

ELSEVIER
BUTTERWORTH
HEINEMANN

11830 Westline Industrial Drive
St. Louis, Missouri 63146

CLINICAL ANATOMY OF THE VISUAL SYSTEM

0-7506-7490-3

Copyright © 2005, 1998 by Elsevier Inc. All rights reserved.

No part of this publication may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, recording, or any information storage and retrieval system, without permission in writing from the publisher. Permissions may be sought directly from Elsevier's Health Sciences Rights Department in Philadelphia, PA, USA: phone: (+1) 215 238 7869, fax: (+1) 215 238 2239, e-mail: healthpermissions@elsevier.com. You may also complete your request on-line via the Elsevier Science homepage (<http://www.elsevier.com>), by selecting 'Customer Support' and then 'Obtaining Permissions'.

NOTICE

Optometry is an ever-changing field. Standard safety precautions must be followed, but as new research and clinical experience broaden our knowledge, changes in treatment and drug therapy may become necessary or appropriate. Readers are advised to check the most current product information provided by the manufacturer of each drug to be administered to verify the recommended dose, the method and duration of administration, and contraindications. It is the responsibility of the licensed prescriber, relying on experience and knowledge of the patient, to determine dosages and the best treatment for each individual patient. Neither the publisher nor the author assumes any liability for any injury and/or damage to persons or property arising from this publication.

The Publisher

Previous edition copyrighted 1998

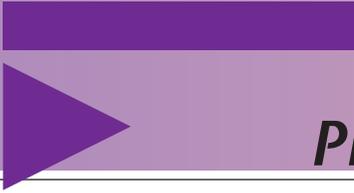
International Standard Book Number 0-7506-7490-3

Publishing Director: Linda Duncan
Managing Editor: Christie M. Hart
Publishing Services Manager: Patricia Tannian
Project Manager: Sarah Wunderly
Senior Design Manager: Gail Morey Hudson

Printed in China

Last digit is the print number: 9 8 7 6 5 4 3 2 1

To
Dan, Tracy, and Ryan,
the loves of my life



Preface

Clinical Anatomy of the Visual System was written to provide the optometry and ophthalmology student, as well as the clinician, with a single text that describes the embryology, anatomy, histology, blood supply, and innervation of the globe and ocular adnexa. The visual and pupillary pathways are covered as well. The text is fully referenced, and information gathered from historical and current literature is well documented. An overview of the visual system as well as a short review of histology is provided in the introductory chapter. Chapters 2 through 5 include the anatomy and the detailed histology of the structures constituting the globe. Each of the three coats of the eye, cornea-sclera, uvea, and retina, is covered in a separate chapter. Included in each is an emphasis on similarities and differences between regions within each coat and notations about layers that are continuous between structures and regions. The crystalline lens is covered in Chapter 5 and the globe is completed in Chapter 6 with descriptions of the chambers of the eye and the material that occupies those spaces.

In my experience, students can more easily grasp the intricacies of ocular development after having a comprehensive understanding of the composition of the structures; therefore, ocular embryology is covered in Chapter 7. The tissue and structures associated with and surrounding the globe are described in the next three chapters. First is a review of the bones and important foramen of the entire skull and then the detail regarding the orbital bones and connective tissue. This is followed by a chapter detailing eyelid structure and histology, including the roles that the muscles and glands have in tear film secretion and drainage. The chapter on the extraocular muscles describes movements that result from contraction of the muscles with the eye in various positions of gaze; an explanation of the clinical assessment of extraocular muscle function based on the anatomy is included.

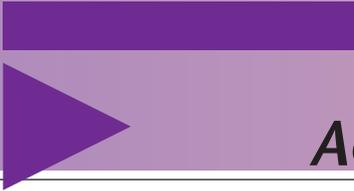
The branches of the internal and the external carotid arteries that supply the globe and adnexa are identified

in Chapter 11. The cranial nerve supply to orbital structures, including both sensory and motor pathways, is clarified, with an emphasis on the clinical relevance and implications of interruptions along the pathways. Significant detail on the relationship between the structures of the visual pathway and neighboring structures and on the orientation of the fibers as they course through the cranium en route to the striate cortex is presented in Chapter 13. Examples are given of characteristic visual field defects associated with injury to various regions of the pathway. The final chapter presents the autonomic pathways to the smooth muscles of the orbit and to the lacrimal gland. The pupillary pathway is included in this chapter, as is a treatment of the more common pupillary abnormalities and the relation between the pathway and the clinical presentation. Some of the common pharmaceutical agents and their actions and pupillary effects are covered as well.

In the format used in the text, terms and names of structures are noted in bold print when they are first described or explained. The name for a structure that is more common in usage is presented first, followed by other terms by which that structure is also known. Current nomenclature tends to use the more descriptive name rather than proper nouns when identifying structures, but that is not always the case, especially when the proper name of an individual has been linked so closely historically (e.g., Schwalbe's line and Schlemm's canal).

Experienced clinicians know that the knowledge of structure provides a good foundation for recognizing and understanding clinical situations, conditions, diseases, and treatments. For this reason clinical comments are included throughout the book to emphasize common clinical problems, disease processes, or abnormalities that have a basis in anatomy.

Lee Ann Remington



Acknowledgments

I have had the pleasure of interacting with numerous bright, engaging students during the past 20 years while teaching ocular and visual anatomy courses at Pacific University College of Optometry. Their questions, corrections, suggestions, and enthusiasm motivate me to continually improve and update my understanding of the process we call vision.

I am also fortunate to work with an extraordinary group of colleagues, the faculty at Pacific, who produce an enjoyable environment conducive to academic growth. I am grateful to Dean Lee Carr for the constant level of support he provides, and to faculty at the college for their encouragement during this process.

I thank Daniel Howells, Nathan Owen, and Blake Simmons for their diligence. These optometry students spent hours during their summer break searching for pertinent literature references for me. Another student,

Neil VanderHorst, spent many hours in the laboratory photographing microscope slides for the text. I appreciate all of their efforts and dedication. The original line drawings included from the first edition were done by Tracey Asmus, O.D.

I am grateful to my husband, Dan, for his patience, encouragement, and loving support during the months spent preparing this manuscript. I am indebted to my children, Tracy and Ryan, for enhancing the joy in my life.

Christie Hart, my editor at Elsevier, has guided me with kindness and tact throughout the entire process, and for that I am grateful. Sarah Wunderly, my project manager at Elsevier, competently combined the text and figures into a cohesive whole. I appreciated her thoughtful and gentle suggestions.



The visual system takes in information from the environment in the form of light and analyzes and interprets it. This process of sight and visual perception involves a complex system of structures, each of which is designed for a specific purpose. The organization of each structure enables it to perform its intended function.

The eye houses the elements that take in light rays and change them to a neural signal; it is protected by its location within the bone and connective tissue framework of the orbit. The eyelids cover and protect the anterior surface of the eye and contain glands that produce the lubricating tear film. Muscles, attached to the outer coat of the eye, control and direct the globe's movement, and the muscles of both eyes are coordinated to provide binocular vision. A network of blood vessels supplies nutrients, and a complex system of nerves provides sensory and motor innervation to the eye and surrounding tissues and structures. The neural signal that carries visual information passes through a complex and intricately designed pathway within the central nervous system, enabling an accurate view of the surrounding environment. This information, evaluated by a process called visual perception, influences myriad decisions and activities.

This book examines the macroscopic and microscopic anatomy of the components in this complex system and the structures that support it.

THE EYE ANATOMIC FEATURES

The eye is a special sense organ made up of three coats, or tunics, as follows:

1. The outer fibrous layer of connective tissue forms the cornea and sclera.
2. The middle vascular layer is composed of the iris, ciliary body, and choroid.
3. The inner neural layer is the retina.

Within this globe are three spaces: the anterior chamber, posterior chamber, and vitreous chamber. The crystalline lens is located in the region of the posterior chamber (Figure 1-1).

The outer dense connective tissue of the eye provides protection for the structures within and maintains the

shape of the globe, providing resistance to the pressure of the fluids inside. The **sclera** is the opaque white of the eye and is covered by the transparent conjunctiva. The transparent **cornea** allows light rays to enter the globe and, by refraction, helps bring these light rays into focus on the retina. The region in which the transition from cornea to sclera and conjunctiva occurs is the **limbus**.

The vascular layer of the eye is the **uvea**, which is made up of three structures, each having a separate function but all are interconnected. Some of the histologic layers are continuous throughout all three structures and are derived from the same embryonic germ cell layer. The **iris** is the most anterior structure, acting as a diaphragm to regulate the amount of light entering the pupil. The two iris muscles control the shape and diameter of the pupil and are supplied by the autonomic nervous system. Continuous with the iris at its root is the **ciliary body**, which produces the components of the aqueous humor and contains the muscle that controls the shape of the lens. The posterior part of the uvea, the **choroid**, is an anastomosing network of blood vessels with a dense capillary network; it surrounds the retina and supplies nutrients to the outer retinal layers.

The neural tissue of the retina, by complex biochemical processes, changes light energy into a signal that can be transmitted along a neural pathway. The signal passes through the retina, exits the eye through the **optic nerve**, and is transmitted to various parts of the brain for processing.

The interior of the eye is made up of three chambers. The **anterior chamber** is bounded in front by the cornea and posteriorly by the iris and anterior surface of the lens. The **posterior chamber** lies behind the iris and surrounds the equator of the lens, separating it from the ciliary body. The anterior and posterior chambers are continuous with one another through the pupil, and both contain aqueous humor that is produced by the ciliary body. The **aqueous humor** provides nourishment for the surrounding structures, particularly the cornea and lens. The **vitreous chamber**, which is the largest space, lies adjacent to the inner retinal layer and is bounded in front by the lens. This chamber contains a gel-like substance, the **vitreous humor**.

The **crystalline lens** is located in the area of the posterior chamber and provides additional refractive

Rights were not granted to include this figure in electronic media.
Please refer to the printed publication.

FIGURE 1-1

The visual system. (From Kronfeld PC: *The human eye*, Rochester, NY, 1943, Bausch & Lomb Press.)

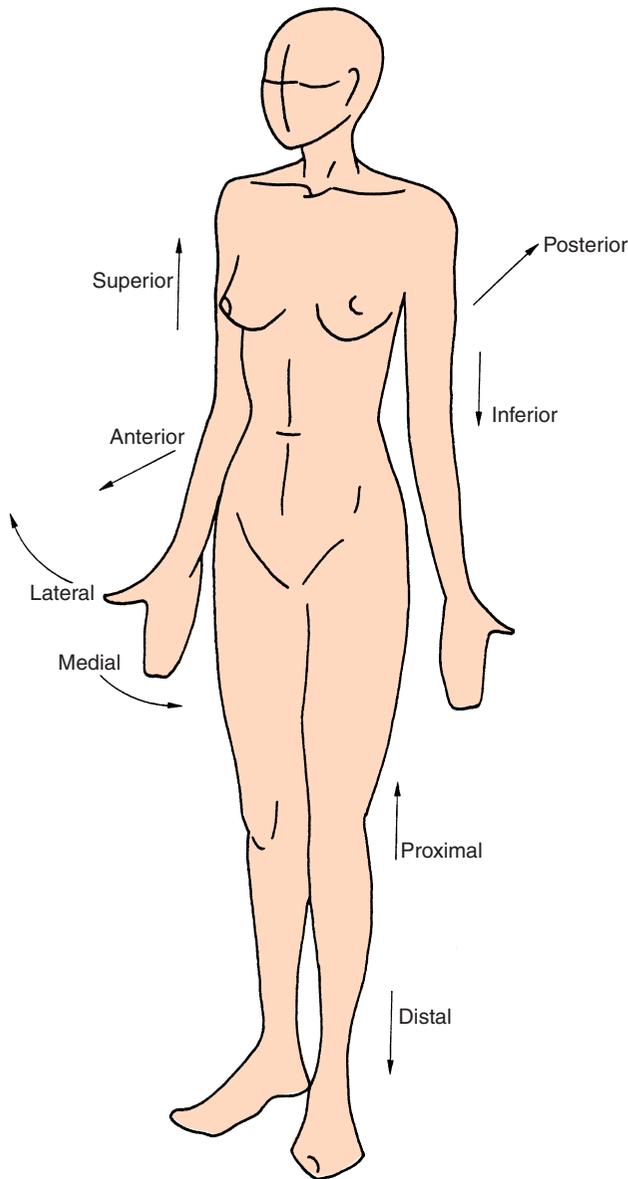


FIGURE 1-2

Anatomic directions. (From Palastanga N, Field D, Soames R: *Anatomy and human movement*, Oxford, England, 1989, Butterworth-Heinemann.)

power for accurately focusing images onto the retina. The lens must change shape to view an object that is close to the eye, through the mechanism of **accommodation**.

ANATOMIC DIRECTIONS AND PLANES

Anatomy is an exacting science, and specific terminology is basic to its discussion. The following anatomic directions should be familiar (Figure 1-2):

- Anterior, or ventral: toward the front
- Posterior, or dorsal: toward the back

- Superior, or cranial: toward the head
- Inferior, or caudal: away from the head
- Medial: toward the midline
- Lateral: away from the midline
- Proximal: near the point of origin
- Distal: away from the point of origin

The following planes are used in describing anatomic structures (Figure 1-3):

- Sagittal: vertical plane running from anterior to posterior locations, dividing the structure into right and left sides.
- Midsagittal: sagittal plane through the midline, dividing the structure into right and left halves.
- Coronal or frontal: vertical plane running from side to side, dividing the structure into anterior and posterior parts.
- Transverse: horizontal plane dividing the structure into superior and inferior parts.

Because the globe is a spheric structure, references to locations can sometimes be confusing. In references to *anterior* and *posterior* locations of the globe, the anterior pole (i.e., center of the cornea) is the reference point. For example, the pupil is anterior to the ciliary body (see Figure 1-1). When layers or structures are referred to as *inner* or *outer*, the reference is to the entire globe unless specified otherwise. The point of reference is the center of the globe, which would lie within the vitreous. For example, the retina is inner to the sclera (see Figure 1-1). In addition, the term *sclerad* is used to mean “toward the sclera,” and *vitread* is used to mean “toward the vitreous.”

REFRACTIVE CONDITIONS

If the refractive power of the optical components of the eye, primarily the cornea and lens, correlate with the distances between the cornea, lens, and retina so that incoming parallel light rays come into focus on the retina, a clear image will be seen. This condition is called **emmetropia** (Figure 1-4, A). No correction is necessary for clear distance vision. In **hyperopia** (farsightedness) the distance from the cornea to the retina is too short for the refractive power of the cornea and lens, thereby causing images that would come into focus *behind* the retina (Figure 1-4, B). Hyperopia can be corrected by placing a convex lens in front of the eye to increase the convergence of the incoming light rays. In **myopia** (nearsightedness), because the lens and cornea are too strong or, more likely, the eyeball is too long, parallel light rays are brought into focus in *front* of the retina (Figure 1-4, C). Myopia can be corrected by placing a concave lens in front of the eye, causing the incoming light rays to diverge.

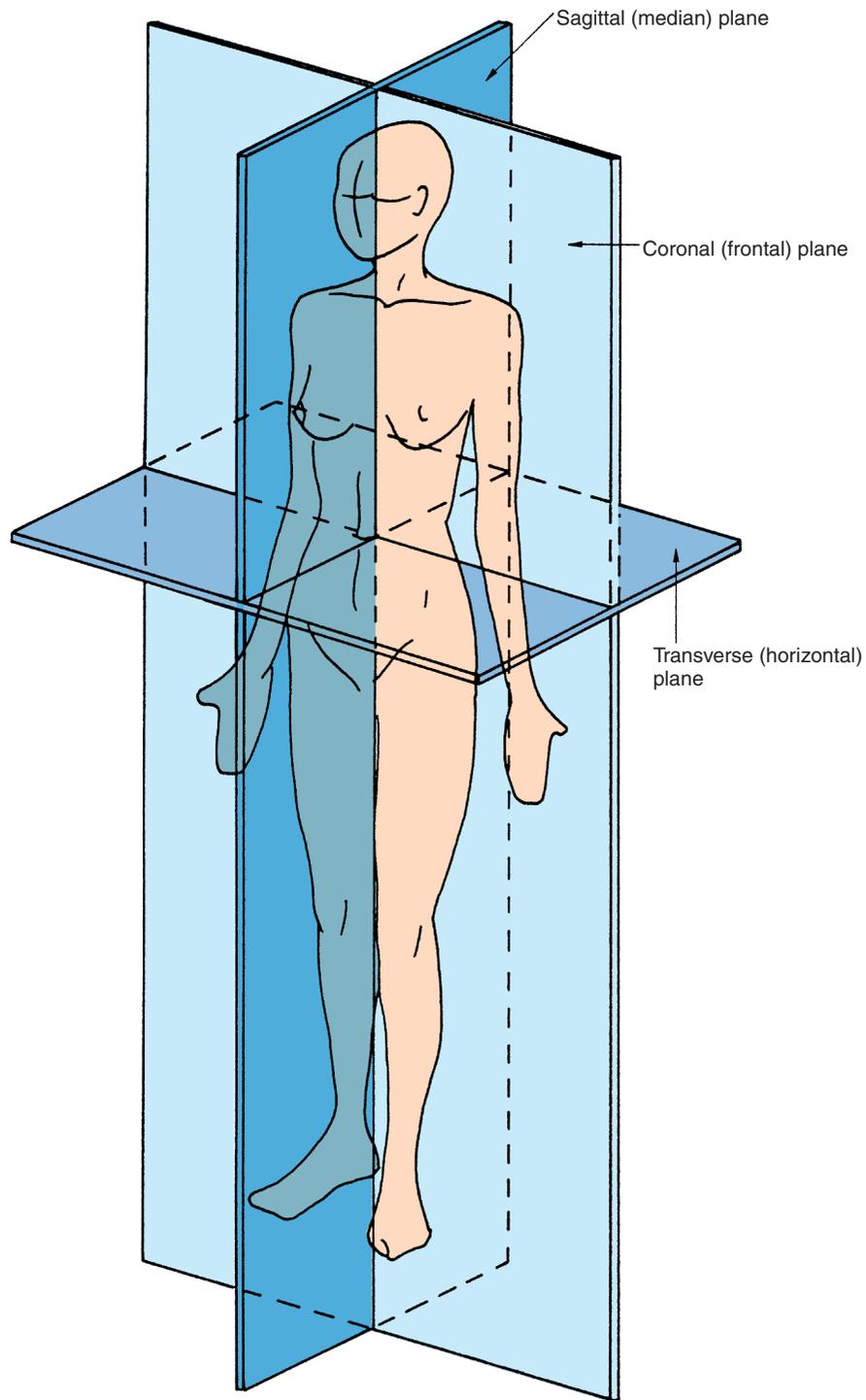
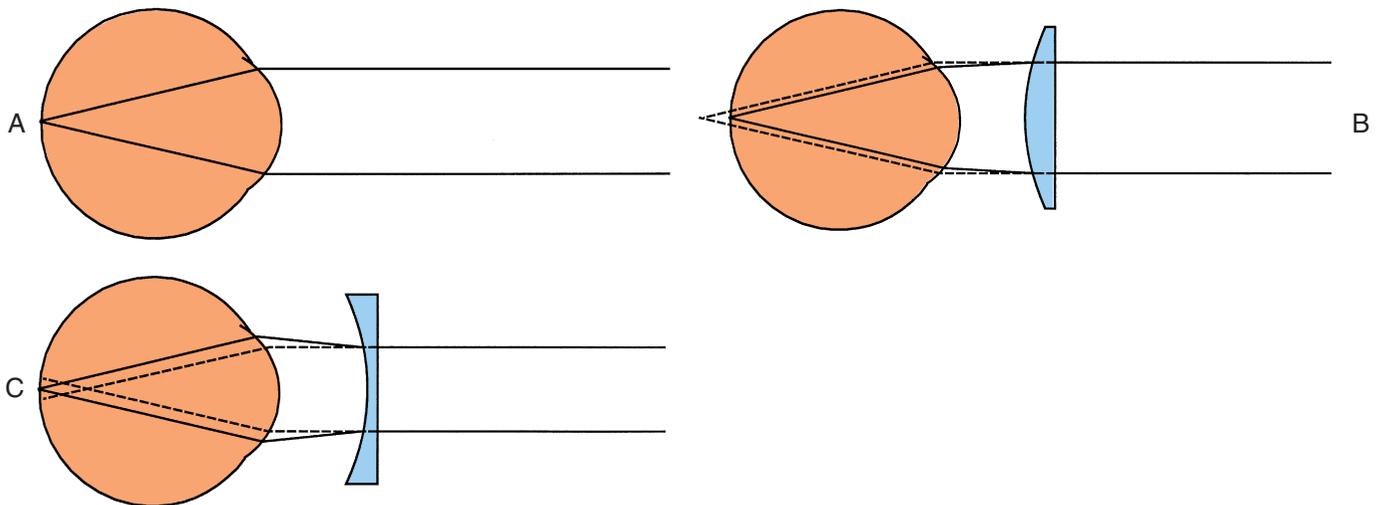


FIGURE 1-3
Anatomic planes. (From Palastanga N, Field D, Soames R: *Anatomy and human movement*, Oxford, England, 1989, Butterworth-Heinemann.)

**FIGURE 1-4**

Refractive conditions. **A**, Emmetropia, in which parallel light comes to a focus on the retina.

B, Hyperopia, in which parallel light comes to a focus behind the retina (*dotted lines*).

A convex lens is used to correct the condition and bring the light rays into focus on the retina.

C, Myopia, in which parallel light comes to a focus in front of retina (*dotted lines*). A concave lens is used to correct the condition and bring the light rays into focus on the retina. (Courtesy Dr. Karl Citek, Pacific University, Forest Grove, Ore.)

OPHTHALMIC INSTRUMENTATION

Various instruments are used to assess the health and function of elements of the visual pathway and the supporting structures. This section briefly describes some of these instruments and the structures examined.

The curvature of the cornea is one of the factors that determine the corneal refractive power. A *keratometer* measures the curvature of the central 3 to 4 mm of the anterior corneal surface and provides information about the power and the difference in curvature between the principle meridians at that location. The smoothness of the corneal surface can also be assessed by the pattern reflected from the cornea during the measuring process. The *automated corneal topographer* maps the corneal surface and gives an indication of curvatures at selected points. This instrument is an important adjunct in the fitting of contact lenses in difficult cases.

The optometric physician can determine the optical power of the eye with a set of lenses and a *retinoscope*. This instrument is beneficial also for assessing the accommodative function of the lens.

The inside of the eye, called the **fundus**, is examined using an *ophthalmoscope*, which illuminates the interior with a bright light. The retina, optic nerve head, and blood vessels can be assessed and information about

ocular and systemic health obtained. This is the only place in the body in which blood vessels can be viewed directly and noninvasively. Various systemic diseases, such as diabetes, hypertension, and arteriosclerosis, can alter ocular vessels. To obtain a more complete view of the inside of the eye, topical drugs are administered to influence the iris muscles, causing the pupil to become enlarged, or mydriatic.

The outside of the globe and the eyelids can be assessed with a *biomicroscope*. This combination of an illumination system and a binocular microscope allows stereoscopic views of various parts of the eye. Particularly beneficial is the view of the transparent structures, such as the cornea and lens. A number of auxiliary instruments can be used with the biomicroscope to measure intraocular pressure and to view the interior of the eye.

Technologic advances have produced instrumentation that can provide three-dimensional mapping of retinal and optic nerve head surfaces and measure the thickness of specific retinal layers.

The visual field is the area that a person sees when looking straight ahead, including those areas seen “out of the corner of the eye.” A *perimeter* is used to test the extent, sensitivity, and completeness of this visual field. Computerized perimeters provide extremely detailed maps of the visual field, as well as statistical information

on the reliability of the test and the probabilities of any defects.

BASIC HISTOLOGIC FEATURES

Because many of the anatomic structures are discussed in this book at the histologic level, this section briefly reviews basic human histology. Other details of tissues are addressed in the pertinent chapters.

All body structures are made up of one or more of the four basic tissues: epithelial, connective, muscle, and nervous tissue. A tissue is defined as a collection of similar cells that are specialized to perform a common function.

EPITHELIAL TISSUE

Epithelial tissue often takes the form of sheets of epithelial cells that either cover the external surface of a structure or that line a cavity. Epithelial cells lie on a basement membrane that attaches them to underlying connective tissue. The basement membrane can be divided into two parts: the **basal lamina**, secreted by the epithelial cell, and the **reticular lamina**, a product of the underlying connective tissue layer.¹ The free surface of the epithelial cell is the *apical* surface, whereas the surface that faces underlying tissue or rests on the basement membrane is the *basal* surface.

