of various diseases have been described. The result is a volume in which both the American Academy of Ophthalmology and Otolaryngology and the Armed Forces Institute of Pathology can be justly proud.

While this Atlas is basically a textbook designed for the graduate student of ophthalmology or pathology, at the same time it serves a reference need for the hospital pathologist who must be expected to cope with the many complexities of ophthalmic pathology.

The staff of the Armed Forces Institute of Pathology takes pride in having been able to assist the authors in the preparation and completion of this very fine contribution to the advancement of pathology.

FRANK M. TOWNSEND, M.D.
COL., U.S.A.F., M.C.

PREFACE TO THE SECOND EDITION

MANY ADVANCES have occurred in ophthalmology and in pathology since the first edition was printed. Not only has knowledge of eye diseases changed, but many of the general concepts of disease and its effects on tissue have undergone considerable revision. Newer methods of investigation of the causes and types of inflammation by immunochemical methods have become available, and histochemical techniques have been originated for detection of chemical changes in tissues in disease states. Former concepts of the anatomy of the ocular structures have been revised as the result of advances in phase microscopy and electron microscopy. Some viruses producing disease of the outer eye have been identified and their pathogenicity has become well known. The biochemist has made great advances in the detection and study of inborn errors of metabolism involving amino acids and other body constituents, and progress has been made toward determining the relationship of lipid metabolism to vascular diseases.

Certain diseases, such as retrolental fibroplasia, have been explained on a rational etiologic basis, reproduced in experimental animals, and virtually extinguished by institution of prophylactic measures. Still other conditions have become apparent as a result of attempts to control disease with new therapeutic agents, e.g., fungal infections superimposed on long-term topical corticosteroid and antibiotic therapy for ulcerative corneal lesions.

All these advances warranted the writing of a second edition of this text. In addition it seemed necessary to develop more fully the presentation of the pathologic anatomy of certain tissues (e.g., retina, optic nerve, and vitreous) which were treated in a somewhat cursory fashion in the first edition.

In preparing the new edition it was decided to revert to the anatomic method of discussing and describing pathologic changes in the eye. This method has the disadvantage of a certain amount of repetition, and the student has to refer to several chapters in order to obtain a complete picture of a certain disease affecting the eye. An attempt

to overcome this drawback has been made in the first chapter by presenting a discussion of certain principles of general pathology which would serve as a background for subsequent chapters. Also it was decided to have a discussion of pathologic entities which affect the entire eye, and a general discussion of ocular injuries before proceeding to individual tissues. A certain amount of repetition is not harmful, and we believe the reader will obtain a complete picture of a disease entity without too much cross reference.

Changing the format has necessitated a certain amount of chopping and reorganization of the plates from the first edition so that they could be integrated with the text. The main criticism of the first edition was the lack of correlation of plates with the text. A large number of new plates have been added to show advances in ocular histology as well as in histochemistry and ophthalmic pathology. Many of these were contributed by authors of articles or chapters on special subjects, and the present authors are grateful to them for permitting their use in this edition. Credit is given in the text for the illustrations.

This revision is so extensive that it could really be termed a new textbook. However, one of the finest parts of the first edition, the illustrations, which were so carefully selected and prepared by Mrs. Helenor Campbell Foerster, have been largely reused. The authors wish, also, to indicate their great appreciation to Miss Eleanor V. Paul who devoted so many hours to the preparation of the new plates for this edition and to reading and correcting manuscript, galleys, and page proof.

We wish to thank the following persons for reading and correcting copy, and furnishing valuable consultation in the preparation of the various chapters: Bernard Becker, M.D., St. Louis; Milton Boniuk, M.D., Houston; Wendell C. Irvine, M.D., Los Angeles; Samuel T. Jones, M.D., Chicago; A. Edward Maumenee, M.D., Baltimore; William K. McEwen, Ph.D., San Francisco; Edith Parkhill, M.D., Rochester, Minnesota; John F. Porterfield, M.D., Columbia, Missouri; Christian Elmore Radcliffe, M.D., Iowa City; Robert N. Shaffer, M.D., San Francisco; and Phillips Thygeson, M.D., San Francisco.