Epithelial cells are classified according to shape. Squamous cells are flat and platelike, cuboidal cells are of equal height and width, and columnar cells are higher than wide. Epithelium consisting of a single layer of cells is referred to as *simple*: simple squamous, simple cuboidal, or simple columnar. *Endothelium* is the special name given to the simple squamous layer that lines certain cavities. Epithelium consisting of several layers is referred to as *stratified* and is described by the shape of the cells in the surface layer. Only the basal or deepest layer of cells is in contact with the basement membrane, and this layer usually consists of columnar cells.

Keratinized, stratified squamous epithelium has a surface layer of squamous cells with cytoplasm that has been transformed into a substance called *keratin*, a tough protective material relatively resistant to mechanical injury, bacterial invasion, and water loss. These keratinized surface cells constantly are sloughed off and are replaced from the layers below, where cell division takes place.

Glandular Epithelium

Many epithelial cells are adapted for secretion and, when gathered into groups, are referred to as *glands*. Glands can be classified according to the manner of

secretion—*exocrine* glands secrete into a duct, whereas *endocrine* glands secrete directly into the bloodstream—or to the mechanism of secretion—*holocrine* glands secrete complete cells laden with the secretory material; *apocrine* glands secrete part of the cell cytoplasm in the secretion; and the secretion of *merocrine* glands is a product of the cell without loss of any cellular components. Glands can also be named according to the nature of their secretion: *mucous*, *serous*, or *sebaceous*.

Intercellular Junctions

Various intercellular junctions join epithelial cells to one another and to adjacent tissue. In a tight (occluding) junction, the outer leaflet of the cell membrane of one cell comes into direct contact with its neighbor. These points of apposition are actually points along ridgelike elevations that fuse with complementary ridges on the surface of the neighboring cell.²

A tight junction that forms a zone or belt around the entire cell and joins it with each of the adjacent cells is called a **zonula occludens** (Figure 1-5). In these zones, row on row of intertwining ridges effectively occlude the intercellular space. For a substance to pass through a sheet of epithelium with cells joined by zonula occludens, the substance must pass *through* the cell itself; it cannot pass *between* cells through the intercellular space. In some instances, ridges are fewer and discontinuous, resulting in a “leaky epithelium.”²

A **zonula adherens**, an intermediate junction, is a similar adhesion zone. However, the adjacent plasma membranes are separated by a narrow intercellular space that contains a specific glycoprotein, cell adhesion molecule, material that contributes to cell stability and adhesion.³ Adjacent to the adhering junction are fine microfilaments that extend from the membrane into the cytoplasm.² These produce relatively firm adhesion. A **terminal bar** consists of a zonula occludens and a zonula adherens side by side, with the tight junction lying nearest the cell apex.^{1,2}

Round, buttonlike intercellular junctions have been called **macula occludens** or **macula adherens**, depending on the type of adhesion.

A **desmosome** (macula adherens) is a strong, spotlike attachment between cells. A dense disc or plaque is present within the cytoplasm adjacent to the plasma membrane at the site of the adherence, and hairpin loops of cytoplasmic filaments called tonofilaments extend from the disc into the cytoplasm, contributing to cell stability. Other filaments, transmembrane linkers, extend from the plaque across the intercellular space, holding the cell membranes together and forming a strong bond.³ The intercellular space contains an acid-rich mucoprotein that acts as a

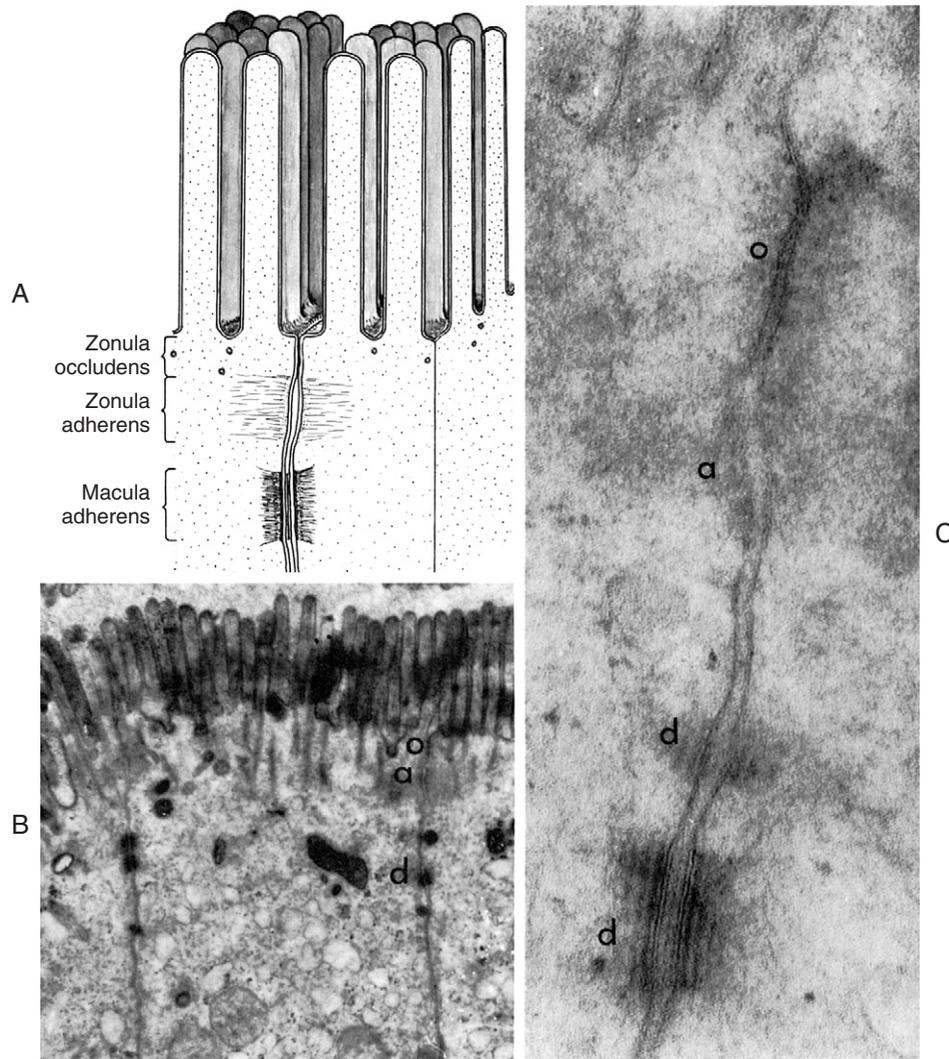


FIGURE 1-5

Junctional complex. **A**, Appearance on electron microscopy of the apical cell interface between two epithelial cells with microvilli on the apical surfaces. **B**, Electron micrograph shows the apical portion of one such cell. ($\times 18,000$.) **C**, Electron micrograph shows features of the junctional complex at high magnification. ($\times 105,000$.) *o*, Zonula occludens; *a*, zonula adherens; *d*, macula adherens, or desmosome. (From Leeson CR, Leeson ST: *Histology*, Philadelphia, 1976, Saunders.)

strong adhesive.² A **hemidesmosome** attaches an epithelial cell to its basement membrane and the underlying connective tissue. Bundles of filaments pass through the cell membrane and the adhesive joining the intracellular plaque to the underlying connective tissue.

A **gap junction**, or communicating junction, is macular in shape. The cells are separated by a thin, intercellular space through which small channels called *connexins* pass, joining the cytoplasm of the two cells.³

These junctions allow for intercellular communication and exchange of ions from one cell to the next.^{1,2}

CONNECTIVE TISSUE

Connective tissue provides structure and support and is a “space filler” for areas not occupied by other tissue. Connective tissue consists of cells, fibers, and ground substance. Ground substance and fibers collectively are called matrix. Connective tissue can be classified as *loose*

or *dense*. Loose connective tissue has relatively fewer cells and fibers per area than dense connective tissue, in which the cells and fibers are tightly packed. Dense connective tissue can be characterized as *regular* or *irregular* on the basis of fiber arrangement.

Among the cells that may be found in connective tissue are fibroblasts (flattened cells that produce and maintain the fibers and ground substance), macrophages (phagocytic cells), mast cells (which contain heparin and histamine), and fat cells. Connective tissue composed primarily of fat cells is called adipose tissue.

The fibers found in connective tissue include flexible collagen fibers with high tensile strength, delicate reticular fibers, and elastic fibers, which can undergo extensive stretching. Collagen fibers are a major component of much of the eye's connective tissue. These fibers are composed of protein macromolecules of tropocollagen that have a coiled helix of three polypeptide chains. The individual polypeptide chains can differ in their amino acid sequences, and the tropocollagen has a banded pattern because of the sequence differences.⁴ Collagen is separated into various types on the basis of such differences, and several types are components of ocular connective tissue structures.

The amorphous ground substance, in which the cells and fibers are embedded, consists of water bound to glycosaminoglycans and long-chain carbohydrates.

MUSCLE TISSUE

Muscle tissue is contractile tissue and can be classified as *striated* or *smooth*, *voluntary* or *involuntary*. Striated muscle has a regular pattern of light and dark bands and is subdivided into skeletal and cardiac muscle. Skeletal muscle is under voluntary control, whereas cardiac muscle is controlled involuntarily. The structure of skeletal muscle and the mechanism of its contraction are discussed in Chapter 10.

The smooth muscle fiber is an elongated, slender cell with a single centrally located nucleus. The tissue is under the involuntary control of the autonomic nervous system.

NERVE TISSUE

Nerve tissue contains two types of cells: **neurons**, which are specialized cells that react to a stimulus and conduct a nerve impulse, and **neuroglia**, which are cells that provide structure and metabolic support. The neuron cell body is the perikaryon, which has several cytoplasmic projections. The projections that conduct impulses *to* the cell body are dendrites (usually several), and the (usually single) projection that conducts impulses *away from* the cell body is an axon. These nerve fibers are either myelinated (enclosed in a lipoprotein material called myelin) or unmyelinated; myelination improves impulse conduction speed.⁵ Both myelinated and unmyelinated fibers are surrounded by Schwann cell cytoplasm; the Schwann cell produces the myelin.

A nerve impulse passes between nerves at a specialized junction, the synapse. As the action potential reaches the presynaptic membrane of an axon, a neurotransmitter is released into the synaptic gap, triggering an excitatory or an inhibitory response in the postsynaptic membrane.

Neuroglial cells outnumber neurons by a ratio of 10 to 50:1, depending on location.⁵ Neuroglial cells include astrocytes, oligodendrocytes, and microglia. **Astrocytes** provide a framework that gives structural support and contributes to the nutrition of neurons. **Oligodendrocytes** produce myelin in the central nervous system, where there are no Schwann cells. **Microglia** possess phagocytic properties and increase in number in areas of damage or disease.⁵

REFERENCES

1. Krause WJ, Cutts JH: Epithelium. In Krause WJ, Cutts JH, editors: *Concise text of histology*, Baltimore, 1981, Williams & Wilkins, p 27.
2. Copenhaver WM, Kelly DE, Wood RL: Epithelium. In Copenhaver WM, Kelly DE, Wood RL, editors: *Bailey's textbook of histology*, ed 17, Baltimore, 1978, Williams & Wilkins, p 103.
3. Fawcett DW, Jensch RP: *Bloom & Fawcett concise histology*, 1997, Chapman & Hall, p 19.
4. Copenhaver WM, Kelly DE, Wood RL: The connective tissues. In Copenhaver WM, Kelly DE, Wood RL, editors: *Bailey's textbook of histology*, ed 17, Baltimore, 1978, Williams & Wilkins, p 142.
5. Krause WJ, Cutts JH: Nervous tissue. In Krause WJ, Cutts JH, editors: *Concise text of histology*, Baltimore, 1981, Williams & Wilkins, p 137.

The outer connective tissue coat of the eye has the appearance of two joined spheres. The smaller, anterior transparent sphere is the cornea and has a radius of curvature of approximately 8 mm. The larger, posterior opaque sphere is the sclera, which has a radius of approximately 12 mm (Figure 2-1, A). The globe is not symmetric; its approximate diameters are 24 mm anteroposterior, 23 mm vertical, and 23.5 mm horizontal.¹

CORNEA

CORNEAL DIMENSIONS

The transparent cornea appears, from the front, to be oval, as the sclera encroaches on the superior and inferior aspects. The anterior horizontal diameter is 12 mm, and the anterior vertical diameter is 11 mm.^{1,2} If viewed from behind, the cornea appears circular, with horizontal and vertical diameters of 11.7 mm (Figure 2-1, B).^{1,3}

In profile, the cornea has an elliptic rather than a spheric shape, the curvature being steeper in the center and flatter near the periphery. The radius of curvature of the central cornea at the anterior surface is 7.8 mm and at the posterior surface is 6.5 mm.^{1,4} The central corneal thickness is 0.53 mm, whereas the corneal periphery is 0.71 mm thick (Figure 2-1, C).^{1,4-6} (All values given are approximations.)

CLINICAL COMMENT: ASTIGMATISM

Astigmatism is a condition in which light rays coming from a point source are not imaged as a point. This results from the unequal refraction of light by different meridians of the refracting elements. Because it is usually elliptic in profile, the cornea contributes to astigmatism in the eye as it refracts light and helps to focus the rays onto the retina. The curvature of the surface of the cornea (central 3 to 4 mm) can be determined by keratometric measurement to give a clinical assessment of the corneal contribution to astigmatism.

Regular astigmatism occurs when the longest radius of curvature and shortest radius of curvature lie 90 degrees apart. The usual presentation occurs when the radius of curvature of the vertical meridian differs from that of the horizontal meridian. The most common situation, called **with-the-rule astigmatism**, occurs when the steepest curvature lies in the vertical meridian. Thus, the vertical

meridian has the shortest radius of curvature. **Against-the-rule** astigmatism is not as common and occurs when the horizontal meridian is the steepest; the greatest refractive power is found in the horizontal meridian. If the meridians that contain the greatest differences are not along the 180- and 90-degree axes (± 30 degrees) but lie along the 45- and 135-degree axes (± 15 degrees), the astigmatism is called **oblique**. **Irregular astigmatism** is an uncommon finding in which the meridians corresponding to the greatest differences are not 90 degrees apart.

In addition to the cornea, the lens is a refractive element that focuses light rays and might contribute to astigmatism. In fact, the tendency of with-the-rule astigmatism to convert to against-the-rule astigmatism with aging is attributable primarily to the lens, which continues to grow throughout life.

CORNEAL HISTOLOGIC FEATURES

The **cornea** is the principal refracting component of the eye. Its transparency and avascularity provide optimal light transmittance. The anterior surface of the cornea is covered by the tear film, and the posterior surface borders the aqueous-filled anterior chamber. At its periphery the cornea is continuous with the conjunctiva and the sclera. From anterior to posterior, the five layers that compose the cornea are epithelium, Bowman's layer, stroma, Descemet's membrane, and endothelium (Figure 2-2).

Epithelium

The outermost layer of stratified corneal **epithelium** is five to seven cells thick and measures approximately 50 μm .^{1,7} The epithelium thickens in the periphery and is continuous with the conjunctival epithelium at the limbus.

The surface layer of corneal epithelium is two cells thick and displays a very smooth anterior surface. It consists of *nonkeratinized* squamous cells, each of which contains a flattened nucleus and fewer cellular organelles than deeper cells. The plasma membrane of the surface epithelial cells is believed to secrete a glycocalyx component that adjoins the mucin layer of the tear film.⁸⁻¹⁰ Many projections located on the apical surface of the outermost cells increase the surface area, thus enhancing the stability of the tear film. The

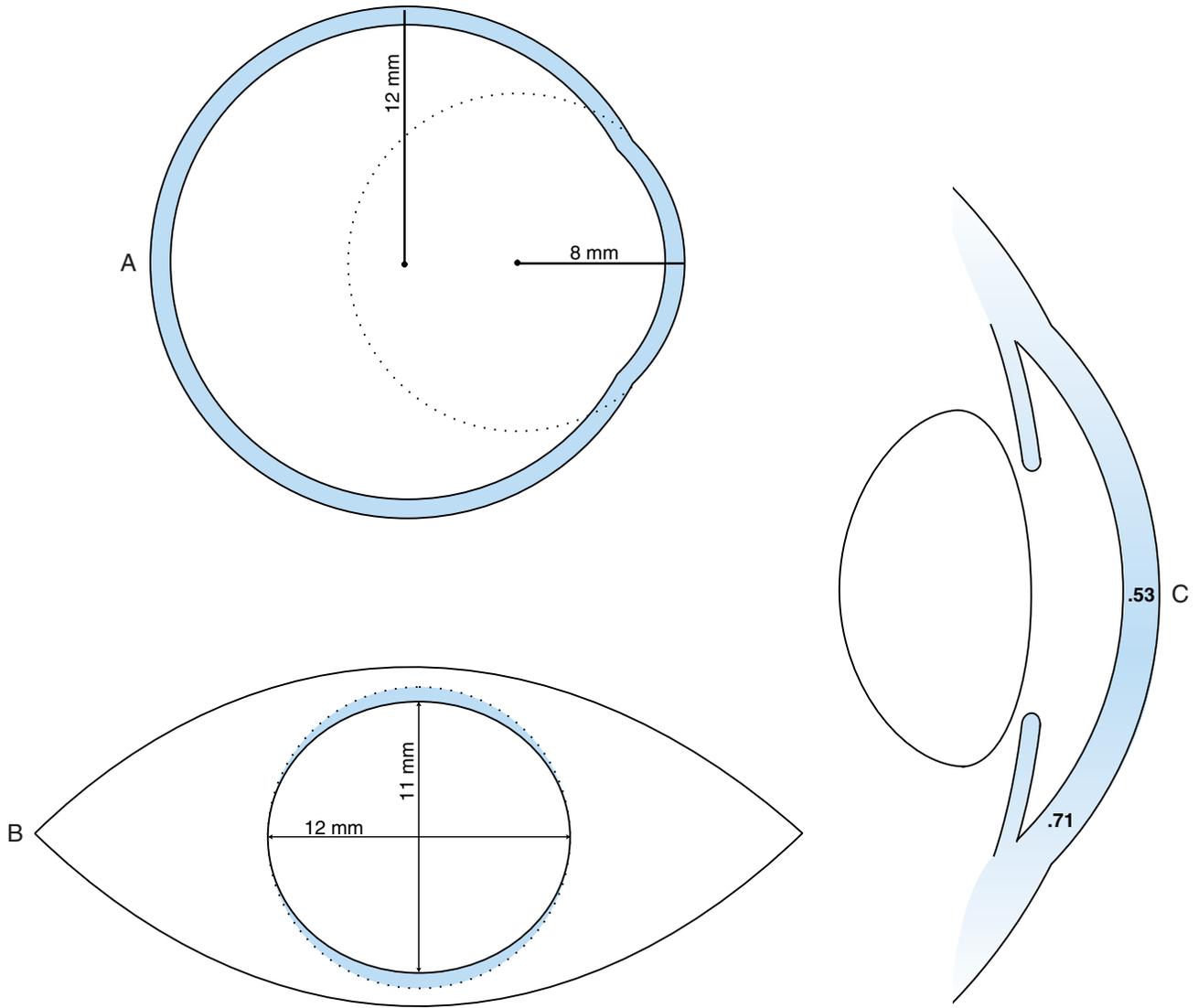


FIGURE 2-1

Corneal dimensions. **A**, Radius of curvature of cornea and sclera. **B**, View from in front of the eye. The sclera encroaches on the corneal periphery inferiorly and superiorly. Dotted lines show the extent of the cornea in the vertical dimension posteriorly. **C**, Sagittal section of cornea showing central and peripheral thickness (0.53 to 0.71 mm).

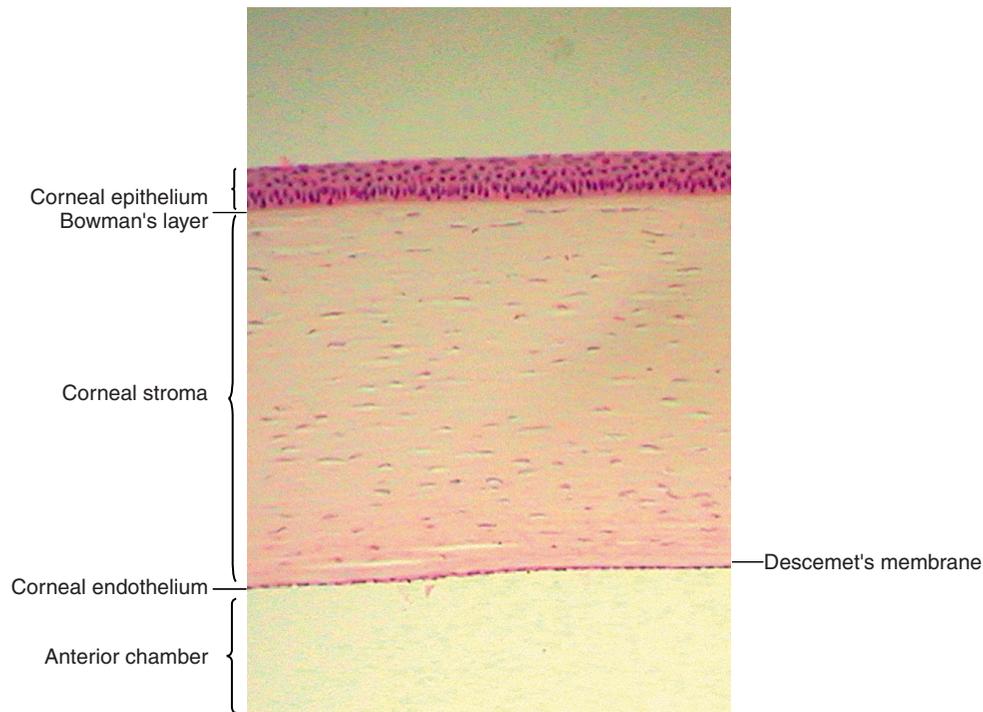


FIGURE 2-2
Light micrograph of corneal layers.

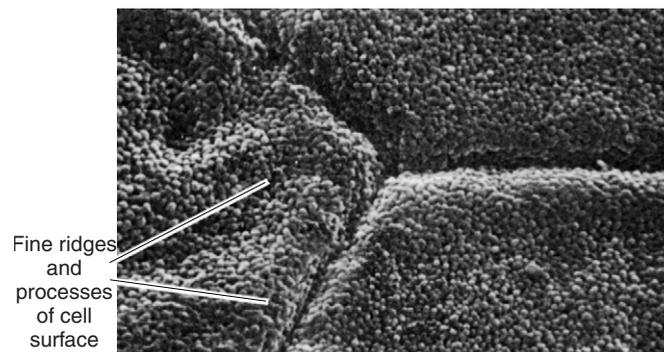


FIGURE 2-3
Scanning electron micrograph of junction of three superficial cells in cornea. ($\times 5000$.) (From Krause WJ, Cutts JH: *Concise text of histology*, Baltimore, 1981, Williams & Wilkins.)

fingerlike projections are **microvilli**, and the ridgelike projections are **microplicae** (Figure 2-3).

Tight junctions (zonula occludens) join the surface cells along their lateral walls, near the apical surface. These junctures provide a barrier to intercellular movement of substances from the tear layer and prevent the uptake of excess fluid from the tear film. A highly effective, semipermeable membrane is produced, allowing

passage of fluid and molecules *through* the cells but not between them. Additional adhesion between the cells is provided by numerous desmosomes.

As the surface cells age, they lose their attachments and are sloughed off, being constantly replaced from the layers below. On scanning electron microscopy the corneal surface is seen to consist of variously sized cells, ranging from small to large. The smaller, lighter cells are

newer replacement cells, whereas the larger, darker cells are those that soon will be sloughed.¹¹

The middle layer of the corneal epithelium is made up of two to three layers of **wing cells**. These cells have winglike lateral processes, are polyhedral, and have convex anterior surfaces and concave posterior surfaces that fit over the basal cells (Figure 2-4). Desmosomes and gap junctions join wing cells to each other, and desmosomes join wing cells to surface and basal cells.¹²

The innermost basal cell layer of the corneal epithelium is a single layer of columnar cells (Figure 2-5). These cells contain oval-shaped nuclei displaced toward the apex and oriented at right angles to the surface. The rounded, apical surface of each cell lies adjacent to the wing cells, and the basal surface attaches to the underlying basement membrane (basal lamina). The basal cells secrete this basement membrane, which attaches the cells to the underlying tissue through hemidesmosomes. Anchoring fibrils pass from these junctions through Bowman's layer into the stroma.¹³ Although less numerous here than in the wing cell layer, desmosomes and gap junctions join the columnar cells; interdigitations and desmosomes connect the basal cells with the adjacent layer of wing cells. The basal layer is the germinal layer where mitosis occurs.