We also wish to thank the following persons for kindly furnishing photographs for some of the chapters: L. Allen, Iowa City; Professor Norman Ashton, London, England; C. H. Binford, M.D., Washington, D.C.; J. M. B. Bloodworth, Jr., M.D., Columbus, Ohio; W. M. Boles, M.D., New Orleans; A. Braley, M.D., Iowa City; H. Burian, M.D., Iowa City; L. L. Calkins, M.D., Kansas City, Missouri; D. G. Cogan, M.D., Boston; F. C. Cordes, M.D., San Francisco; L. Feeney, San Francisco; B. S. Fine, M.D., Washington, D.C.; L. K. Garron, M.D., San Francisco; J. W. Henderson, M.D., Rochester, Minnesota; A. S. Holmberg, M.D., Sweden; S. T. Jones, M.D., Chicago; A. Kallos, M.D., New York; H. Q. Kirk, M.D., Oak Park, Illinois; B. A. Klien, M.D., Chicago; T. Kuwabara, M.D., Boston; H. Lund, M.D., Greensboro, North Carolina; A. E. Maumenee, M.D., Baltimore; E. Okun, M.D., St. Louis; A. B. Reese, M.D., New York; B. Rones, M.D., Washington, D.C.; R. N. Shaffer, M.D., San Francisco; G. D. Theobald, M.D., Oak Park, Illinois; P. Thygeson, M.D., San Francisco; A. J. Tousimis, Washington, D.C.; J. A. C. Wadsworth, M.D., New York; and J. R. Wolter, M.D., Ann Arbor.

We wish to thank the Council of the American Academy of Ophthalmology and Otolaryngology for their very earnest support of this revision, and Col. Frank M Townsend, Director of the Armed Forces Institute of Pathology for his assistance in providing the use of the outstanding Medical Illustration Service of the Institute for many of the illustrations. Mr. John Dusseau, of the Saunders Company, has rendered invaluable aid at many of the meetings of the committee and we are very grateful for his excellent advice.

MICHAEL J. HOGAN
LORENZ E. ZIMMERMAN

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Chapter I

General Pathology

INFLAMMATION

Definition

Inflammation may be defined as a series of local tissue reactions which take place at the site of injury. According to Ehrich and to Selye, these reactions follow a repetitive pattern regardless of the specific agent responsible for the injury. They include (1) an initial shock phase characterized physiologically by a disturbance of equilibrium and pathologically by necrosis or degeneration produced by the injurious agent, (2) a reactive countershock phase in which the acute exudative inflammatory reaction attempts to overcome the irritant, (3) an adaptive phase of great variability marked by features of subacute or chronic inflammation, progressing ultimately to (4) a reparative phase in which homeostasis is restored or (4a) exhaustion of local defensive mechanisms, with uncontrolled necrosis or degeneration. Selye has grouped these reactions to local injury under the heading of "local adaptation syndrome" and he has described experiments which support his belief that the local and the general adaptation syndromes are closely interrelated.

Causes and Mechanisms

Inflammation is not synonymous with infection; in fact, most injurious agents are noninfectious. All types of trauma are capable of provoking the cardinal features of inflammation. Abrasions, lacerations, foreign bodies, heat, cold, acids, alkalis, radiant energy, hypersensitivity reactions, in fact any stimulus capable of irritating (overstimulating) cells may be considered etiologic factors. Moreover the stimulus need not be exogenous. Noxious substances liberated from dead or dying tissues are effective irritants. Thus occlusion of the local blood supply to a tissue leading to its destruction may be attended by systemic as well as local signs of inflammation.

In ophthalmology we see many excellent examples of noninfectious agents which set up an inflammatory reaction. Corneal ulcers, for example, often provoke an iritis and sterile pus accumulates in the anterior chamber (hypopyon). Virtually every ocular injury and every surgical procedure is complicated by some degree of inflammation. Those which are attended by great tissue destruction, hemorrhage, the presence of foreign bodies, or infection generally will be complicated by more severe degrees of inflammation. One of the most significant clinical examples of purely endogenous but noninfectious inflammation encountered by the ophthalmologist

is produced by malignant melanomas (and less frequently retinoblastomas) which outgrow or obstruct their blood supply and become necrotic. Eyes containing such tumors frequently are treated with antibiotics in the belief that the endophthalmitis or panophthalmitis is of bacterial origin. Another example is lens-induced uveitis.