The basal cells are joined to the basement membrane by hemidesmosomes. Opposite the plaque, fine anchoring fibrils form a complex branching and anastomosing network that runs from the basement membrane through Bowman's layer and penetrates 1.5 to 2 μm into the stroma.¹³⁻¹⁸ The linkage between the hemidesmosome and the anchoring network is likely composed of basement membrane components.⁵ The anchoring fibrils attach to anchoring plaques of extracellular matrix within the stroma.^{16,19}

Epithelial Replacement

Maintenance of the smooth corneal surface depends on replacement of the surface cells that constantly are being shed into the tear film. Cell proliferation occurs in the basal layer, basal cells move up to become wing cells, and wing cells move up to become surface cells. Only the cells in contact with the basement membrane have the ability to divide; the cells that are displaced into the wing cell layers lose this ability.²⁰ Stem cells located in a 0.5- to 1-mm-wide band around the corneal periphery are the source for renewal of the corneal basal cell layer. A slow migration of basal cells occurs from the periphery toward the center of the cornea.^{21,22} Turn-over time for the entire corneal epithelium is approximately 7 days, which is more rapid than for other epithelial tissues.^{23,24} Repair to corneal epithelial tissue proceeds quickly; minor abrasions heal within hours, and larger ones often heal overnight. If the basement

membrane is damaged, however, complete healing with replacement basement membrane and hemidesmosomes can take months.^{14,15}

Despite cells constantly being sloughed, the barrier function is maintained as the cell below moves into position to replace the one that has been shed. Tight junctions are present exclusively between the squamous cells that occupy the superficial position. The protein components necessary to form these junctions are not present in the basal cells but are increasingly present as the cells move up to the surface.²⁵

The basal cell layer is constantly losing and reestablishing the hemidesmosome junctions as cells divide and move up into the wing cell layers. The plaque sites remain present in the stroma for reattachment.¹⁵

CLINICAL COMMENT: RECURRENT CORNEAL EROSION

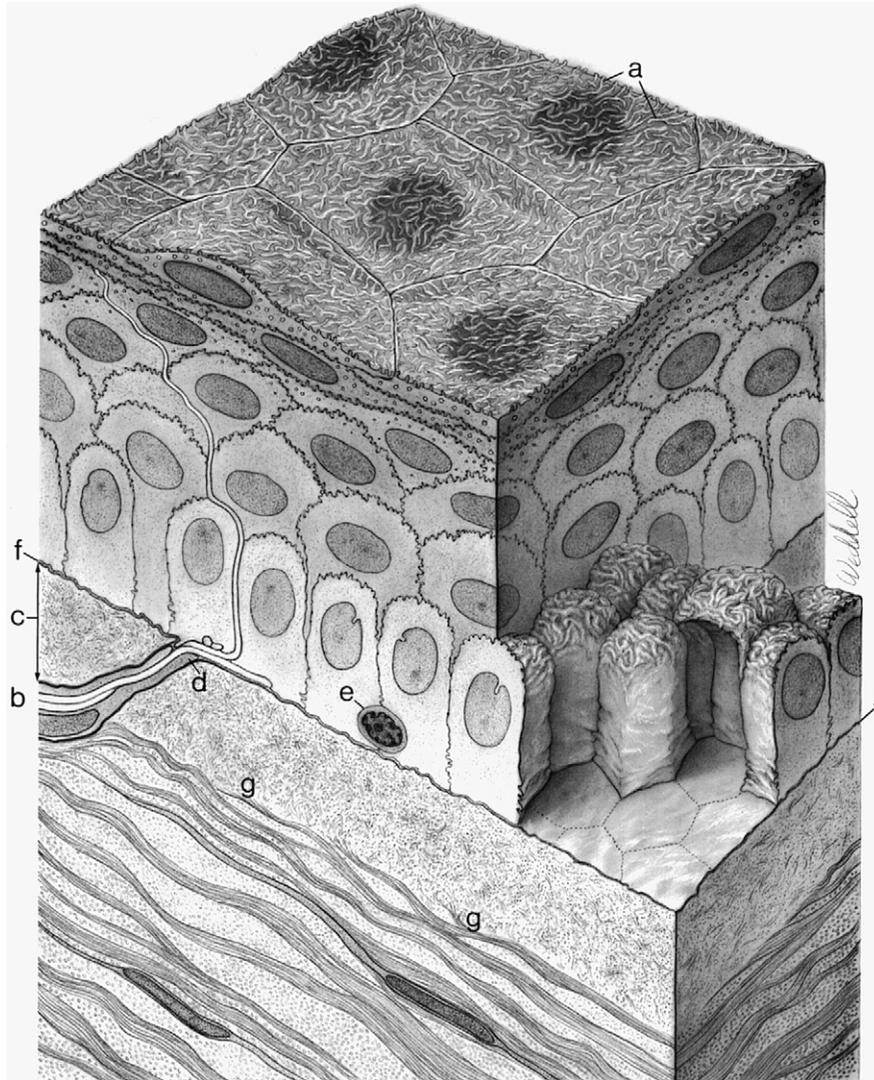
Recurrent corneal erosion is a condition in which the corneal epithelium sloughs off either continually or periodically. This condition may occur because of either poor attachment between the epithelium and its basement membrane or poor attachment between the basement membrane and the underlying tissue. Recurrent corneal erosion can occur after incomplete healing of an abrasion in which the hemidesmosomes are malformed or it may be caused by an epithelial basement membrane dystrophy stemming from defective nutrition or metabolism.⁵

Age-related changes also can play a role in recurrent corneal erosion. Epithelium continues to secrete basement membrane throughout life; in the corneal epithelium the thickness of the basement membrane doubles by 60 years of age. In addition, areas of reduplication of the membrane can occur with aging.²⁶ As the basement membrane thickens or as reduplication occurs, the thickness of the membrane can exceed the length of the anchoring fibrils, allowing sloughing of epithelial layers.

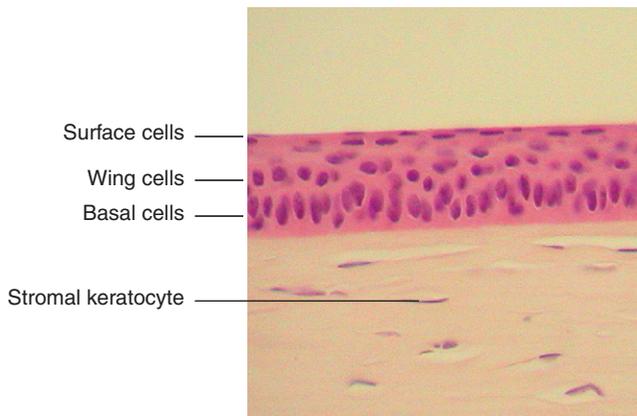
Corneal erosions are very painful because the dense network of sensory nerve endings in the epithelium is disrupted. A number of treatments may be used. Acute cases may be patched and antibiotic ointment applied to allow healing of the surface without the shearing effect of opening and closing of the eyelids. Bandage soft contact lenses or collagen shields often are applied in chronic situations to alleviate pain.²⁶⁻²⁹ For cases in which the suspected cause is a faulty basement membrane, treatment might include corneal puncture, in which multiple perforations are made through the epithelial layers to induce new basement membrane formation and adhesion³⁰⁻³² (Figure 2-6). If reduplication is the cause of corneal erosion, the doubled membrane can be removed.³²

Bowman's Layer

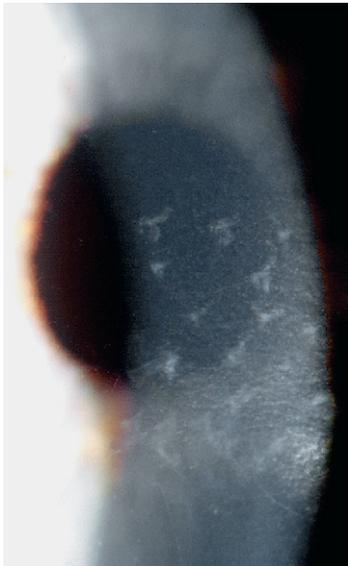
The second layer of the cornea is approximately 8 to 14 μm thick.^{1,7,33} **Bowman's layer** is a dense, fibrous sheet of interwoven collagen fibrils randomly arranged in a mucoprotein ground substance. The fibrils have a diameter of 20 to 25 nm, run in various directions, and

**FIGURE 2-4**

Three-dimensional drawing of corneal epithelium showing five layers of cells. Polygonal shape of basal and surface cells and their relative size are apparent. Wing cell processes fill spaces formed by dome-shaped apical surface of basal cells. Turnover time for these cells is 7 days, and during this time the columnar basal cell gradually is transformed into a wing cell and then into a thin, flat surface cell. During this transition, cytoplasm changes and Golgi apparatus becomes more prominent. Numerous vesicles develop in the superficial wing and surface layers, and glycogen appears in surface cells. Intercellular space separating the outermost surface cells is closed by a zonula occludens, forming a barrier that prevents passage of precorneal tear film into corneal stroma. Cell surface shows extensive net of microplacae (a) and microvilli that might be involved in retention of the precorneal film. Corneal nerve (b) passes through Bowman's layer (c); the nerve loses its Schwann cell sheath near basement membrane (d) of basal epithelium. It then passes as a naked nerve between the epithelial cells toward the superficial layers. Lymphocyte (e) is seen between two basal epithelial cells. Basement membrane is seen at f. Some of the most superficial corneal stromal lamellae (g) are seen curving forward to merge with Bowman's layer. The regular arrangement of the corneal stromal collagen differs from the random disposition in Bowman's layer. (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

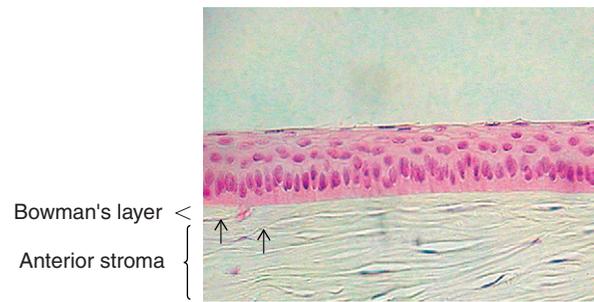
**FIGURE 2-5**

Light micrograph of corneal epithelium showing columnar basal cells, wing cells, and squamous surface cells of cornea; Bowman's layer and anterior stroma are also evident. (Courtesy Patrick Caroline, Oregon Health Sciences University, Portland, Ore.)

**FIGURE 2-6**

Corneal puncture. In recurrent corneal erosion defective adhesion of the epithelium and basement membrane complex to underlying stroma exists. A hypodermic needle is passed through epithelium and anterior stroma to create focal areas of scarring that help to cause "spot welds." (From Krachmer JH, Palay DA: *Cornea color atlas*, St Louis, 1995, Mosby.)

are not ordered into bundles. Bowman's layer sometimes is referred to as a "membrane," but it is more correctly a *transition layer* to the stroma rather than a true membrane. It differs from the stroma in that it is acellular and contains collagen fibrils of a smaller diameter. The pattern of the anterior surface is irregular and reflects the contour of the bases of the basal cells of the epithelium. Posteriorly, as the layer transitions into

**FIGURE 2-7**

Light micrograph of corneal epithelium, Bowman's layer, and anterior stroma. There is a change in the direction of the superficial lamellae as they curve forward to merge with Bowman's layer (*arrows*).

stroma, the fibrils gradually adopt a more orderly arrangement and begin to merge into bundles that intermingle with those of the stroma (Figure 2-7). The posterior surface is not clearly defined.³³

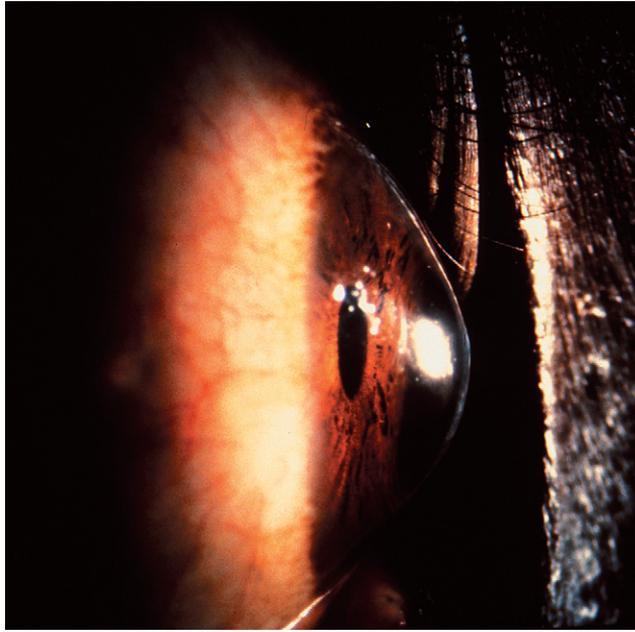
Bowman's layer is produced prenatally by the epithelium and is not believed to regenerate. Therefore, if injured, the layer usually is replaced by epithelial cells or stromal scar tissue. However, Bowman's layer is very resistant to damage by shearing, penetration, or infection. Speculation continues regarding the function of Bowman's layer and whether it is necessary to maintain corneal function. No long-term effects have been documented in patients with Bowman's layer removed by photorefractive keratoplasty, a procedure performed since the late 1980s.³⁴

Corneal nerves passing through Bowman's layer typically lose their Schwann cell covering and pass into the epithelium as naked nerves (see Figure 2-4). The layer tapers and ends at the corneal periphery and does not have a counterpart in either the conjunctiva or the sclera.

CLINICAL COMMENT: KERATOCONUS

Keratoconus is a corneal dystrophy that first presents with focal disruptions of basement membrane and Bowman's layer. Possible causes include metabolic and nutritional disturbances. The process usually begins in the central cornea; the stroma eventually degenerates and thins, and the affected area projects outward in a cone shape because of the force exerted on the weakened areas by intraocular pressure (Figure 2-8). Folds occur in the posterior stroma and Descemet's membrane.^{35,36}

Spectacles may be used for a time for correction of refractive error, but with increasing irregular astigmatism, rigid gas-permeable contact lenses usually are necessary to achieve best corrected vision.³⁷ When contact lenses no longer correct vision, penetrating keratoplasty may be performed to replace the defective cornea with a donor cornea.

**FIGURE 2-8**

Keratoconus. (Courtesy Patrick Caroline, Pacific University College of Optometry, Forest Grove, Ore.)

Stroma or Substantia Propria

The middle layer of the cornea is approximately 500 μm thick, or about 90% of the total corneal thickness⁷ (see Figure 2-2). The **stroma (substantia propria)** is composed of collagen fibrils, keratocytes, and extracellular ground substance.

The **collagen fibrils** have a uniform 25- to 35-nm diameter and run parallel to one another, forming flat bundles called **lamellae**.³³ The 200 to 300 lamellae are distributed throughout the stroma and lie parallel to the corneal surface. Each contains uniformly straight collagen fibrils arranged with regular spacing, sometimes described as a “latticework.” The fibrils are also oriented parallel to the corneal surface. Adjacent lamellae lie at angles to one another, but all fibrils within a lamella run in the same direction (Figure 2-9). Each lamella extends across the entire cornea, and each fibril runs from limbus to limbus. Interweaving occurs between the lamellae.^{38,39}

The arrangement of the lamellae varies slightly within the stroma. In the anterior one third of the stroma, the lamellae are thin (0.5 to 30 μm wide and 0.2 to 1.2 μm thick), and they branch and interweave more than in the deeper layers.^{33,40} In the posterior two thirds of the stroma, the arrangement is more regular, and the lamellae

become larger (100 to 200 μm wide and 1 to 2.5 μm thick).³³

In the innermost layer, adjacent to Descemet’s membrane, the fibrils interlace to form a thin collagenous sheet that contributes to the binding between stroma and Descemet’s membrane.³³

Keratocytes (corneal fibroblasts) are flattened cells that lie between and occasionally within the lamellae⁴¹ (Figure 2-10). The cells are not distributed randomly; a corkscrew pattern is recognizable from anterior to posterior, with the density higher in anterior stroma.⁴² Keratocytes have extensive branching processes joined by gap junctions along the lateral extensions as well as the anteroposterior branches.^{43,44} These are active cells that maintain the stroma by synthesizing collagen and extracellular matrix components. Other cells may be found between lamellae, including white blood cells, lymphocytes, macrophages, and polymorphonuclear leukocytes, which may increase in number in pathologic conditions.

Ground substance fills the areas between fibrils, lamellae, and cells. It contains proteoglycans, macromolecules with a carbohydrate **glycosaminoglycan (GAG)** portion. GAGs are hydrophilic, negatively charged carbohydrate molecules located at specific sites around

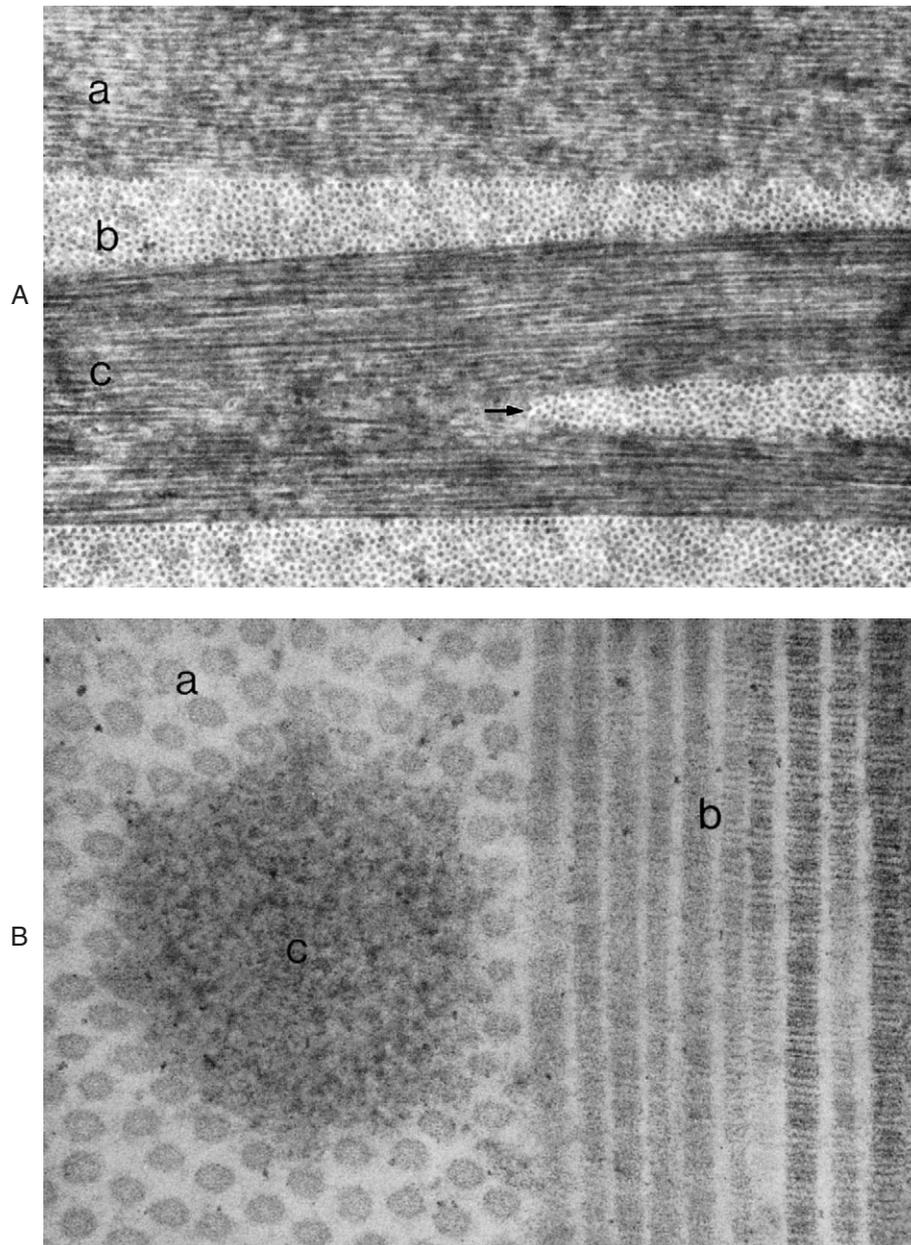
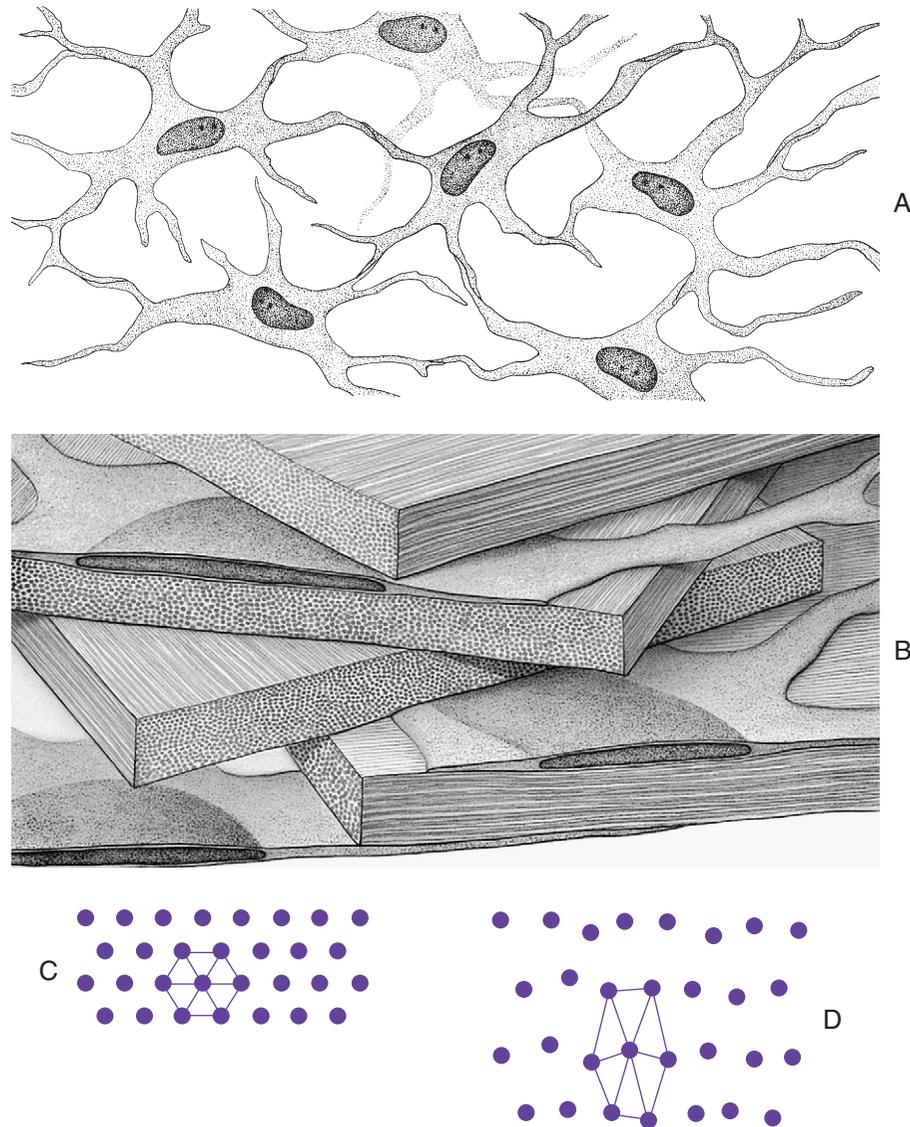
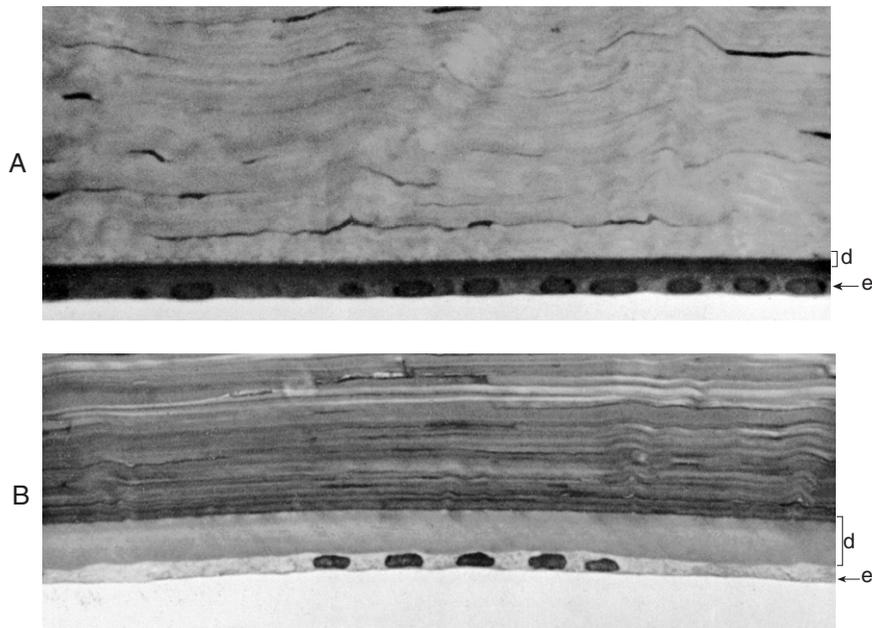


FIGURE 2-9

Corneal stroma. **A**, View of lamellae cut in three planes. The upper lamella (*a*) is cut obliquely, the next (*b*) is cut in cross section, and the third (*c*) is cut longitudinally. This lamella splits into two lamellae (*arrow*). ($\times 28,000$.) **B**, Cross-sectional (*a*) and longitudinal (*b*) views of the two lamellae. The fibrils measure 340 to 400 angstroms (\AA) in diameter and are separated from each other by a space measuring 200 to 500 \AA . Large, round granular mass (*c*) is observed within the lamella cut in cross section. Such masses are seen in most of the collagenous tissues of the eye and may represent a stage in formation of the mature fiber. ($\times 104,000$.) (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

**FIGURE 2-10**

Summary diagram of corneal stroma. **A**, Fibroblasts. Diagram shows six fibroblasts lying between stromal lamellae. Cells are thin and flat with long processes that contact fibroblast processes of other cells lying in same plane. These cells once were believed to form a true syncytium, but electron microscopy has disproved this theory. There is almost always a 200-Å-wide intercellular space that separates the cells. Unlike fibroblasts elsewhere, these cells occasionally join one another at a macula occludens. **B**, Lamellae. Cornea is composed of orderly, dense, fibrous connective tissue. Its collagen, which is a stable protein with an estimated half-life of 100 days, forms many lamellae. Collagen fibrils within a lamella are parallel to one another and run the full length of cornea. Successive lamellae run across cornea at an angle to one another. Three fibroblasts are seen between the lamellae. **C**, Theoretic orientation of corneal collagen fibrils. Each of the fibrils is separated from the others by an equal distance. Maurice⁴⁶ has explained the transparency of cornea on the basis of this equidistant separation. As a result of this arrangement, stromal lamellae form a three-dimensional array of diffraction gratings. Scattered rays of light passing through such a system interact with one another in an organized way, resulting in elimination of scattered light by destructive interference. Mucoproteins, glycoproteins, and other components of ground substance are responsible for maintaining proper position of fibrils. **D**, Orientation of collagen fibrils in an opaque cornea. Diagram shows that orderly position of fibrils has been disturbed. Because of this disarrangement, scattered light is not eliminated by destructive interference, and cornea becomes hazy. Edematous fluid in ground substance also produces clouding of cornea by disturbing interfibrillar distance. (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

**FIGURE 2-11**

Thickness of Descemet's membrane changes with increasing age. **A**, Eye of 1½-year-old child. Light micrograph showing the endothelium (*e*) and Descemet's membrane (*d*), which are approximately the same thickness. (×500.) **B**, Eye of 50-year-old adult. Descemet's membrane (*d*) is a little more than double the thickness of the endothelium (*e*). (×800.) (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders, p 94.)

each collagen fibril. GAGs attract and bind with water, maintaining the precise spatial relationship between individual fibrils, and are one reason for the relatively high stromal hydration.⁴⁵

The very regular arrangement of the stromal components, as well as the small diameter of the fibrils, contributes to stromal transparency.⁴⁶ Studies have shown that the distance between areas of different refractive indices can affect transparency. If the change in the index of refraction occurs across a distance that is less than one half the wavelength of light, destructive interference occurs, and light scattering is reduced significantly.^{40,47} In the stroma the very specific spacing between the fibrils allows destructive interference of rays reflecting from adjacent fibrils. Although the components of the epithelium, Bowman's layer, and Descemet's membrane are arranged irregularly, the scattering particles are separated by such small distances that light scattering is minimal in these layers.⁴⁰ The cornea scatters less than 1% of the light that enters it.^{7,48}

Descemet's Membrane

Descemet's membrane is considered the basement membrane of the endothelium. It is produced constantly

and therefore thickens throughout life, such that it has doubled by age 40 years.²⁶ In children it is 5 μm thick and will increase to approximately 15 μm over a lifetime (Figure 2-11).

Descemet's membrane consists of two laminae. The anterior lamina, approximately 3 μm thick, exhibits a banded appearance and is a latticework of collagen fibrils secreted during embryonic development. The posterior lamina is nonbanded and homogeneous; it is the portion secreted by the endothelium throughout life.⁴⁹

Although no elastic fibers are present, the collagen fibrils are arranged in such a way that Descemet's membrane exhibits an elastic property; if torn, the membrane will curl into the anterior chamber. Descemet's membrane is very resistant to trauma, proteolytic enzymes, and some pathologic conditions and can be regenerated if damaged. A thickened area of collagenous connective tissue may be seen at the membrane's termination in the limbus; this circular structure is called **Schwalbe's line** (or ring).

The method of attachment between Descemet's membrane and the neighboring layers is poorly understood. Attachment sites between the stroma and Descemet's membrane are relatively weak; the mem-

brane can be detached easily from posterior stroma.¹⁹ The adhesions between Descemet's membrane and the endothelium are not the typical hemidesmosomes but some variation.⁵⁰

Endothelium

The innermost layer of the cornea, the **endothelium**, lies adjacent to the anterior chamber and is composed of a single layer of flattened cells. It normally is 5 μm thick.⁷ The basal part of each cell rests on Descemet's membrane, and the apical surface, from which microvilli extend, lines the anterior chamber (Figure 2-12).

Endothelial cells are polyhedral: five-sided and seven-sided cells can be found in normal cornea, but 70% to 80% are hexagonal.^{5,51} The very regular arrangement of these cells is described as the **endothelial mosaic** (Figure 2-13).

Although Descemet's membrane is considered the basement membrane, no hemidesmosomes join it to the endothelium.⁵² Extensive interdigitations join the lateral walls of the cells, and gap junctions provide intercellular communication.¹² Tight junctional complexes joining the endothelial cells are located near the cell apex; these are a series of macula occludens rather than zonula occludens.^{53,54}

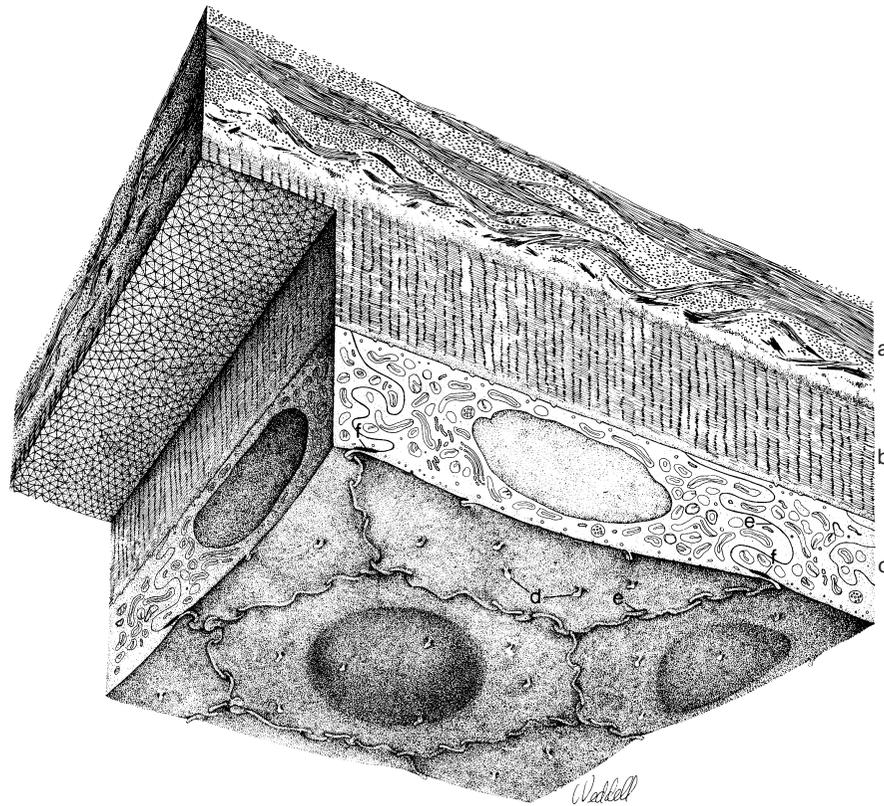
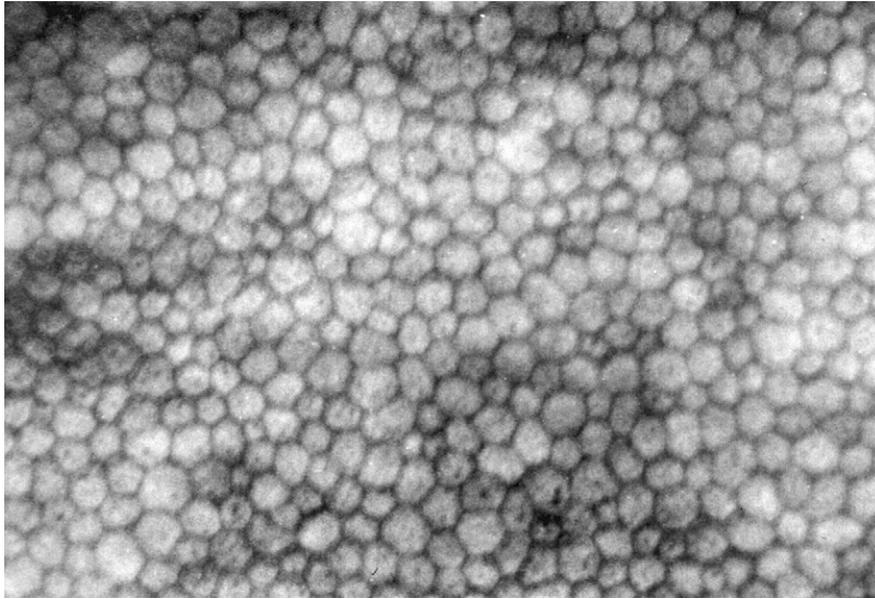


FIGURE 2-12

Three-dimensional drawing of deep cornea showing deepest corneal lamellae (a), Descemet's membrane (b), and endothelium (c). The deeper stromal lamellae split, and some branches curve posteriorly to merge with Descemet's membrane. Descemet's membrane is seen in meridional and tangential planes. Collagenous lattice of this membrane has intersecting filaments that form nodes. These nodes are separated from one another by 100 \AA and are exactly superimposed on one another to form a linear pattern in meridional sections. Endothelial cells are polygonal, measuring approximately 3.5 μm in thickness and 7 to 10 μm in length. Microvilli (d) protrude into anterior chamber from posterior cell, and marginal folds (e) at intercellular junctions project into anterior chamber. Intercellular space near anterior chamber is closed by a tight junction (f). Cytoplasm contains an abundance of rod-shaped mitochondria. Nucleus is round and flattened in anteroposterior axis. (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

**FIGURE 2-13**

Endothelial mosaic. (Courtesy Patrick Caroline, Pacific University College of Optometry, Forest Grove, Ore.)

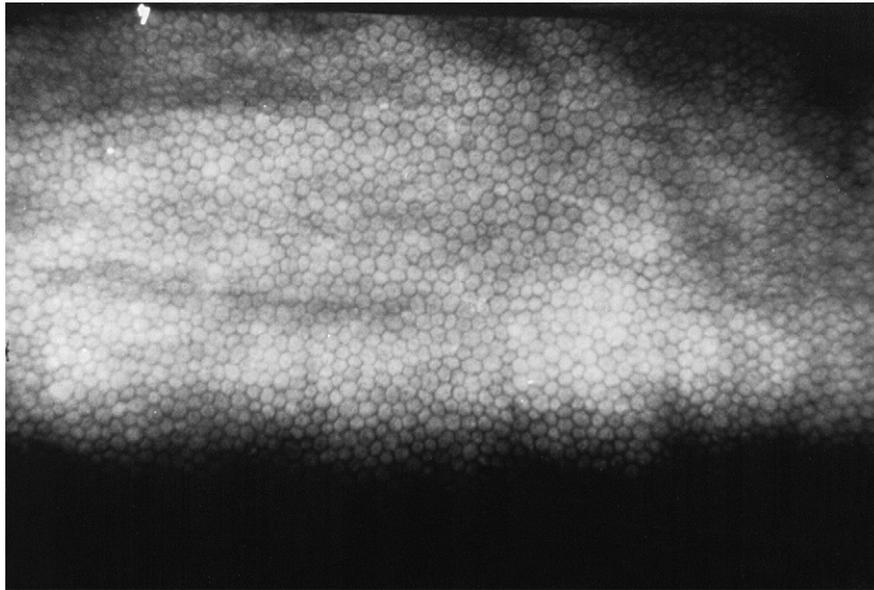
The barrier formed by these adhesions is slightly leaky; in experiments, large molecules have penetrated the intercellular spaces.⁵⁵ This incomplete barrier allows the entrance of nutrients, including glucose and amino acids, from the aqueous humor. Excess water that accompanies these nutrients must be moved out of the cornea if proper hydration is to be maintained. Metabolic pump mechanisms are active throughout the cells of the endothelium and function continually to move ions across the cell membranes. With changes in solute concentration, water flows down the concentration gradient, thus maintaining a balance of fluid movement across the endothelium. The endothelial cell is rich in cellular organelles; mitochondria reflect high metabolic activity and are more numerous in these cells than in any other cells of the eye, except the retinal photoreceptor cells.⁷

Endothelial cells do *not* divide and replicate. Studies now suggest that endothelial cells in the adult possess proliferative capacity but are in an arrested phase in the cell cycle. The cell-to-cell contact may be one factor that maintains this layer in the nonproliferative state.^{50,52,56} Even in children, cells migrate and spread out to cover a defect, with resultant cell thinning. The cell density (cells per unit area) of the endothelium decreases normally with aging because of cell disintegration; density ranges from 3000 to 4000 cells/mm² in children to 1000 to 2000 cells/mm² at age 80 years.^{5,53,57,58} The minimum cell density necessary for adequate function is in the range of 400 to 700 cells/mm.^{2,59} Disruptions to the

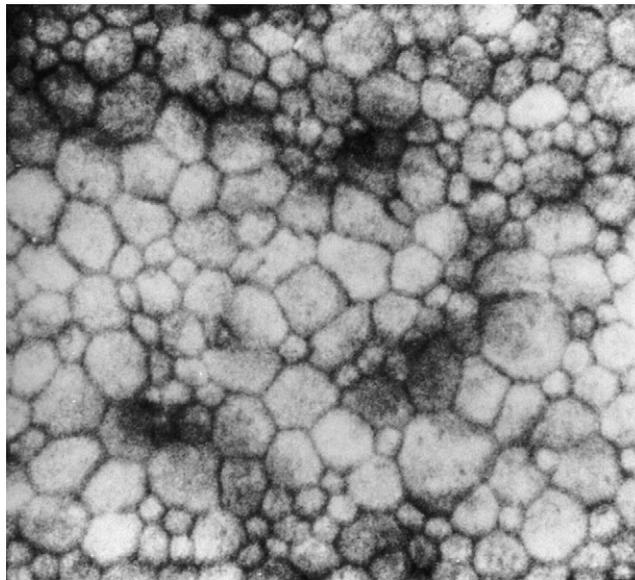
endothelial mosaic can include endothelial cell loss or an increase in the variability of cell shape (**pleomorphism**) or size (**polymegathism**) (Figure 2-14). The active pump function can be detrimentally affected by polymegathism or morphologic changes, although the endothelial barrier function is not compromised by a moderate loss of cells.⁶⁰ An excessive loss of cells can disrupt the intercellular junctions and allow excess aqueous to flow into the stroma, and the endothelial pumps may be unable to compensate for this loss of barrier function.

CLINICAL COMMENT: HASSALL-HENLE BODIES AND GUTTATA

*The endothelium can produce mounds of basement membrane material, which are seen as periodic thickenings in Descemet's membrane that bulge into the anterior chamber. Those located near the corneal periphery are called **Hassall-Henle bodies**. These bodies are a common finding, and their incidence increases with age. Such deposits of basement membrane in central cornea are called **corneal guttata** and are indicative of endothelial dysfunction. The endothelium that covers these mounds is thinned and altered, and the endothelial barrier may be compromised. Both Hassall-Henle bodies and guttata are visible as dark areas when viewed with specular reflection with the biomicroscope. These may be interpreted as holes in the endothelium but the endothelium is merely displaced posteriorly from the plane of reflection (Figure 2-15).*



A



B

FIGURE 2-14

Endothelial integrity can be evaluated by determining the coefficient of variation (CV) of cell size. Normal endothelium has a CV of 0.25. **A**, Endothelium of healthy 25-year-old non-contact lens wearer. Endothelial cell density is 2000 cells/mm², hexagonality is 69%, and CV is 0.25. **B**, Endothelium of 40-year-old patient who has worn polymethyl methacrylate contact lenses for 23 years. Endothelial cell density is 1676 cells/mm², hexagonality is 24%, and CV is 0.66. (**A** courtesy Dr. Scott MacRae, Oregon Health Sciences University, Portland; **B** from MacRae SM, Matsuda M, Shellans S et al: *Am J Ophthalmol* 102:50, 1986.)

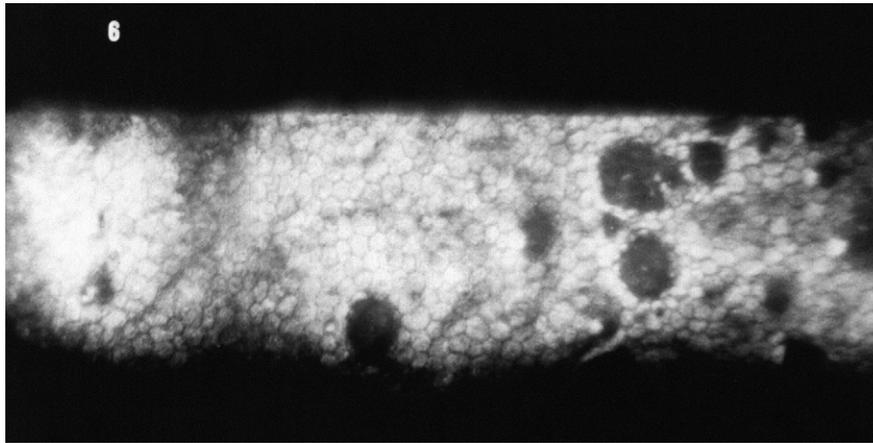


FIGURE 2-15

Guttata. Endothelium of a patient with Fuchs' endothelial dystrophy. Numerous guttata are evident by the dark areas; endothelial cell density is 1600 cells/mm². (Courtesy Dr. Scott MacRae, Oregon Health Sciences University, Portland, Ore.)

CLINICAL COMMENT: EFFECTS OF CONTACT LENSES

Clinical studies indicate that epithelial thinning, stromal thinning, and a decreased number of keratocytes are associated with long-term extended wear of contact lenses.^{61,62} Numerous studies show that contact lens wear can induce changes in the regularity of the endothelial mosaic.⁶³⁻⁶⁷ Pleomorphism and polymegathism have been documented after only 6 years of either rigid gas-permeable or soft contact lens wear, although cell density remained normal.^{68,69}

CORNEAL FUNCTION

The cornea has two primary functions: to refract light and to transmit light. Factors that affect the amount of corneal refraction include (1) the curvature of the anterior corneal surface, (2) the change in refractive index from air to cornea (actually the tear film), (3) corneal thickness, (4) the curvature of the posterior corneal surface, and (5) the change in refractive index from cornea to aqueous humor. The total refractive power of the eye focused at infinity is between 60 and 65 diopters (D), with 43 to 48 D attributable to the cornea.⁵

In the transmission of light through the cornea, it is important that minimal scattering and distortion occur. Scattering of incident light is minimized by the smooth optical surface formed by the corneal epithelium and its tear film covering. The regular arrangement of the surface epithelial cells provides a relatively smooth surface, and

the tear film fills in slight irregularities between cells. The absence of blood vessels and the maintenance of the correct spatial arrangement of components account for minimal scattering and distortion as light rays pass through the tissue. Because the stroma makes up 90% of the cornea, the regularity of spacing between the collagen fibrils is an important consideration in maintenance of corneal transparency. When the stroma is 75% to 80% water, the negatively charged molecules located around each collagen fibril maintain this precise arrangement by their bonds with the water molecules, and corneal transparency is optimal.^{5,70}

CLINICAL COMMENT: ULTRAVIOLET RADIATION

The cornea transmits light with wavelengths between 310 and 2500 nm^{48,71} and acts as an ultraviolet (UV) filter absorbing light in the UV range of wavelengths between 240 and 310 nm.^{72,73} The epithelium and Bowman's layer appear to be the site for this UV absorbance.⁷² Acute exposure to UV radiation can result in a painful photokeratitis, such as occurs with exposure to sunlamps, tanning beds, or a welder's arc. Chronic exposure can result in keratopathies affecting the epithelium and anterior stroma or can cause endothelial pleomorphism.⁷⁴

CORNEAL HYDRATION

A number of factors help to maintain the correct amount of corneal hydration. The tight zonular junctions that

join surface cells of the epithelium restrict the amount of fluid entering from the tear film; fluid must be transported across the cell. Tight junctions that join the endothelial cells provide an effective, if somewhat leaky, barrier to influx of water from the aqueous humor. Pumps in the plasma membrane of the epithelium and endothelium maintain the correct amount of hydration; the endothelial Na^+/K^+ -ATPase pump is the most important. In addition to the pump mechanisms, recent studies suggest that water channels called **aquaporins** are located in the plasma membrane of the endothelial cell and play a role in fluid movement.⁷⁵

In the properly hydrated cornea, the endothelial tight junctions are leaky enough to permit circulation of water with no net flow (i.e., balance is maintained as nutrients pass into and waste moves out of the cornea).⁷⁶ Fluid that leaks into the stroma with the nutrients is balanced by active transport, which exchanges ions through the pump mechanisms. Apparently, the pumps operate at a constant rate, and the leak depends on the swelling pressure of the stroma; the rate of leakage is proportional to the pressure gradient across the endothelium.^{77,78} This is a self-adjusting, homeostatic mechanism.

If fluid is retained, the ground substance expands in stromal edema, thereby increasing the spacing between collagen fibrils. In an edematous stroma, fluid accumulates between and within the lamellae, causing loss of transparency.⁴⁰ The edema occurs in the spaces between fibrils, not within the fibrils themselves.

CLINICAL COMMENT: CORNEAL EDEMA

Damage to either the epithelium or the endothelium can cause edema of the cornea, resulting in impaired visual acuity. Generally, with minor epithelial disruption, the edema is restricted to epithelium. With more extensive damage, however, the localized area of edema spreads into the stroma. Endothelial damage is more likely to cause generalized stromal edema. In an acute episode of high-pressure glaucoma, the intraocular pressure can overcome the transport activity of the endothelium and force fluid from the aqueous humor into the stroma.

An increase in fluid retention thickens the stroma; no change in the anterior curvature occurs, but changes do occur posteriorly.⁷⁹ The more closely packed lamellae in the anterior cornea may make the anterior stroma more resistant to edema than the posterior stroma, with the larger spaces between lamellae in the posterior stroma allowing more fluid collection.⁴² The posterior stroma and Descemet's membrane buckle, producing vertical lines called striae, which may be visible on biomicroscopy.^{80,81}

CORNEAL WOUND HEALING

Damaged corneal epithelium regenerates quickly. Initially, basal cells migrate over the damaged area, and

as healing progresses, the cells are replaced. Hemidesmosomes in the basal cell layer disappear near the wound edge, and the cells flatten and are transformed into motile cells migrating across the defect, covering it with a one cell-thick layer.^{14,15,82,83} A concomitant increase in the cell volume increases the surface area of the individual cell, and the columnar appearance of the cell is lost. After the defect is covered, cell proliferation fills in the defect, and tight adhesions are established once again. If the basement membrane is intact, this healing takes only days, but if the basement membrane is damaged, several weeks will be needed for recovery.¹⁷

Bowman's layer will not regenerate if damaged but will be replaced either by stroma-like fibrous tissue or by epithelium.