Vascular and Cellular Aspects

Initial changes in ground substance. According to McCutcheon, the series of events which take place when tissues are irritated generally are described as vascular and cellular, but these, as Zweifach has shown by micromanipulative procedures, are preceded by alterations in the ground substance at the site of injury. In the conjunctiva, for example, the connective tissue matrix is normally a gel which impedes the spread of particulate matter. The earliest alterations observed after micro-injury occur at the site of trauma. The state of the ground substance is converted from gel to sol and particulate matter now flows freely through the injured tissues. Comparable connective tissue changes can be reproduced by trypsin, hyaluronidase, a variety of bacterial toxins and snake venom, but significantly not by histamine or heparin.

Local vascular response. The vascular inflammatory response to minimal trauma begins several minutes later. The terminal arteriole dilates and the endothelium of capillaries and venules downstream from the site of micro-injury shows a greatly increased affinity (stickiness) for particulate matter and circulating cells. This is a transient reaction which cannot be reproduced by histamine. With more intense injury blood platelets and leukocytes adhere to the vessel wall in greater numbers and over larger areas. These same areas become much more permeable, leaking colloids as well as water. With even more severe degrees of local injury the capillary walls become pervious to red blood cells and thrombi tend to form.

Reflex vascular phenomena. The vascular phenomena just described were found by Zweifach to be purely localized and not associated with recognizable increase in regional blood flow. After the injection of such irritants as xylol or tissue extracts, there ensues a widespread axon reflex-type of vasodilatation mainly affecting the arteriolar vessels. This gives rise to an active hyperemia which is associated with a great increase in volume of the capillary bed. Microscopic examination reveals large numbers of dilated capillaries (Fig. 1). Normally only a small fraction of

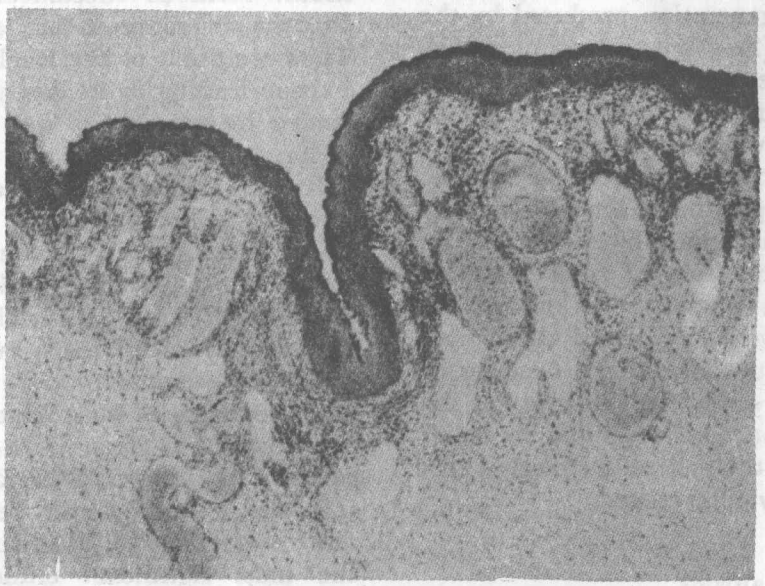

Figure 1. Active Hyperemia
There is an extreme degree of dilatation of the conjunctival blood and lymphatic capillaries. ×50. AFIP Acc. 484173.

the capillaries are functioning at a given moment, but in acutely inflamed tissues the majority of them are not only open but they are dilated. This change in function of capillaries can be studied easily in the conjunctival capillaries with the slit lamp. Active hyperemia thus accounts for two of the cardinal signs of inflammation, increased redness (rubor) and warmth (calor) of the tissue. These vascular phenomena, reflex arteriolar dilatation and endothelial damage, can be reproduced by histamine but they are not abolished by antihistaminics after microinjection of chemical irritants. Adrenal cortical extract diminishes the degree of reactive hyperemia of acute inflammation.