When stroma is damaged, keratocytes increase in number and synthesize the connective tissue components. The characteristics of the replacement tissue are slightly different from those of the original tissue, and a scar may result. The diameter of regenerated corneal stromal collagen is larger than normal, comparable to that found in the sclera.⁷ The fibrils across the defect are not as well organized, and the tensile strength of the collagen fibrils in the repaired cornea is diminished.⁸⁴

Descemet's membrane is a strong, resistant membrane and, if damaged, can be regenerated by the endothelial cells that secrete it. Endothelial cells are not replaced when damaged but migrate to cover the area, causing the cells involved to enlarge and flatten, resulting in a decrease in cell density.

The biomolecular factors that influence the healing processes in the cornea are not fully understood, especially considering that the cornea lacks a vascular supply. Factors identified thus far include epidermal growth factor, which enhances epithelial and endothelial healing, and fibronectin and cell surface proteoglycans, which promote epithelial cell adhesion, motility, and proliferation.⁸⁵⁻⁹³

CORNEAL PHYSIOLOGIC PROPERTIES

The cornea is metabolically active and depends on oxygen, derived primarily from the atmosphere and absorbed through the tear film, with small amounts also absorbed from the aqueous humor and limbal capillaries.^{94,95} Nutrients are obtained from limbal capillaries and the aqueous humor. (For details on the complexities of corneal physiology, the reader is referred to a text on physiology of the eye.)

CORNEAL BLOOD SUPPLY

The cornea is avascular and obtains its nourishment by diffusion from the aqueous humor in the anterior

chamber and from the conjunctival and episcleral capillary networks located in the limbus. Absence of blood vessels is a contributing factor in corneal transparency, and vessel growth into the stroma may be impeded because of the stroma's compact composition. Studies are ongoing to determine whether an antiangiogenic substance inhibiting the ingrowth of vessels is present in corneal tissue.⁹⁶

CLINICAL COMMENT: CORNEAL NEOVASCULARIZATION

*In response to oxygen deprivation, the body may produce new blood vessels in an attempt to supply the oxygen-depleted area. This growth of abnormal blood vessels is termed **neovascularization**. In a contact lens wearer, neovascularization is usually an indication that the cornea is not receiving enough oxygen. It can be a sign of a poorly fitting or poorly moving lens or a thick edge. The incidence of neovascularization is higher in soft contact lens wearers than in those wearing rigid gas-permeable lenses and increases in those who wear their lenses for extended periods.*

New vessels extend from the conjunctival loops into the cornea (Figure 2-16). Careful monitoring of patients with neovascularization and elimination of the causative factor may prevent extensive neovascularization. When the oxygen supply to the cornea resumes, the vessels will no longer carry blood, but the structures will remain and atrophy. These are known as ghost vessels and appear as fine white lines on biomicroscopy.

Corneal infections also may induce neovascularization in the body's attempt to increase blood supply to the affected area.

CORNEAL INNERVATION

The cornea is densely innervated with sensory fibers. Seventy to 80 large nerves, branches of the anterior ciliary and short ciliary nerves, enter the peripheral stroma. Approximately 2 to 3 mm after they pass into the cornea, the nerves lose their myelin sheath, but the covering from the Schwann cell remains.^{97,98} Considerable branching occurs, and three nerve networks are formed. One network is located in midstroma, and a subepithelial network is located in the region of Bowman's layer and anterior stroma. Branches from this second network enter the epithelium, where the final nerve network is located (see Figure 12-2).

As the nerves pass through Bowman's layer, the Schwann cell covering is lost, and the fibers terminate as naked nerve endings between the tightly packed epithelial cells.^{7,98} No nerve endings are located in Descemet's membrane or the endothelium. Any abrasion of the cornea, even a superficial one, is quite painful because of the density of this sensory innervation.

In addition to the rich sensory innervation, the cornea contains sympathetic nerve fibers that have physiologic

roles in the regulation of corneal epithelial metabolism, proliferation, and wound healing.⁹⁹

SCLERA

The sclera forms the posterior five sixths of the connective tissue coat of the globe. The sclera maintains the shape of the globe, offering resistance to internal and external forces, and provides an attachment for the extraocular muscle insertions. The thickness of the sclera varies from 1 mm at the posterior pole to 0.3 mm just behind the rectus muscle insertions.^{1,100-102}

HISTOLOGIC FEATURES

Episclera

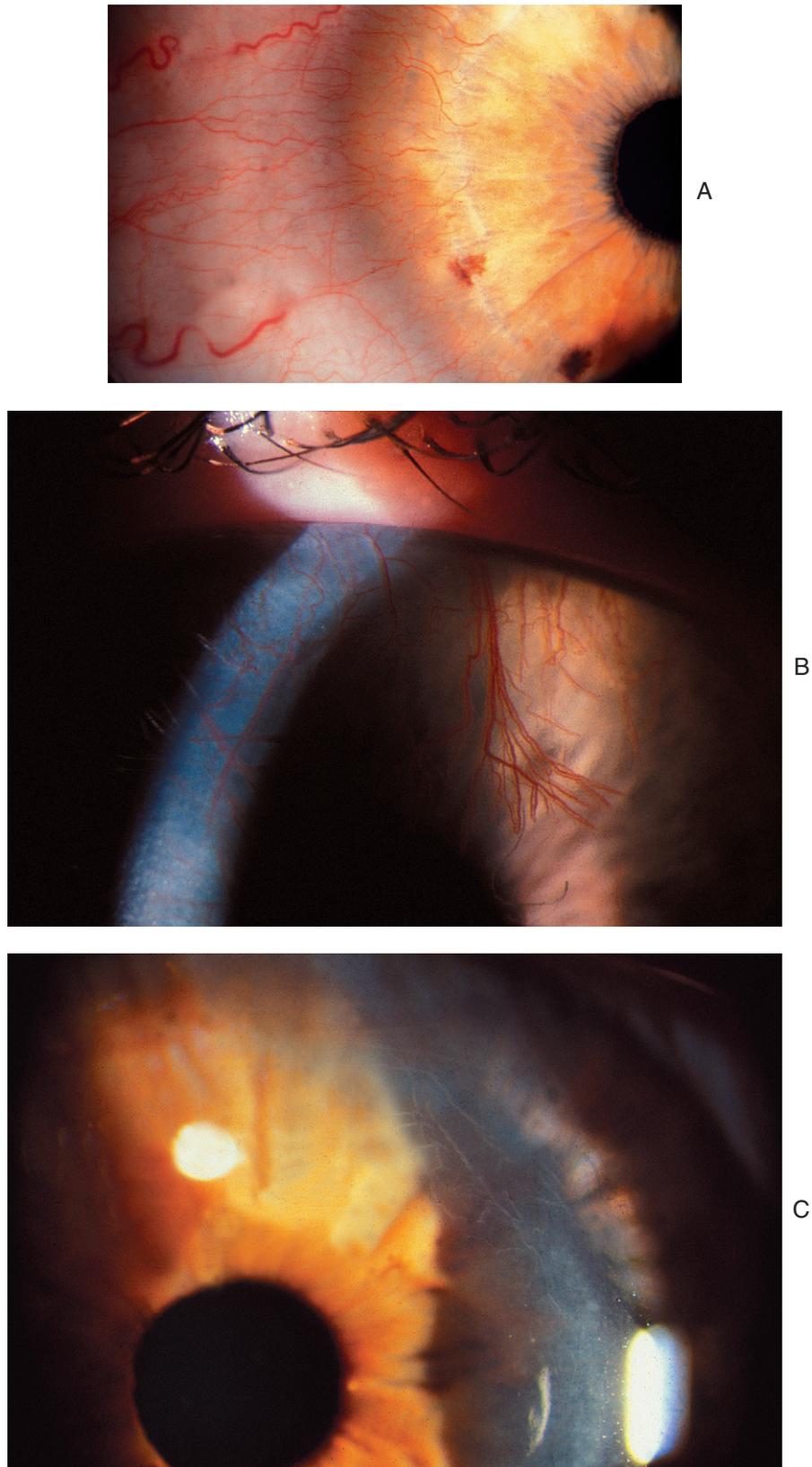
The **episclera** is a loose, vascularized, connective tissue layer that lies just outer to the sclera. The larger episcleral vessels are visible through the conjunctiva. Branches of the anterior ciliary arteries form a capillary network in the episclera just anterior to the rectus muscle insertions and surrounding the peripheral cornea. The episclera, which is joined to Tenon's capsule by strands of connective tissue, becomes thinner toward the back of the eye.

CLINICAL COMMENT: CILIARY INJECTION

*The episcleral network becomes congested in **ciliary injection**, giving the limbus a light-purple or rose coloration in serious corneal inflammation or diseases of the iris or ciliary body.*

Sclera

The **sclera** is a thick, dense connective tissue layer that is continuous with the corneal stroma at the limbus. The diameter of the collagen fibrils in this tissue varies from 25 to 230 nm. These fibrils are arranged in irregular bundles that branch and interlace.^{33,103} Bundle widths and thicknesses vary, with the external bundles narrower and thinner than the deeper bundles. The orientation of the bundles is very irregular compared with bundles in the cornea. The bundles in the outer regions of the sclera run approximately parallel to the surface, with interweaving between the bundles, whereas in the inner regions the bundles run in all directions.³³ This random arrangement and the amount of interweaving may contribute to the strength and flexibility of the eye. Generally, the fibrils parallel the limbus anteriorly; the pattern becomes meridional near the rectus muscle insertions and circular around the optic nerve exit. The collagen of the extraocular muscle tendon at its insertion merges and interweaves with the fibrils of the sclera.¹⁰⁴

**FIGURE 2-16**

A, Early neovascularization from conjunctival loops. **B**, Several large vessels have invaded the corneal stroma. **C**, Corneal ghost vessels remain after vessels empty. (**A** Courtesy Family Vision Center, Pacific University, Forest Grove, Ore. **B**, **C** Courtesy Dr. Christina Schneider.)

Elastic fibers are found occasionally in the sclera between and sometimes within bundles.^{33,105,106} Fibroblasts are also present, although they are less numerous than in the cornea. The stromal ground substance is similar to the corneal ground substance but contains fewer GAGs.⁷⁰ The innermost aspect of the sclera merges with the choroidal tissue in the suprachoroid layer.

CLINICAL COMMENT: SCLERA IN MYOPIC DEVELOPMENT

Early childhood growth of the eye requires coordinated changes in the refractive components and in eye size for the eye to become emmetropic (see Chapter 1). When these factors are not coordinated, refractive error develops. A myopic eye generally is larger than emmetropic or hyperopic eyes, and changes in scleral tissue may be a factor when emmetropization does not occur. The progression of myopia caused by axial elongation in a highly myopic eye often causes scleral thinning, particularly at the posterior pole. Biochemical studies have established that collagen and glycosaminoglycan content are reduced in the myopic eye, which is consistent with scleral thinning.^{107,108}

SCLERAL SPUR

The **scleral spur** is a region of circularly oriented collagen bundles that extends from the inner aspect of the sclera.¹ In its entirety the scleral spur is actually a ring, although on cross section it appears wedge shaped, resembling a spur (Figure 2-17). At the spur's posterior edge, its fibers blend with the more obliquely arranged scleral fibers.¹ The posterior scleral spur is the origin of the longitudinal ciliary muscle fibers, and most of the trabecular meshwork sheets attach to its anterior aspect, such that the collagen of the spur is continuous with that from the trabeculae.

SCLERAL OPACITY

The opacity of the sclera depends on a number of factors, including the number of GAGs, the amount of water, and the size and distribution of the collagen fibrils. The sclera contains one-fourth the number of GAGs that are present in the cornea, and as a probable consequence, the sclera is relatively dehydrated (68%) compared with the cornea.¹⁰¹ The greater variation in fibril size and the irregular spacing between scleral components induce light scattering, which renders the sclera opaque.³³

SCLERAL COLOR

The anterior sclera is visible through the conjunctiva and, if healthy, is white but may appear colored as a

result of age or disease. In the newborn the sclera has a bluish tint because it is almost transparent and the underlying pigmented vascular uvea shows through. The sclera also may appear blue in connective tissue diseases that cause scleral thinning. The sclera might appear yellow in the presence of fatty deposits, which can occur with age. Likewise, in liver disease the sclera may appear yellow because of the buildup of metabolic wastes.

SCLERAL FORAMINA AND CANALS

The sclera contains a number of foramina and canals. The anterior scleral foramen is the area occupied by the cornea. The optic nerve passes through the posterior scleral foramen, which is bridged by a network of scleral tissue called the **lamina cribrosa**. It is similar to a sieve, with interwoven collagen fibrils forming canals through which the optic nerve bundles pass.^{104,109} The lamina cribrosa is the weakest area of the outer connective tissue tunic.¹

CLINICAL COMMENT: OPTIC NERVE CUPPING

Because it is the weakest area of the outer connective tissue layer, the lamina cribrosa is the area that will most likely be affected by increased pressure inside the eye. A cupping out or ectasia of the center area of the surface of the optic nerve may be evident in patients with elevated intraocular pressure and is one of the clinical signs sometimes noted in glaucoma.

The canals that pass through the sclera carry nerves and vessels and are possible routes by which disease can exit or enter the eye. The canals are designated by their location. The *posterior* apertures are located around the posterior scleral foramen and are the passages for the posterior ciliary arteries and nerves. The *middle* apertures lie approximately 4 mm posterior to the equator and carry the vortex veins (Figure 2-18). The *anterior* apertures are near the limbus at the muscle insertions and are the passages for the anterior ciliary vessels, which are branches from the muscular arteries.

SCLERAL BLOOD SUPPLY

Because it is relatively inactive metabolically, the sclera has a minimal blood supply. A number of vessels pass through the sclera to other tissues, but the sclera is considered avascular because it contains no capillary beds. Nourishment is furnished by small branches from the episcleral and choroidal vessels and branches of the long posterior ciliary arteries.¹⁰¹

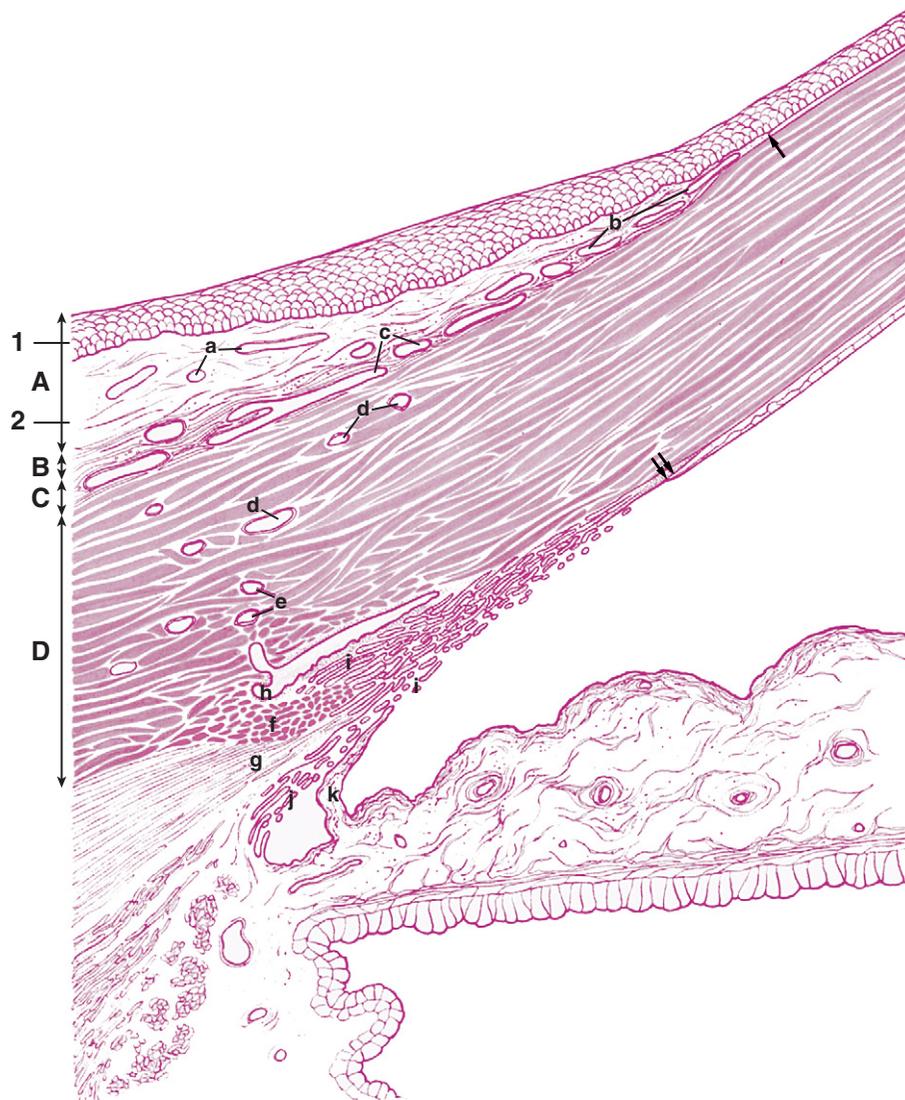
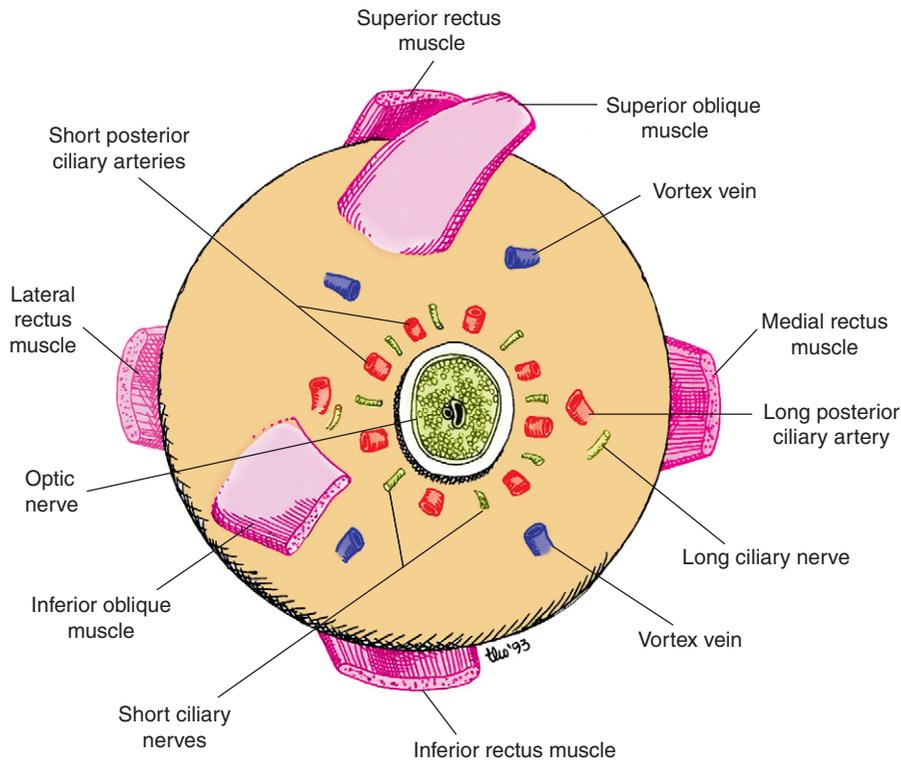


FIGURE 2-17

Limbus. Limbal conjunctiva (A) is formed by an epithelium (1) and a loose connective tissue stroma (2). Tenon's capsule (B) forms a thin, poorly defined connective tissue layer over episclera (C). Limbal stroma occupies the area (D) and is composed of scleral and corneal tissues that merge in this region. Conjunctival stromal vessels are also seen (a). They form peripheral corneal arcades (b), which extend anteriorly to termination of Bowman's layer (arrow). Episcleral vessels (c) are cut in different planes. Vessels forming intrascleral (d) and deep scleral plexus (e) are shown within limbal stroma. Scleral spur has coarse and dense collagen fibers (f). Anterior part of longitudinal portion of ciliary muscle (g) merges with scleral spur and trabecular meshwork. Lumen of Schlemm's canal (h) and loose tissues of its wall are seen clearly. Sheets of the trabecular meshwork (i) are outer to cords of uveal meshwork (j). An iris process (k) is seen to arise from iris surface and join trabecular meshwork at level of anterior portion of scleral spur. Descemet's membrane terminates (double arrows) within anterior portion of the triangle, outlining aqueous outflow system. (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

**FIGURE 2-18**

Posterior sclera. Optic nerve passes through the posterior scleral foramen; long and short ciliary arteries and nerves pass through the posterior apertures; and vortex veins pass through the middle apertures.

SCLERAL INNERVATION

Sensory innervation is supplied to the posterior sclera by branches of the short ciliary nerves; the remainder of the sclera is served by branches of the long ciliary nerves.¹⁰¹

LIMBUS

The **limbus**, located at the corneoscleral junction, is a band approximately 1.5 to 2 mm wide that encircles the periphery of the cornea. The radius of curvature abruptly changes at this junction of cornea and sclera, creating a shallow, narrow furrow, the **external scleral sulcus**. Internally at this juncture, there is a larger furrow, the **internal scleral sulcus**, which has a scooped-out appearance.

Histologically, the anterior boundary of the limbus consists of a plane connecting the termination of Bowman's layer and the termination of Descemet's membrane (see Figure 2-17). The posterior boundary is a plane perpendicular to the surface of the globe and passing through the posterior edge of the scleral spur.¹¹⁰

These boundaries are used in this discussion, although clinically the boundaries are not as definitive.

The limbus is the transitional zone between cornea and conjunctiva and between cornea and sclera. Some layers of the cornea continue into the limbal area, and others terminate (see Figure 2-17). In the limbus, (1) the very regular squamous corneal epithelium becomes the thicker columnar conjunctival epithelium, (2) the very regular corneal stroma becomes the irregularly arranged scleral stroma, (3) the corneal endothelial sheet becomes discontinuous to wrap around the strands of the trabecular meshwork, (4) Bowman's layer and Descemet's membrane terminate at the anterior border, and (5) the conjunctival stroma, episclera, and Tenon's capsule begin within the limbal area.

LIMBAL HISTOLOGIC FEATURES

At the limbus the epithelium increases from a layer five cells thick to a layer 10 to 15 cells thick (Figure 2-19).^{1,110,111} Melanocytes may be present in the basal layer, and pigmentation may be evident in the limbus and

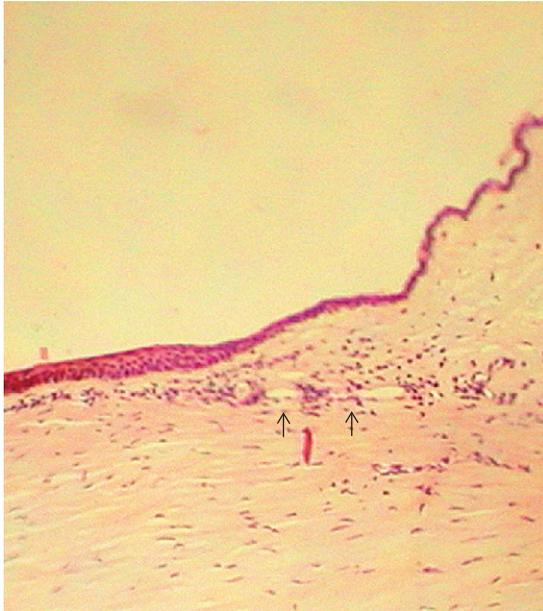


FIGURE 2-19

Light micrograph showing limbal area, cornea to left, conjunctiva and sclera to right. The loose connective tissue of the conjunctival stroma appears inner to the thickened epithelium. Episcleral vessels (*arrows*), cut in cross section, are outer to dense connective tissue of sclera.

conjunctiva, especially in darker-skinned individuals. Bowman's layer tapers and terminates.

The limbus contains the transition from the very regular corneal lamellae to the irregular and random organization of collagen bundles in the sclera. This change is gradual such that, as the transparent cornea merges into the opaque sclera, no line of demarcation can be identified. The scleral fibrils extend further anteriorly on the external than on the internal side of the limbus.² Within the limbal stroma at the corneal periphery, a distinct group of collagen fibrils has been identified that lies circumferentially, forming an annulus. This ring structure is postulated to help maintain the correct corneal curvature.¹¹²

Descemet's membrane tapers at the anterior limbal boundary, and the posterior nonbanded portion becomes interlaced with the connective tissue of the anterior sheets of the trabecular meshwork. The corneal endothelium continues into the anterior chamber angle as the endothelial covering of the sheets of the trabecular meshwork.^{19,53}

The conjunctival submucosa begins in the limbus and has no counterpart in the cornea. This stromal tissue forms mounds that project toward the surface epithelium at the limbus, giving an undulating appearance. The basal layer of the epithelium follows these ridges, called papillae, which are also found near

the eyelid margin. Papillae give the inner aspect of the epithelium a wavy appearance, although the surface remains smooth.

Tenon's capsule lies just inner to the conjunctival submucosa, and the episclera is inner to Tenon's capsule. Both begin in the limbus but do not continue into the cornea. Tenon's capsule, the episclera, and the conjunctival stroma fuse in the anterior limbal area.²

PALISADES OF VOGT

The **palisades of Vogt** are radial projections of limbal epithelium and stroma that extend into the cornea in spokelike fashion.¹⁶ On biomicroscopy these projections appear as thin, gray pegs approximately 0.5 mm wide and 2 to 4 mm long.¹¹⁰ The surface of the limbal area where the palisades of Vogt arise remains flat. The epithelium in this area is the suspected site of stem cell origin, the source of corneal epithelial basal cell replication.¹¹³⁻¹¹⁵

LIMBAL BLOOD VESSELS AND LYMPHATICS

Capillary loops from conjunctival and episcleral vessels form networks in the limbus, which surround the cornea and provide nourishment to the avascular corneal tissue. Limbal veins collect blood from the anterior conjunctival veins and drain into the radial episcleral veins, which then empty into the anterior ciliary veins.¹¹⁶ Lymphatic channels located in the limbal area do not enter the cornea.

CELL REPLACEMENT

In the limbal basal epithelial layer, a cell has been identified that is smaller and darker staining than the usual epithelial cells. It has histochemical features suggestive of stem cells, with the capacity for cell proliferation.^{20,117-122} Centripetal movement from the limbal area is responsible for the migration and replacement of corneal epithelial basal cells in both normal cell replacement and wound healing.¹⁵

LIMBAL PHYSIOLOGIC FEATURES

The limbus has two functions: to provide nutrients to adjacent tissue and to provide a pathway for the drainage of aqueous humor from the eye. The vessels that loop in the conjunctival and episcleral tissue of the limbus provide some metabolites for the peripheral cornea. The structures in the internal scleral sulcus, the trabecular meshwork and the canal of Schlemm, that provide the major route for drainage of the aqueous humor are discussed in Chapter 6.

CLINICAL COMMENT: PRK AND LASIK

Reducing myopic refractive error can be accomplished by remodeling the corneal curvature either by a method of contact lens fitting (orthokeratology) or by procedures that remove corneal tissue.

In orthokeratology a rigid contact lens is fit that gradually changes corneal shape. This lens is worn for a certain period, often overnight, and with time causes the center of the cornea to flatten. Wearing time is gradually reduced, and a minimal wearing time may be established that maintains the corrected corneal shape.

The earliest surgical procedure for modifying corneal curvature, radial keratotomy (RK), involved radial incisions from the corneal periphery to a point just outside the pupillary zone. This weakened the corneal periphery and the normal pressure within the eye, pushed the periphery out, thus flattening central cornea, shortening the optical length of the eye, and reducing myopia. Numerous complications resulted, the most serious of which was endothelial compromise when the incision involved the endothelium.

Greatly improved procedures have enhanced the methods for corneal restructuring and in these procedures corneal stroma is removed. In photorefractive keratoplasty (PRK) the epithelium is removed first, usually by mechanical means, then Bowman's layer and anterior stroma are ablated by laser. Bowman's layer does not regenerate, and the basement membrane of the epithelium must be laid down on the remaining stromal surface. In laser-assisted in situ keratomileusis (LASIK) an incision is made to produce a flap consisting of epithelium and Bowman's layer. This flap is folded back, and stroma is removed by laser. The flap is laid back down, and the edges seal as the epithelium heals. In both procedures anterior stroma is removed, and one study has shown that this is the most rigid or stable area of the stroma.⁴² Speculation continues about long-term effects resulting from loss of Bowman's layer, although none has been determined. Some endothelial cell loss is reported but has not been found to be clinically significant.¹²³⁻¹²⁷ The role of Bowman's layer in UV absorption may be one of the considerations when deciding between PRK and LASIK.

The reduction of corneal thickness may have other clinical effects. Studies have shown a correlation between corneal thickness and the measurement of intraocular pressure (IOP) and between corneal thickness and the incidence of glaucoma.^{128,129} The clinician must be aware of the increased risk of inaccurate IOP readings, as well as any implications for glaucoma risk, in patients who have had removal of stromal tissue.^{130,131} Pachometry (measurement of corneal thickness) may be a relevant addition to the diagnosis of glaucoma.

AGING CHANGES IN CORNEA AND SCLERA

Aging does produce changes in corneal appearance, but most are not detrimental to vision.

Iron deposits in epithelial cell cytoplasm, more concentrated in the basal cells,¹³² produce a horizontal



FIGURE 2-20

The white limbal band of corneal arcus. (From Kanski JJ, Nischal JJ: *Ophthalmology: clinical signs and differential diagnosis*, St Louis, 1998, Mosby.)

pigmented line, the *Hudson-Stähli line*, often evident at the level of the lower lid margin. Degeneration of Bowman's layer produces the *limbal girdle of Vogt*. This yellowish white opacity is located at the 3 and 9 o'clock positions, interpalpebrally, but does not encircle the cornea. A clear interval separating the opacity from the limbus may or may not be seen. The area may include degeneration of anterior stroma, calcium deposits, and hypertrophy of the overlying epithelium.

Corneal arcus is the most common corneal aging change. An annular yellow-white deposit located within peripheral stroma is evident (Figure 2-20). This ring is separated from the limbus by a zone of clear cornea. The deposits are cholesterol and cholesterol esters and can result from age or elevated blood cholesterol levels. With time the arcus can extend anteriorly to Bowman's layer or into central cornea. There is no clinical significance in elderly persons, but in those under age 40, hyperlipidemia should be suspected.

Hassell-Henle bodies, located in peripheral Descemet's membrane and described earlier, are of no clinical significance.

Aging changes in the corneal endothelium include decrease in cell density, polymegathism, and pleomorphism.^{57,58,133} Pigment deposits on the posterior cornea that have a vertical orientation are called *Krukenberg's spindle*, and their incidence increases with age.

There is no evident change in the wavelengths transmitted by the aging cornea.¹³⁴

A decrease in corneal sensitivity corresponds to a loss of corneal nerves with age.¹³⁵

Fatty deposits may cause the sclera to appear yellow. The fibers of the lamina cribrosa become stiffer and less resilient with age. Changes in the laminar pores in the

aged lamina cribrosa may make the nerve fibers passing through the openings more susceptible to injury, contributing to an increased susceptibility to glaucomatous damage.¹³⁶⁻¹³⁹

REFERENCES

- Warwick R: *Eugene Wolff's anatomy of the eye and orbit*, ed 7, Philadelphia, 1976, Saunders, p 30.
- Van Buskirk EM: The anatomy of the limbus, *Eye* 3:101, 1989.
- Duke-Elder WS: *Textbook of ophthalmology*, St Louis, 1946, Mosby, p 40.
- Martola E, Baun J: Central and peripheral corneal thickness, *Arch Ophthalmol* 79:28, 1968.
- Pepose JS, Ubels JL: The cornea. In Hart WM Jr, editor: *Adler's physiology of the eye: clinical application*, ed 9, St Louis, 1992, Mosby, p 29.
- Siu A, Herse P: The effect of age on human corneal thickness: statistical implications of power analysis, *Acta Ophthalmol (Copenh)* 71(1):51, 1993.
- Hogan MJ, Alvarado JA: The cornea. In Hogan MJ, Alvarado JA, Weddell JE, editors: *Histology of the human eye*, Philadelphia, 1971, Saunders, p 55.
- Gipson IK, Yankauckas M, Spurr-Michaud SJ et al: Characteristics of a glycoprotein in the ocular surface glycocalyx, *Invest Ophthalmol Vis Sci* 33:218, 1992.
- Nichols B, Dawson CR, Togni B: Surface features of the conjunctiva and cornea, *Invest Ophthalmol Vis Sci* 24:570, 1983.
- Watanabe H, Fabricant M, Tisdale AS et al: Human corneal and conjunctival epithelia produce a mucin-like glycoprotein for the apical surface, *Invest Ophthalmol Vis Sci* 36(2):337, 1995.
- Pfister RR: The normal surface of corneal epithelium: a scanning electron microscope study, *Invest Ophthalmol* 12:654, 1973.
- Williams KK, Watsky MA: Dye spread through gap junctions in the corneal epithelium of the rabbit, *Curr Eye Res* 16:445, 1997.
- Gipson IK, Spurr-Michaud SJ, Tisdale AS: Anchoring fibrils form a complex network in human and rabbit cornea, *Invest Ophthalmol Vis Sci* 28(2):212, 1987.
- Gipson IK, Spurr-Michaud S, Tisdale A et al: Reassembly of the anchoring structures of the corneal epithelium during wound repair in the rabbit, *Invest Ophthalmol Vis Sci* 30:425, 1989.
- Gipson IK, Spurr-Michaud SJ, Tisdale AS: Hemidesmosome and anchoring fibril collagen appears synchronously during development and wound healing, *Dev Biol* 126:253, 1988.
- Gipson IK: The epithelial basement membrane zone of the limbus, *Eye* 3:132, 1989.
- Khodadoust AA, Silverstein AM, Kenyon KR et al: Adhesion of regenerating epithelium, *Am J Ophthalmol* 65(3):339, 1968.
- Tisdale AS, Spurr-Michaud SJ, Rodrigues M et al: Development of the anchoring structures of the epithelium in rabbit and human fetal corneas, *Invest Ophthalmol Vis Sci* 29(5):727, 1988.
- Binder PS, Rock ME, Schmidt KC et al: High-voltage electron microscopy of normal human cornea, *Invest Ophthalmol Vis Sci* 32:2234, 1991.
- Kruse FE: Stem cells and corneal epithelial regeneration, *Eye* 8:170, 1994.
- Throft R: The X,Y,Z hypothesis of corneal epithelial maintenance, *Invest Ophthalmol Vis Sci* 24(10):1442, 1983.
- Tseng SCG: Concept and application of limbal stem cells, *Eye* 3:141, 1989.
- Hanna C, O'Brien JE: Cell production and migration in the epithelial layer of the cornea, *Arch Ophthalmol* 64:536, 1960.
- Hanna C, Bicknell BA, O'Brien JE: Cell turnover in the adult human eye, *Arch Ophthalmol* 65:695, 1961.
- McCartney ND, Cantu-Crouch D: Rabbit corneal epithelial wound repair: tight junction reformation, *Curr Eye Res* 11:15, 1991.
- Alvarado J, Murphy C, Juster R: Age-related changes in the basement membrane of the human corneal epithelium, *Invest Ophthalmol Vis Sci* 24(8):1015, 1983.
- Bartlett JD, Jaanus SD: *Clinical ocular pharmacology*, ed 2, Boston, 1989, Butterworth, p 379.
- Susicky P: Use of soft contact lenses in the treatment of recurrent corneal erosions, *Cesk Oftalmol* 46(5):381, 1990 (abstract).
- Robin JB, Keys CK, Kaminski LA et al: The effect of collagen shields on rabbit corneal reepithelialization after chemical debridement, *Invest Ophthalmol Vis Sci* 31(7):1294, 1990.
- Gegel HS: Successful treatment of recurrent corneal erosion with Nd:YAG anterior stromal puncture, *Am J Ophthalmol* 110(4):404, 1990.
- Katsev DA, Kincaid MC, Fouraker BD et al: Recurrent corneal erosion: pathology of corneal puncture, *Cornea* 10(5):418, 1991.
- Pfister RR: Clinical measures to promote corneal epithelial healing, *Acta Ophthalmol Suppl* 202:73, 1992.
- Komai Y, Ushiki T: The three-dimensional organization of collagen fibrils in the human cornea and sclera, *Invest Ophthalmol Vis Sci* 32:2244, 1991.
- Wilson SE, Hong JW: Bowman's layer structure and function: critical or dispensable to corneal function? A hypothesis, *Cornea* 19(4):417, 2000.
- Bron AJ: Keratoconus, *Cornea* 7(3):163, 1988.
- Chi HH, Katzin HM, Teng CC: Histopathology of keratoconus, *Am J Ophthalmol* 42:847, 1956.
- Astin C: Contact lens fitting after anterior segment disease, *Contact Lens J* 20(5):11, 1992.
- Radner W, Zehetmayer M, Aufreiter R et al: Interlacing and cross-angle distribution of collagen lamellae in the human cornea, *Cornea* 17(5):537, 1998.
- Radner W, Mallinger R: Interlacing of collagen lamellae in the midstroma of the cornea, *Cornea* 21(6):598, 2002.
- Goldman J, Benedek G, Dohlman C et al: Structural alterations affecting transparency in swollen human corneas, *Invest Ophthalmol* 7(5):501, 1968.
- Poole CA, Brookes NH, Clover GM: Keratocyte networks visualized in the living cornea using vital dyes, *J Cell Sci* 106:685, 1993.
- Müller LJ, Pels E, Vrensen GF: The specific architecture of the anterior stroma accounts for maintenance of corneal curvature, *Br J Ophthalmol* 85:437, 2001.
- Müller LJ, Pels L, Vrensen GF: Novel aspects of the ultrastructural organization of human corneal keratocytes, *Invest Ophthalmol Vis Sci* 36(13):2557, 1995.
- Snyder MC, Bergmanson JP, Doughty MJ: Keratocytes: no more the quiet cells, *J Am Optom Assoc* 69:180, 1998.
- Scott JE, Haigh M: "Small" proteoglycan: collagen interactions. Keratin sulfate proteoglycan associates with rabbit corneal collagen fibrils at the "a" and "c" bands, *Biosci Rep* 5:765, 1965.
- Maurice DM: The structure and transparency of the cornea, *J Physiol* 136:263, 1957.
- Farrell RA, McCally RL, Tatham PE: Wave-length dependencies of light scattering in normal and cold swollen rabbit corneas and their structural implications, *J Physiol* 233:589, 1973.
- Edelhauser HF, Ubels JL: The cornea and the sclera. In Kaufman PL, Alm A, editors: *Adler's physiology of the eye: clinical application*, ed 10, St Louis, 2003, Elsevier Science, p 47.
- Johnson DG, Bourne WM, Campbell RJ: The ultrastructure of Descemet's membrane, *Arch Ophthalmol* 100:1942, 1982.
- Joyce NC: Proliferative capacity of the corneal endothelium, *Prog Ret Eye Res* 22:359, 2003.

51. Doughty MJ: Toward a quantitative analysis of corneal endothelial cell morphology: a review of techniques and their application, *Optom Vis Sci* 66:626, 1989.
52. Joyce NC, Harris DL, Mello DM: Mechanisms of mitotic inhibition in corneal endothelium: contact inhibition and TGF- β 2, *Invest Ophthalmol Vis Sci* 43:2152, 2002 (abstract).
53. Waring GO, Bourne WM, Edelhauser HF et al: The corneal endothelium: normal and pathologic structure and function, *Ophthalmology* 89(6):531, 1982.
54. Barry PA, Petroll WM, Andrews PM et al: The spatial organization of corneal endothelial cytoskeletal proteins and their relationship to the apical junctional complex, *Invest Ophthalmol Vis Sci* 36(6):1115, 1995.
55. Kaye GI, Sibley RC, Hoefle FB: Recent studies on the nature and function of the corneal endothelial layer, *Exp Eye Res* 15:585, 1973.
56. Senoo T, Joyce NC: Cell cycle kinetics in corneal endothelium from old and young donors, *Invest Ophthalmol Vis Sci* 41:660, 2000.
57. Mustonen RK, McDonald MB, Srivannaboon S et al: Normal human corneal cell populations evaluated by in vivo scanning slit confocal microscopy, *Cornea* 17(5):485, 1998.
58. Abib FC, Barreto J Jr: Behavior of corneal endothelial density over a lifetime, *J Cataract Refract Surg* 27:1574, 2001.
59. Bourne WM, McCarey BE, Kaufman HE: Specular microscopy of the human corneal endothelium in vivo, *Am J Ophthalmol* 81:319, 1976.
60. Bergmanson JP: Histopathological analysis of corneal endothelial polymegathism, *Cornea* 11:133, 1992.
61. Efron N, Perez-Gomez I, Morgan PB: Confocal microscopic observations of stromal keratocytes during extended contact lens wear, *Clin Exp Optom* 85(3):156, 2002.
62. Lui ZG, Pflugfelder SC: The effect of long-term contact lens wear on corneal thickness, curvature, and surface regularity, *Ophthalmology* 107:105, 2000.
63. Connor CG, Zagrod ME: Contact lens-induced corneal endothelial polymegathism: functional significance and possible mechanisms, *Am J Optom Physiol Opt* 63:539, 1986.
64. Holden BA, Sweeney DF, Vannas A et al: Effects of long-term extended contact lens wear on the human cornea, *Invest Ophthalmol Vis Sci* 26:1489, 1985.
65. Holden BA, Vannas A, Nolsso L et al: Epithelial and endothelial effects from the extended wear of contact lenses, *Curr Eye Res* 4:739, 1985.
66. Matsuda M, Inaba M, Suda T: Corneal endothelial changes associated with aphakic extended contact lens wear, *Arch Ophthalmol* 106:70, 1988.
67. MacCrae SM, Matsuda M, Shellans S et al: The effects of hard and soft contact lenses on the corneal endothelium, *Am J Ophthalmol* 102:50, 1986.
68. Esgin H, Erda N: Corneal endothelial polymegathism and pleomorphism induced by daily-wear rigid gas-permeable contact lenses, *CLAO J* 28(1):40, 2002.
69. Chang SW, Hu FR, Lin LLK: Effects of contact lenses on corneal endothelium: a morphological and functional study, *Ophthalmologica* 215:197, 2001.
70. McCulley JP: The circulation of fluid at the limbus (flow and diffusion at the limbus), *Eye* 3:114, 1989.
71. Boettner EA, Wolter JR: Transmission of the ocular media, *Invest Ophthalmol Vis Sci* 1:776, 1962.
72. Koložvári L, Nógrádi A, Hopp B et al: UV absorbance of the human cornea in the 240- to 400-nm range, *Invest Ophthalmol Vis Sci* 43(7):2165, 2002.
73. Ringvold A: Corneal epithelium and UV-protection of the eye, *Acta Ophthalmol Scand* 76:149, 1998.
74. Karai I, Matsumura S, Takise S et al: Morphological change in the corneal endothelium due to ultraviolet radiation in welders, *Br J Ophthalmol* 68:544, 1984.
75. Li J, Kuang K, Nielsen S et al: Molecular identification and immunolocalization of the water channel protein aquaporin 1 in CBCECs, *Invest Ophthalmol Vis Sci* 40:1288, 1999 (abstract).
76. Liebovitch LS, Weinbaum S: A model of epithelial water transport: the corneal endothelium, *Biophys J* 35:315, 1981.
77. Baum JP, Maurice DM, McCarey BE: The active and passive transport of water across the corneal endothelium, *Exp Eye Res* 39:335, 1984.
78. O'Neal MR, Polse KA: In vivo assessment of mechanisms controlling corneal hydration, *Invest Ophthalmol Vis Sci* 26:849, 1985.
79. Rom ME, Keller WB, Meyer CJ et al: Relationship between corneal edema and topography, *CLAO J* 21(3):191, 1995.
80. Wechsler S: Striate corneal lines, *Am J Optom Physiol Opt* 51:852, 1974.
81. Erickson P, Comstock TL, Doughty MJ et al: The cornea swells in the posterior direction under hydrogel contact lenses, *Ophthalm Physiol Opt* 19(6):475, 1999.
82. Crosson CE, Klyce SD, Beuerman RW: Corneal epithelial wound closure, *Invest Ophthalmol Vis Sci* 27(4):464, 1986.
83. Tervo T, van Setten GB, Päällysaho T et al: Wound healing of the ocular surface, *Ann Med* 24:19, 1992.
84. Davison PF, Galbary EJ: Connective-tissue remodeling in corneal and scleral wounds, *Invest Ophthalmol Vis Sci* 27(10):1478, 1986.
85. Brazzell RK, Stern ME, Aquavella JV et al: Human recombinant epidermal growth factor in experimental corneal wound healing, *Invest Ophthalmol Vis Sci* 32(2):336, 1991.
86. Hoppenreijns VP, Pels E, Vrensen GF et al: Effects of human growth factor on endothelial wound healing of human corneas, *Invest Ophthalmol Vis Sci* 33(6):1946, 1992.
87. Hoppenreijns VP, Pels E, Vrensen GF et al: Platelet-derived growth factor: receptor expression in corneas and effects on corneal cells, *Invest Ophthalmol Vis Sci* 34(3):637, 1993.
88. Kim LS, Oh JS, Kim IS et al: Clinical efficacy of topical homologous fibronectin in persistent corneal epithelial disorders, *Korean J Ophthalmol* 6(1):12, 1992.
89. Mooradian DL, McCarthy JB, Skubitz AP et al: Characterization of FM-C/H-V, a novel synthetic peptide from fibronectin that promotes rabbit corneal epithelial cell adhesion, spreading, and motility, *Invest Ophthalmol Vis Sci* 34(1):153, 1993.
90. Pastor JC, Calonge M: Epidermal growth factor and corneal wound healing, *Cornea* 11(4):311, 1992.
91. Rieck P, Hartmann C, Jacob C et al: Human recombinant bFGF stimulates corneal endothelial wound healing in rabbits, *Curr Eye Res* 11(12):1161, 1992.
92. Schultz G, Chegini N, Grant M et al: Effects of growth factors on corneal wound healing, *Acta Ophthalmol Suppl* 202:60, 1992.
93. Fullwood NJ, Davies Y, Nieduszynski IA et al: Cell surface-associated keratan sulfate on normal and migrating corneal endothelium, *Invest Ophthalmol Vis Sci* 37(7):1256, 1996.
94. Hill RM, Fatt I: How dependent is the cornea on the atmosphere? *J Am Optom Assoc* 5:873, 1964.
95. Smelser GK, Ozanics V: Importance of atmospheric oxygen for maintenance of the optical properties of the human cornea, *Science* 115:140, 1952.
96. Klintworth GK, Burger PC: Neovascularization of the cornea: current concepts of its pathogenesis, *Int Ophthalmol Clin* 23(1):27, 1981.
97. Lawrenson JG, Ruskell GL: The structure of corpuscular nerve endings in the limbal conjunctiva of the human eye, *J Anat* 177:75, 1991.
98. Müller LJ, Pels E, Vrensen GF: Ultrastructural organization of human corneal nerves, *Invest Ophthalmol Vis Sci* 37(4):476, 1996.