Inflammatory edema. In time or with severe degrees of injury, blood flow through this widely dilated capillary bed becomes sluggish and finally may cease in some vessels. The vessel walls become more permeable, first for water, then for blood proteins, and later for blood cells. Capillaries which normally would permit passage of only one or two cells at a time become widened to a diameter of 25 or more cells (Fig. 2). The interstitial spaces between vessels appear waterlogged. If much protein has escaped, this tissue juice will stain pink with eosin, the intensity of eosin-staining increasing with protein content. Because of its smaller molecular size albumin escapes first, later the globulins and fibrinogen (Fig. 3). The greater concentration of these plasma proteins in the tissue fluids constitutes one of the main differences between inflammatory exudates and other types of edema (transudates). The lymphatics soon enlarge because of this edema. Normal lymphatics are difficult to demonstrate by ordinary histology but in acutely inflamed tissues these vessels are easy to find because of their large numbers and great size.

The inflammatory edema causes the tissues to swell. This swelling accounts for the other two cardinal signs of inflammation, tumor and dolor. Zweifach found that adrenal cortical extract increased the vascular hyporeactivity during acute inflammation, and as a result of this effect there was loss of fluid from the damaged capillaries. The degree of edema depends partly on the amount of fluid leaking from the irritated vascular bed and partly on the efficiency of the lymphatic drain-

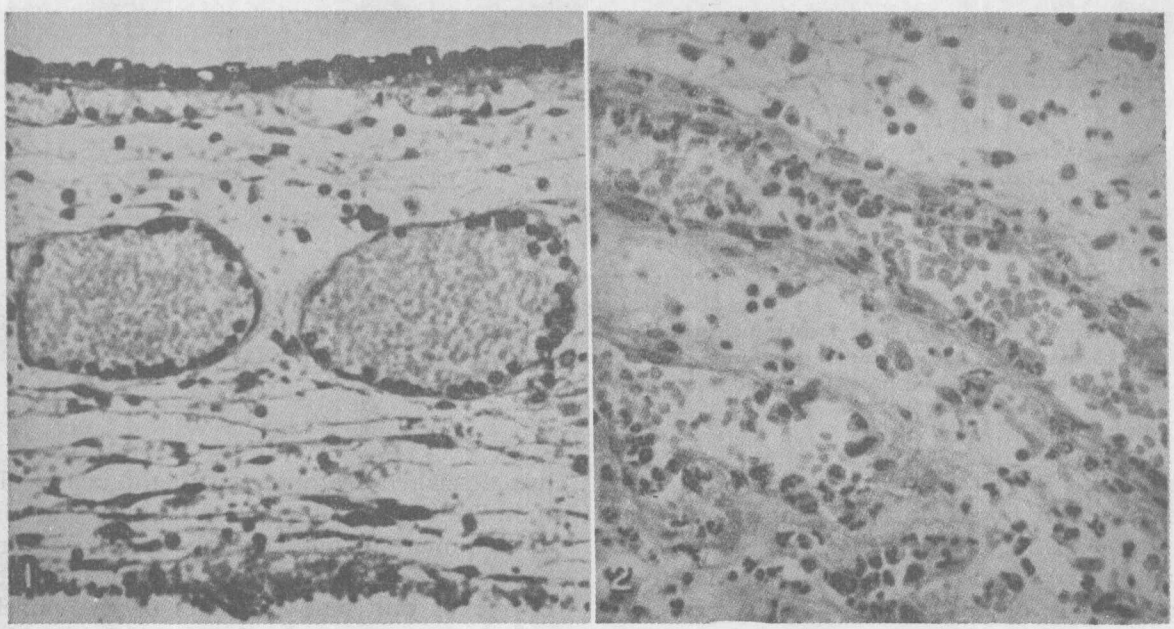

Figure 2. Inflammation

1. Dilatation and engorgement of choroidal vessels. Margination of leukocytes. Edema of surrounding tissue which contains red blood cells. × 145. AFIP Acc. 164016.