99. Oliveira-Soto L, Efron N: Morphology of corneal nerves using confocal microscopy, *Cornea* 20(4):374, 2001.
100. Meyer E, Ludatscher RN, Miller B et al: Connective tissue of the orbital cavity in retinal detachment: an ultrastructural study, *Ophthalmic Res* 24:365, 1992.
101. Hogan MJ, Alvarado JA: The sclera. In Hogan MJ, Alvarado JA, Weddell JE, editors: *Histology of the human eye*, Philadelphia, 1971, Saunders, p 183.
102. Olsen TW, Aaberg SY, Geroski DH et al: Human sclera: thickness and surface area, *Am J Ophthalmol* 125:237, 1998.
103. Quantock AJ, Meek KM: Axial electron density of human sclera, *Biophys J* 54:159, 1988.
104. Thale A, Tillmann B: The collagen architecture of the sclera: SEM and immunohistochemical studies, *Anat Anz* 175:215, 1993.
105. Marshall GE: Human scleral elastic system: an immunoelectron microscopic study, *Br J Ophthalmol* 79:57, 1995.
106. Alexander RA, Garner A: Elastic and precursor fibres in the normal human eye, *Exp Eye Res* 36:305, 1983.
107. McBrien NA, Cornell LM, Gentle A: Structural and ultrastructural changes to the sclera in a mammalian model of high myopia, *Invest Ophthalmol Vis Sci* 42:2179, 2001 (abstract).
108. McBrien NA, Gentle A: The role of visual information in the control of scleral matrix biology in myopia, *Curr Eye Res* 23(5):319, 2001.
109. Elkington AR, Inman CB, Steart PV et al: The structure of the lamina cribrosa of the human eye: an immunocytochemical and electron microscopical study, *Eye* 4:42, 1990.
110. Hogan MJ, Alvarado JA: The limbus. In Hogan MJ, Alvarado JA, Weddell JE, editors: *Histology of the human eye*, Philadelphia, 1971, Saunders, p 112.
111. Kikkawa DO, Lucarelli MJ, Shovlin JP et al: Ophthalmic facial anatomy and physiology. In Kaufman PL, Alm A, editors: *Adler's physiology of the eye: clinical application*, ed 10, St Louis, 2003, Elsevier Science, p 16.
112. Newton RH, Meek KM: Circumcorneal annulus of collagen fibrils in the human limbus, *Invest Ophthalmol Vis Sci* 39(7):1125, 1998.
113. Davanger M, Evensen A: Role of the pericorneal papillary structure in renewal of corneal epithelium, *Nature* 229:560, 1971.
114. Dua HS, Azuara-Blanco A: Limbal stem cells of the corneal epithelium, *Surv Ophthalmol* 44(5):415, 2000.
115. Kinoshita S, Wakako A, Chie S et al: Characteristics of the human ocular surface epithelium, *Prog Ret Eye Res* 20(5):639, 2001.
116. Meyer PAR: The circulation of the human limbus, *Eye* 3:121, 1989.
117. Cotsarelis G, Cheng SZ, Dong E et al: Existence of slow-cycling limbal epithelial basal cells that can be preferentially stimulated to proliferate, *Cell* 57:201, 1989.
118. Ebato B, Friend J, Throft RA: Comparison of central and peripheral human corneal epithelium in tissue culture, *Invest Ophthalmol Vis Sci* 28:1450, 1987.
119. Lauweryns B, van den Oord JJ, De Vos R et al: A new epithelial cell type in the human cornea, *Invest Ophthalmol Vis Sci* 34(6):1983, 1993.
120. Thoft RA, Wiley LA, Sundarraj N: The multipotential cells of the limbus, *Eye* 3:109, 1989.
121. Zieske JD, Bukusoglu G, Yankauckas MA: Characterization of a potential marker of corneal epithelial stem cells, *Invest Ophthalmol Vis Sci* 33(1):143, 1992.
122. Wolosin JM, Xiong X, Schütte M et al: Stem cells and differentiation stages in the limbo-corneal epithelium, *Prog Ret Eye Res* 19(2):223, 2000.
123. Pallikaris JG, Siganos DS: Laser in situ keratomileusis to treat myopia: early experience, *J Cataract Refract Surg* 23:39, 1997.
124. Collins MJ, Carr JD, Stulting RD et al: Effects of laser in situ keratomileusis (LASIK) on the corneal endothelium 3 years postoperatively, *Am J Ophthalmol* 131:1, 2001.
125. Jabbur NS: Endothelial cell studies in patients after photorefractive keratectomy for hyperopia, *J Refract Surg* 19:142, 2003.
126. Fagerholm P: Phototherapeutic keratectomy: 12 years of experience, *Acta Ophthalmol Scand* 81(1):1, 2003.
127. Simarop P, Kosalprapai K, Chuckpaiwong V: Effect of laser in situ keratomileusis on the corneal endothelium, *J Refract Surg* 19:S237, 2003.
128. Brandt JD, Beiser JA, Kass MA et al: Central corneal thickness in the Ocular Hypertension Treatment Study (OHTS), *Ophthalmology* 108(10):1779, 2001.
129. Bhan A, Browning AC, Shah S et al: Effect of corneal thickness on intraocular pressure measurements with the pneumotonometer, Goldmann applanation tonometer, and Tono-Pen, *Invest Ophthalmol Vis Sci* 43(5):1389, 2002.
130. Rashad KM, Bahnassy AA: Changes in intraocular pressure after laser in situ keratomileusis, *J Refract Surg* 17(4):420, 2001.
131. Arimoto A, Shimizu K, Shoji N et al: Underestimation of intraocular pressure in eyes after laser in situ keratomileusis, *Jpn J Ophthalmol* 46(6):645, 2002.
132. Barraquer-Somers E, Chan CC, Green WR: Corneal epithelial iron deposition, *Ophthalmology* 90:729, 1983.
133. Bourne WM, Nelson LR, Hodge DO: Central corneal endothelial cell changes over a ten-year period, *Invest Ophthalmol Vis Sci* 38(3):779, 1997.
134. Van den Berg TJ, Tan KE: Light transmittance of the human cornea from 320-700 nm for different ages, *Vis Res* 34(11):1453, 1994.
135. Hollingsworth J, Perez-Gomez I, Mutalib HA et al: A population study of the normal cornea using an in vivo, slit-scanning confocal microscope, *Optom Vis Sci* 78(10):706, 2001.
136. Albon J, Karwatowski WS, Easty DL et al: Age-related changes in the non-collagenous components of the extracellular matrix of the human lamina cribrosa, *Br J Ophthalmol* 84:311, 2000.
137. Sawaguchi S, Yue BY, Fukuchi T et al: Collagen fibrillar network in the optic nerve head of normal monkey eyes and monkey eyes with laser-induced glaucoma: a scanning electron microscopic study, *Curr Eye Res* 18(2):143, 1999.
138. Albon J, Purslow PP, Karwatowski WS et al: Age-related compliance of the lamina cribrosa in human eyes, *Br J Ophthalmol* 84:318, 2000.
139. Albon J, Karwatowski WS, Avery N et al: Changes in the collagenous matrix of the aging human lamina cribrosa, *Br J Ophthalmol* 79:368, 1995.

The middle layer of the eye, the **uvea (uveal tract)**, is composed of three regions: from front to back, the iris, ciliary body, and choroid. The uvea sometimes is called the vascular layer because its largest structure, the choroid, is composed mainly of blood vessels, which supply the outer retinal layers.

IRIS

The **iris** is a thin, circular structure located anterior to the lens, often compared to a diaphragm of an optical system. The center aperture, the **pupil**, actually is located slightly nasal and inferior to the iris center.¹ Pupil size regulates retinal illumination. The diameter can vary from 1 mm to 9 mm depending on lighting conditions. The pupil is very small (**miotic**) in brightly lit conditions and fairly large (**mydriatic**) in dim illumination. The average diameter of the iris is 12 mm, and its thickness varies. It is thickest in the region of the **collarette**, a circular ridge approximately 1.5 mm from the pupillary margin. This slightly raised jagged ridge was the attachment site for the fetal pupillary membrane during embryologic development.^{1,2} The collarette divides the iris into the **pupillary zone**, which encircles the pupil, and the **ciliary zone**, which extends from the collarette to the **iris root** (Figure 3-1). The color of these two zones often differs.

The pupillary margin of the iris rests on the anterior surface of the lens and, in profile, the iris has a truncated cone shape such that the pupillary margin lies anterior to its peripheral termination, the iris root (Figure 3-2). The root, approximately 0.5 mm thick, is the thinnest part of the iris and joins the iris to the anterior aspect of the ciliary body (Figure 3-3)¹. The iris divides the anterior segment of the globe into anterior and posterior chambers, and the pupil allows the aqueous humor to flow from the posterior into the anterior chamber with no resistance.

CLINICAL COMMENT: BLUNT TRAUMA

*With blunt trauma to the eye or head, the thin root may tear away from the ciliary body, creating a condition called **iridodialysis**, which can result in damaged blood vessels and nerves. Blood may hemorrhage into either the anterior or the posterior chamber, or both, and nerve damage may cause sector paralysis of the iris muscles.*

HISTOLOGIC FEATURES OF IRIS

The iris can be divided into four layers: (1) the anterior border layer, (2) stroma and sphincter muscle, (3) anterior epithelium and dilator muscle, and (4) posterior epithelium.

Anterior Border Layer

The surface layer of the iris, the **anterior border layer**, is a thin condensation of the stroma. In fact, some do not consider this to be a separate layer. It is composed of fibroblasts, pigmented melanocytes, and collagen fibrils. The highly branching processes of the cells interweave to form a meshwork in which the fibroblasts are on the surface and the melanocytes are located below^{1,2} (Figure 3-4). The thickness of the melanocyte layer may vary throughout the iris, with accumulations of melanocytes forming elevated frecklelike masses, evident in the anterior border layer. The density and arrangement of the meshwork differ among irises and are contributing factors in iris color. The collagen fibrils are arranged in radial columns that are seen easily as white fibers in light-colored irises.³

The anterior border layer is absent at the oval-shaped iris crypts. Near the root, extensions of this layer form finger-shaped iris processes that can attach to the trabecular meshwork. The number of these processes varies, but they usually do not impede aqueous outflow. The anterior border layer ends at the root.

Iris Stroma and Sphincter Muscle

The connective tissue **stroma** is composed of pigmented and nonpigmented cells, collagen fibrils, and extensive ground substance. The pigmented cells include melanocytes and clump cells, whereas the nonpigmented cells are fibroblasts, lymphocytes, macrophages, and mast cells.¹ Although melanocytes and fibroblasts have many branching processes, the cells are widely spaced in the stroma, so their branches do not form a meshwork. **Clump cells** are large, round, darkly pigmented cells and are variously described as “displaced neuroectodermal cells” or more likely “altered macrophages.”^{1,3} Clump cells usually are located in the pupillary portion of the stroma, often near the sphincter muscle (Figure 3-5).

The iris arteries are branches of a circular vessel, the **major circle of the iris**, located in the ciliary body near the iris root. The iris vessels usually follow a radial course from the iris root to the pupil margin. These vessels were historically thought to have an especially

thick tunica adventitia and have been called “thick-walled blood vessels.”¹⁻³ Improved histologic staining has shown, however, that the bundles of collagen fibrils encircling the vessels are continuous with the collagen network of the stroma and not part of the actual vessel wall. This fibril network anchors the vessels in place and protects them from kinking and compression during extensive iris movement in miosis and mydriasis.⁴ An incomplete circular vessel, the **minor circle of the iris**, is located in the iris stroma in the region of the collarette and is a remnant of embryologic development. The iris capillaries are not fenestrated and form part of the blood-aqueous barrier.¹ The iris stroma is continuous with the stroma of the ciliary body.

The **sphincter muscle** lies within the stroma (see Figure 3-5) and is composed of smooth-muscle cells joined by tight junctions.¹ As its name implies, the sphincter is a circular muscle 0.75 to 1 mm wide, encircling the pupil and located in the pupillary zone of the stroma^{1,2} (Figure 3-6). The sphincter muscle is anchored firmly to adjacent stroma and retains its function even if severed radially.¹ Contraction of the sphincter causes the pupil to constrict in *miosis*. The muscle is innervated by the parasympathetic system.

CLINICAL COMMENT: IRIDECTOMY

*In some cases of glaucoma, to facilitate the movement of aqueous from the posterior chamber to the anterior chamber, an **iridectomy** is performed. In this surgical procedure a wedge-shaped, full-thickness section of tissue is removed from the iris. If the sphincter muscle is cut during this procedure, the ability of the muscle to contract is not lost. **Iridotomy**, a similar procedure in which an opening is made in the iris without excising tissue, often is accomplished using a laser, and the muscle is usually not involved.*

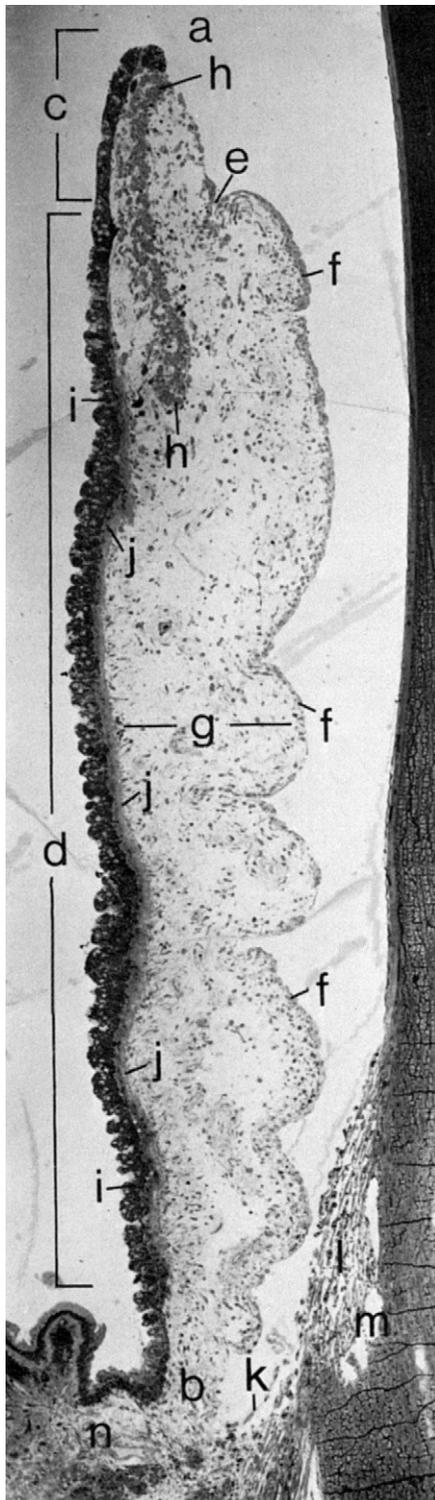


FIGURE 3-1

Light micrograph of the iris and anterior chamber. The cornea, anterior chamber angle, trabecular meshwork, canal of Schlemm, and part of the ciliary body are included. Anterior and posterior iris contraction furrows are accentuated by slight dilation of pupil. Pupil and pupillary ruff are at *a*, and iris root is at *b*. Pupillary portion of iris is at *c*, and ciliary portion is at *d*. Collarette (*e*) and minor arterial circle of the iris lie at the junction of these two portions. Cellular anterior border layer (*f*) is distinct from loosely arranged stromal tissue (*g*). Sphincter muscle lies in the stroma (*h*). Posterior iris shows posterior (*i*) and anterior (*j*) epithelium; the latter forms the dilator muscle. Anterior chamber angle shows part of a uveal band (*k*). Trabecular meshwork (*l*) and canal of Schlemm (*m*) lie external to chamber angle. Ciliary body and its muscle are posterior to iris (*n*). (×60.) (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

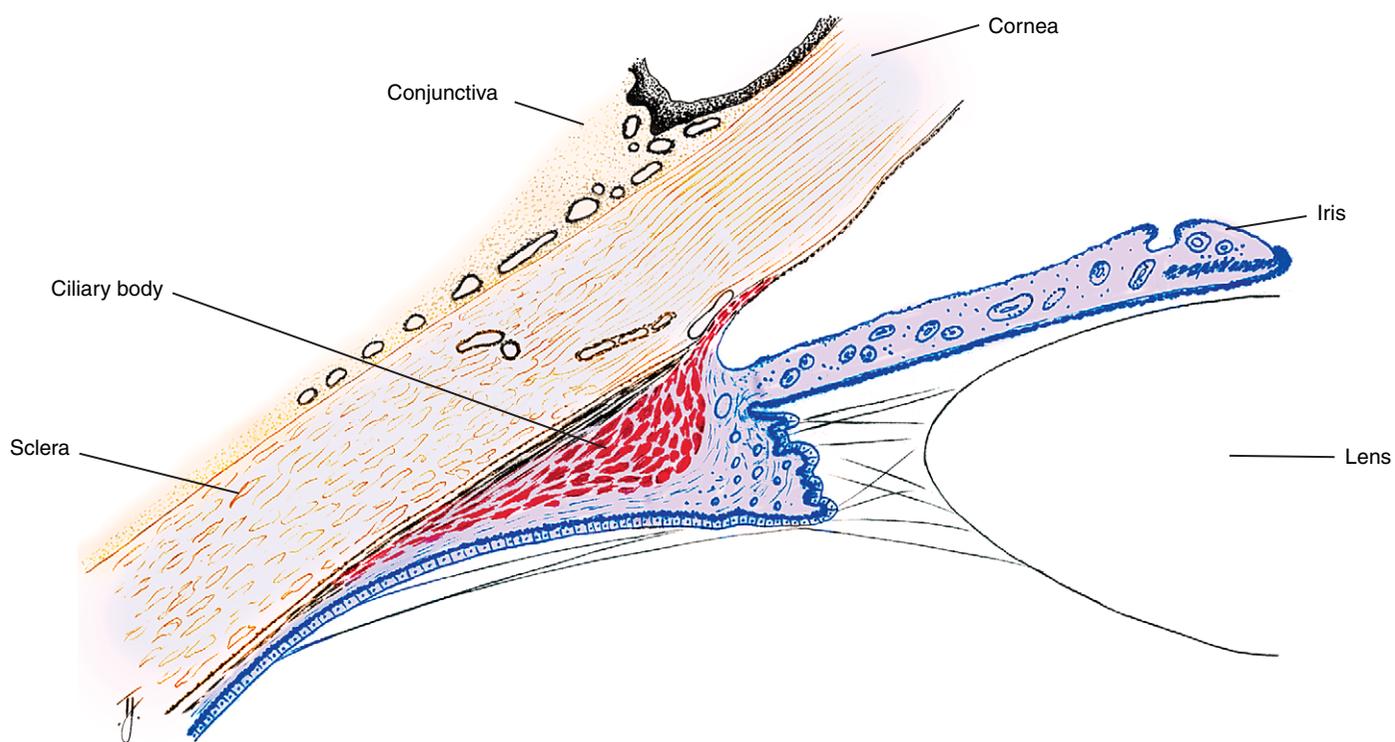


FIGURE 3-2
Periphery of anterior segment of the globe.

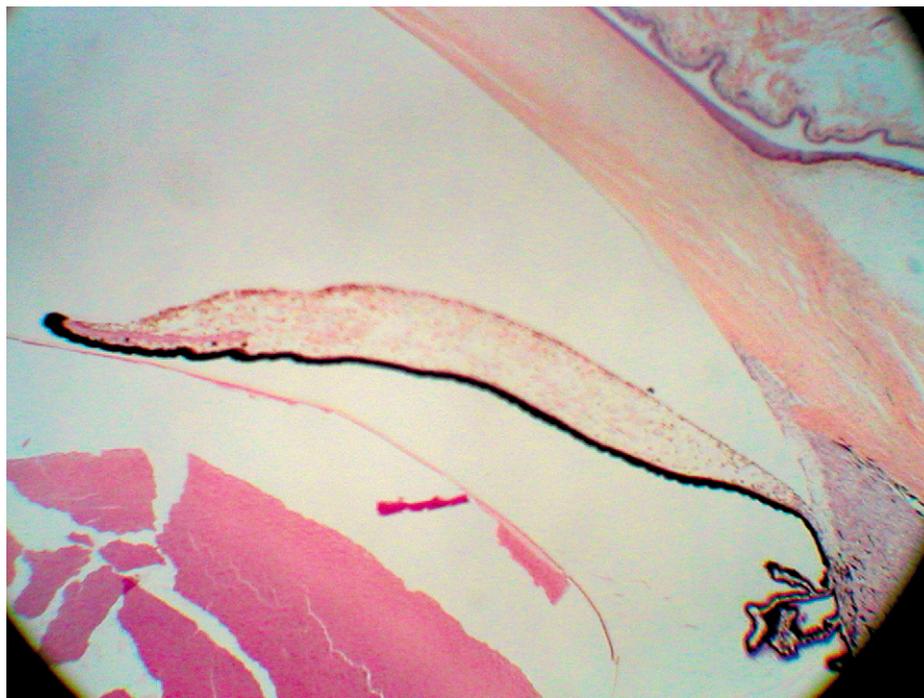


FIGURE 3-3
Light micrograph of anterior segment section. The pupillary zone of the iris rests on lens, lens fibers are fragmented, the iris root is evident at its attachment to the ciliary body; remnants of the zonular fibers are seen between lens equator and ciliary process.

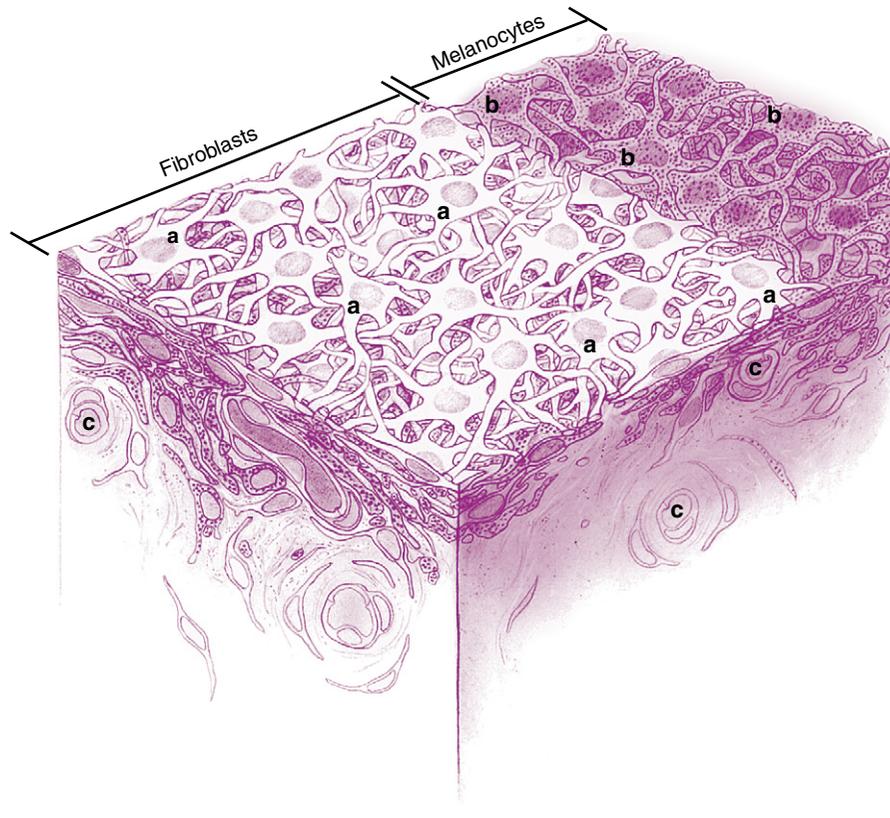


FIGURE 3-4

Anterior layers of the iris. Anterior border layer is covered by a single layer of fibroblasts (*a*), the long, branching processes of which interconnect. Branching processes of fibroblasts form variably sized openings on iris surface. Beneath the layer of fibroblasts is a fairly dense aggregation of melanocytes and a few fibroblasts. The superficial layer of fibroblasts has been removed at *b* to show these cells. Number of cells in anterior border layer is greater than that in underlying stroma. Iris stroma contains a number of capillaries (*c*), which may be quite close to the surface. (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

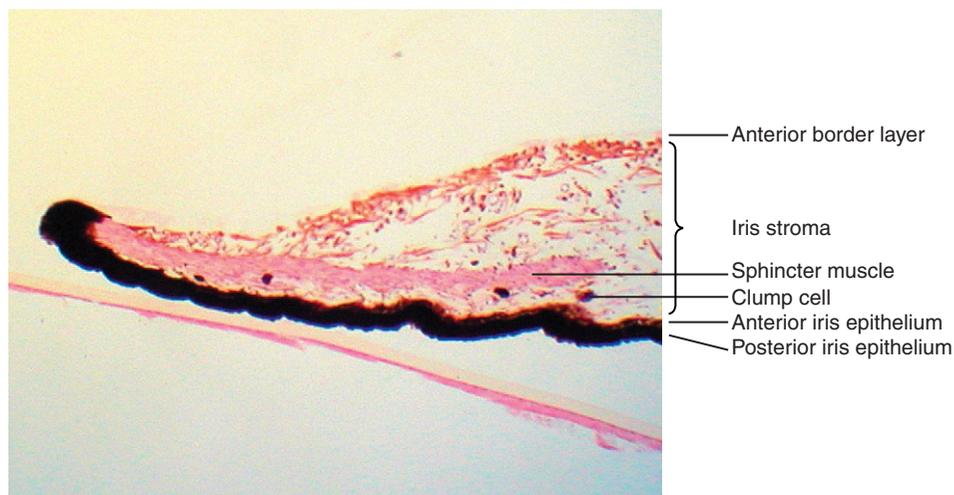


FIGURE 3-5

Light micrograph of transverse section of pupillary portion of the iris showing the sphincter muscle. Clump cells are evident between the muscle and the anterior epithelium.