2. Polymorphonuclear leukocytes escaping through vessel wall. ×400. AFIP Acc. 291365.

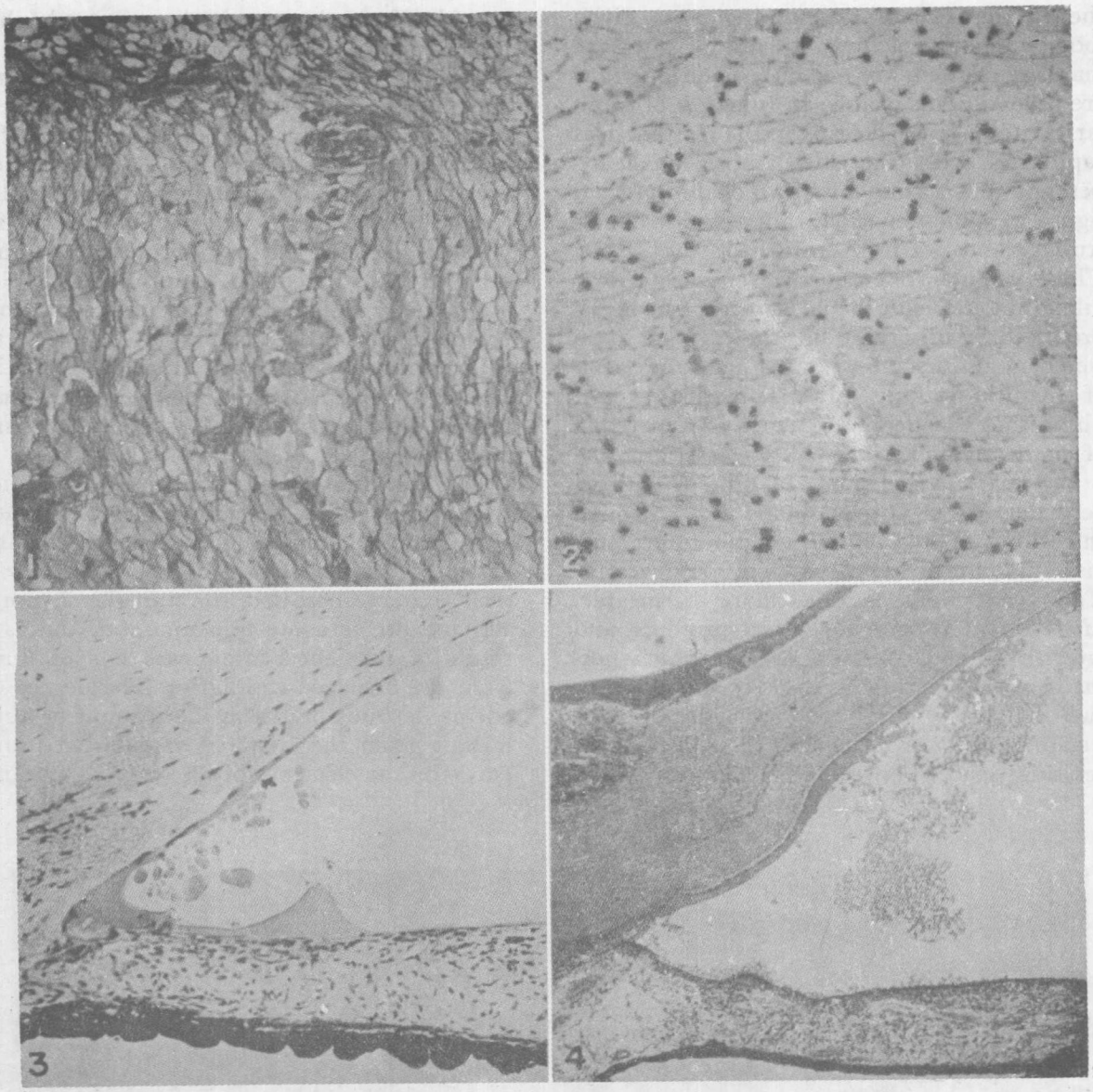

Figure 3. Inflammatory Exudates

1. Edema. Serous exudate between nerve fibers in papilledema. ×275. AFIP Acc. 185418.
2. Fibrin with enmeshed polymorphonuclear leukocytes. Note nodal points of fibrin. ×320. AFIP Acc. 48306.
3. Serous exudate with globular precipitate in anterior chamber. ×125. AFIP Acc. 167332.
4. Granular precipitated proteins in anterior chamber. ×48. AFIP Acc. 266650.

age. With the escape of fibrinogen there is a tendency for fibrin clots to form, not only in the interstitial spaces, but also within the lymphatics. Thus the initial inflammatory edema may become accentuated by a superimposed lymphedema resulting from obstructed lymph vessels.

All of the vascular aspects of inflammation just described are observed in the ocular tissues. In fact, hyperemia of the iris and the development of an "aqueous flare" without the presence of cells in the anterior chamber is one of our best examples of the purely vascular component of the inflammatory reaction.

For those who like to think teleologically