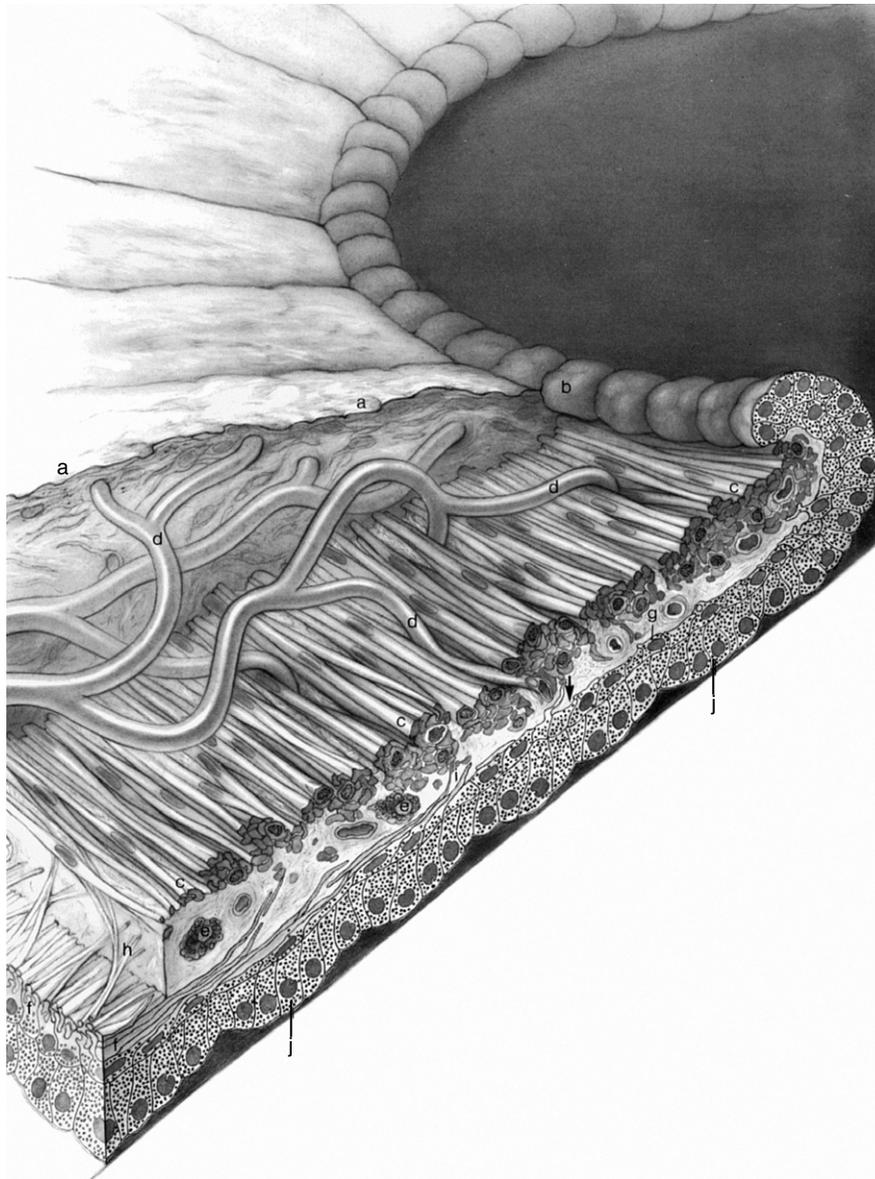


FIGURE 3-6

Pupillary portion of the iris. Dense cellular anterior border layer (*a*) terminates at pigment ruff (*b*) in pupillary margin. Sphincter muscle is at *c*. The arcades (*d*) from the minor circle of iris extend toward pupil and through sphincter muscle. Sphincter muscle and iris epithelium are close to each other at the pupillary margin. Capillaries, nerves, melanocytes, and clump cells (*e*) are found within and around the muscles. The three to five layers of dilator muscle (*f*) gradually diminish in number until they terminate behind midportion of sphincter muscle (*arrow*), leaving low, cuboidal epithelial cells (*g*) to form the anterior epithelium of pupillary margin. Spurlike extensions from dilator muscle form Michel's spur (*h*) and Fuchs' spur (*i*), which extend anteriorly to blend with sphincter muscle. Posterior epithelium (*j*) is formed by tall columnar cells with basally located nuclei. Its apical surface is contiguous with apical surface of anterior epithelium. (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

Anterior Epithelium and Dilator Muscle

Posterior to the stroma are two layers of epithelium. The first of these, the epithelial layer lying nearest to the stroma, is the **anterior iris epithelium**, which is composed of the unique myoepithelial cell. The apical portion is pigmented cuboidal epithelium joined by tight junctions and desmosomes, whereas the basal portion is composed of elongated, contractile, smooth muscle processes (Figure 3-7). The muscle fibers extend into the stroma, forming three to five layers of dilator muscle joined by tight junctions (Figure 3-8).

The **dilator muscle** is present from the iris root to a point in the stroma below the midpoint of the sphincter.¹ Near the termination of the dilator muscle, small projections insert into the stroma or, more accurately, into the sphincter^{1,2} (see Figure 3-6). Because the fibers are arranged radially, contraction of the dilator muscle pulls the pupillary portion toward the root, thereby enlarging the pupil in *mydriasis*. The dilator is sympathetically innervated.

The anterior epithelium continues to the pupillary margin as cuboidal epithelial cells, and the epithelium continues posteriorly as the pigmented epithelium of the ciliary body.

Posterior Epithelium

The second epithelial layer posterior to the stroma is the **posterior iris epithelium**, a single layer of heavily pigmented, approximately columnar cells joined by tight junctions and desmosomes.^{2,3} In the periphery the posterior iris epithelium begins to lose its pigment as it continues into the ciliary body as the nonpigmented epithelium. A thin basement membrane covers the basal aspect of this cellular layer, lining the posterior chamber.

The anterior and posterior iris epithelial layers are positioned *apex to apex*, a result of events during embryologic development. Apical microvilli extend from both surfaces, and desmosomes join the two apical surfaces. The epithelial cells curl around from the posterior iris to the anterior surface at the pupillary margin, forming the pigmented **pupillary ruff** (or frill), which encircles the pupil; this normally has a serrated appearance (see Figure 3-6).

CLINICAL COMMENT: IRIS SYNECHIAE

An **iris synechia** is an abnormal attachment between the iris surface and another structure. In a **posterior synechia** the posterior iris surface is adherent to the anterior lens surface. In an **anterior synechia** the anterior iris surface is adherent to the corneal endothelium or the trabecular meshwork. Synechiae can occur as a result of a sharp blow to the head or a whiplash-type movement that brings the

two structures forcefully together. Alternatively, cells and debris from a uveal infection that are circulating in the aqueous humor can make the surfaces “sticky” and so cause synechiae.⁵

If a posterior synechia involves a large portion of the pupillary margin, aqueous will accumulate in the posterior chamber. Continual production of aqueous causes the pressure in the posterior chamber to increase, which in turn causes the iris to bow forward in a configuration called *iris bombé*. This can push the peripheral iris against the trabecular meshwork, setting the stage for a dramatic increase of intraocular pressure (IOP). A drug-induced dilation usually will break a posterior synechia. The break usually occurs between the epithelial layers, leaving remnants of the posterior epithelium on the anterior surface of the lens.

An anterior synechia usually occurs at the iris periphery and involves the meshwork. It is called a **peripheral anterior synechia (PAS)**. Aqueous outflow is impeded by a PAS, causing an increase in IOP if the adhesion occupies a considerable amount of the trabecular meshwork.

ANTERIOR IRIS SURFACE

Thin, radial, collagenous columns or trabeculae are evident in lightly pigmented irises. Thicker, radially oriented, branching trabeculae encircle depressions or openings in the surface called **crypts**.³ Crypts are located on both sides of the collarette (**Fuchs' crypts**) and near the root (peripheral crypts). They allow the aqueous quick exit and entrance into spaces in the iris stroma as the volume of the iris changes with iris dilation and contraction.

Circular contraction folds, evident on the anterior surface of the ciliary zone, result from tissue moving toward the iris root during pupillary dilation. Figure 3-9 shows the topography of the anterior and posterior iris surfaces.

POSTERIOR IRIS SURFACE

The posterior surface of the iris is fairly smooth, but when viewed with magnification, small circular furrows are evident near the pupil. **Radial contraction furrows (of Schwalbe)** are located in the pupillary zone, and the deeper **structural furrows (of Schwalbe)** run throughout the ciliary zone and continue into the ciliary body as the valleys between the ciliary processes.¹⁻³ Also found on the posterior surface are circular contraction folds similar to those seen on the anterior surface.

IRIS COLOR

Iris color depends on the arrangement and density of connective tissue components in the anterior border layer and stroma, melanocyte density,³ and pigment density within the melanocyte.⁶ An iris appears blue for

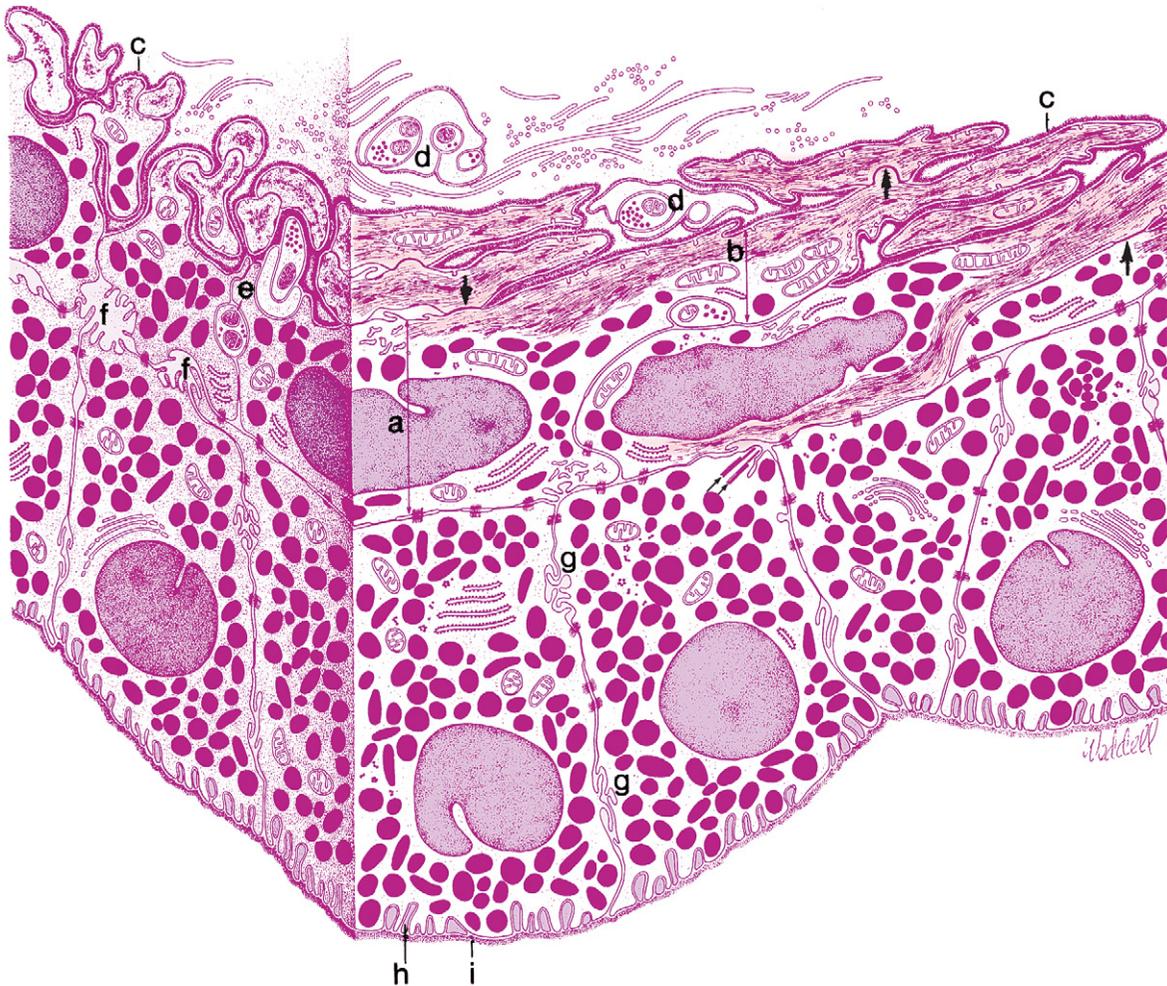


FIGURE 3-7

Posterior epithelial layers. Anterior iris epithelium has two morphologically distinct portions: apical epithelial portion (*a*) and basal muscular portion (*b*). Cytoplasm of basal portion is filled with myofibrils and moderate number of mitochondria. Tonguelike muscular processes overlap, creating three to five layers. Tight junctions (*arrows*), such as those in sphincter muscle, are found between dilator muscle cells. A basement membrane (*c*) surrounds the muscle processes. Unmyelinated nerves and associated Schwann cells (*d*), as well as a few naked axons, innervate sphincter muscle. Axon (*e*) is in close contact with anterior epithelium, separated from it by a space measuring 200 Å wide. Cytoplasm of epithelial portions contains cell organelles, melanin granules, nucleus, and bundles of myofilaments. Most intercellular junctions present here are macula occludens, and only a few desmosomes are present; desmosomes are not found in muscular portion. Apical surface of anterior epithelium is contiguous with that of posterior epithelium. Desmosomes and tight junctions join the two layers, but some areas of separation (*f*) exist between the cells. The spaces so formed are filled with microvilli, and an occasional cilium also is found here (*double arrows*). Posterior pigmented iris epithelium shows lateral interdigitations (*g*) and areas of infolding along its basal surface (*h*). A typical basement membrane (*i*) is found on the basal side as well. Numerous tight junctions and desmosomes occur along lateral and apical walls. Cytoplasm of this epithelium contains numerous melanin granules, measuring approximately 0.8 μm in cross section and up to 2.5 μm in length. Stacks of cisternae of rough-surfaced endoplasmic reticulum, clustered unattached ribosomes, mitochondria, and a Golgi apparatus are typically observed. (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

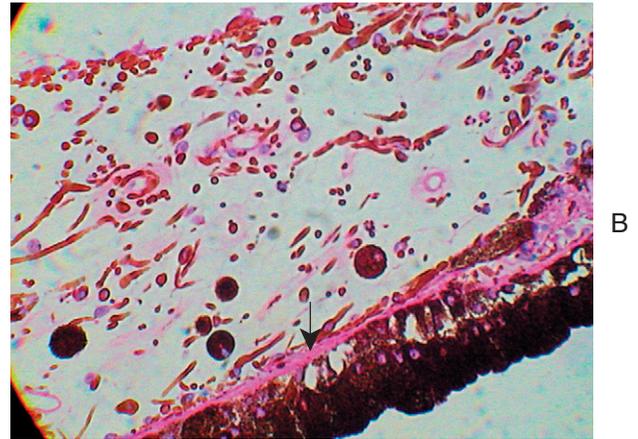
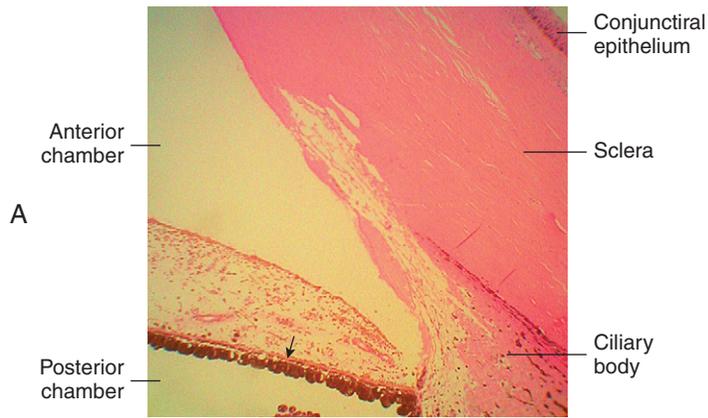


FIGURE 3-8

A, Light micrograph of ciliary portion of iris. Dilator muscle is evident as pink band (*arrow*) anterior to pigmented epithelium. **B**, Light micrograph of epithelial iris layers, strands of dilator (*arrow*) evident above pigmented portion of anterior iris epithelium.

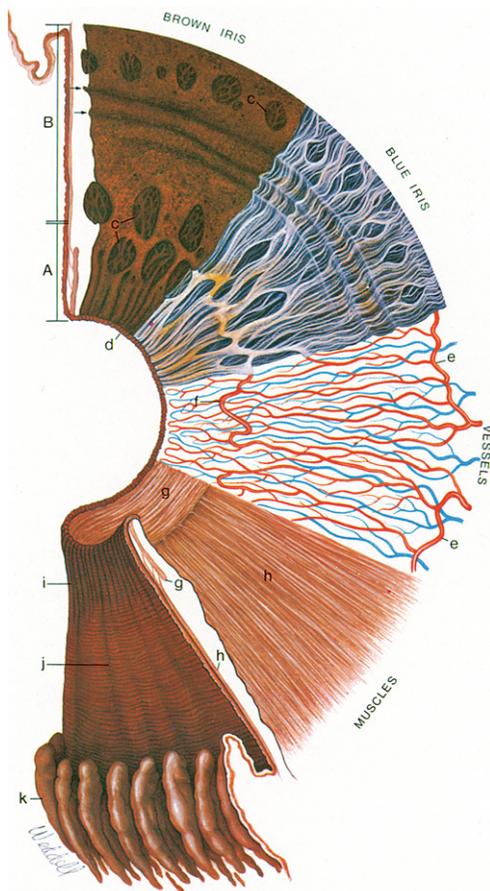


FIGURE 3-9

Surfaces and layers of the iris. Beginning at the upper left and proceeding clockwise, the iris cross-section shows the pupillary (*A*) and ciliary portions (*B*), and the surface view shows a brown iris with its dense, matted anterior border layer. Circular contraction furrows are shown (*arrows*) in the ciliary portion of the iris. Fuchs' crypts (*c*) are seen at either side of the collarette in the pupillary and ciliary portion and peripherally near the iris root. The pigment ruff is seen at the pupillary edge (*d*). The blue iris surface shows a less dense anterior border layer and more prominent trabeculae. The iris vessels are shown beginning at the major arterial circle in the ciliary body (*e*). Radial branches of the arteries and veins extend toward the pupillary region. The arteries form the incomplete minor arterial circle (*f*), from which branches extend toward the pupil, forming capillary arcades. The sector below it demonstrates the circular arrangement of the sphincter muscle (*g*) and the radial processes of the dilator muscle (*h*). The posterior surface of the iris shows the radial contraction furrows (*i*) and the structural folds of Schwalbe (*j*). Circular contraction folds also are present in the ciliary portion. The pars plicata of the ciliary body is at (*k*). (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

the same reason that the sky is blue; the wavelength seen results from light scatter caused by the arrangement and density of the connective tissue components. Other colors are caused by the amount of light absorption, which depends on the pigment density within the melanocytes. If the iris is heavily pigmented, the anterior surface appears brown and smooth, even velvety, whereas in a lighter iris, the collagen trabeculae are evident and the color ranges from grays to blues to greens depending on the density of pigment and collagen. A freckle or a nevus is an area of hyperpigmentation, an accumulation of melanocytes, and frequently is seen in the anterior border layer. In all colored irises, the two epithelial layers are heavily pigmented. Only in the albino iris do the epithelial layers lack pigment.³

CLINICAL COMMENT: PIGMENTARY DISPERSION SYNDROME

In **pigmentary dispersion syndrome**, pigment granules are shed from the posterior iris surface and are dispersed into the anterior chamber. They can be deposited on the iris, lens, or corneal endothelium or in the trabecular meshwork, where they might compromise aqueous outflow.⁴ Significant pigment loss will be evident on transillumination of the iris when the red fundus reflex shows through in the depigmented areas.

CLINICAL COMMENT: HETEROCHROMIA

Heterochromia of the iris is a condition in which one iris differs in color from the other or portions of one iris differ in color from the rest of the iris. This can be either congenital or a sign of uveal inflammation. If congenital, a disruption of the sympathetic innervation may be suspected.^{4,7} A history regarding iris coloration should be elicited.

CILIARY BODY

When viewed from the front of the eye, the **ciliary body** is a ring-shaped structure. Its width is approximately 5.9 mm on the nasal side and 6.7 mm on the temporal side.² The posterior area of the ciliary body, which terminates at the ora serrata, appears fairly flat, but the anterior ciliary body contains numerous folds or processes that extend into the posterior chamber. In sagittal section the ciliary body has a triangular shape, the base of which is located anteriorly; one corner of the base lies at the scleral spur, the iris root extends from the approximate center of the base, and a portion of the base borders the anterior chamber. The outer side of the triangle lies against the sclera, and the inner side lines the posterior chamber and a small portion of the vitreous cavity (Figure 3-10). The apex is located at the ora serrata.

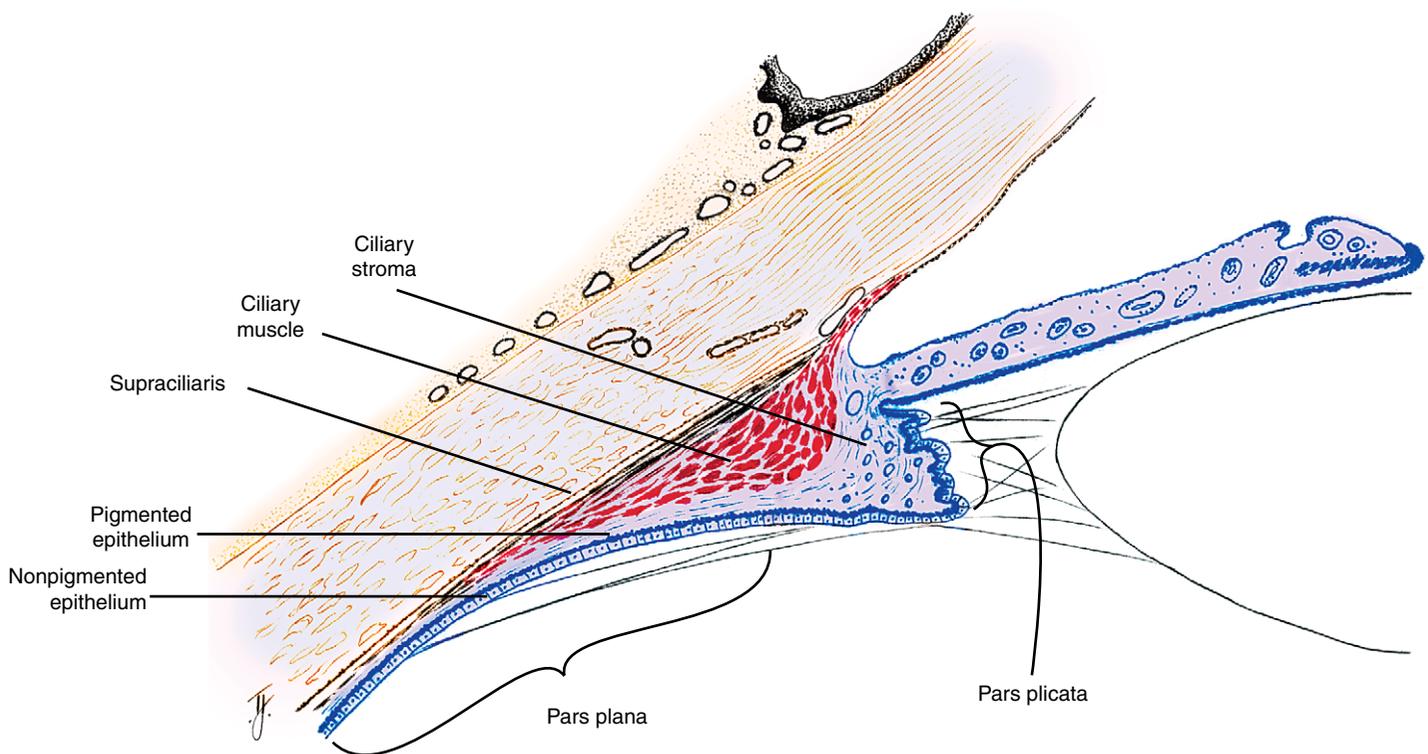


FIGURE 3-10

Partitions and layers of ciliary body.

The ciliary body can be divided into two parts: the pars plicata (corona ciliaris) and the pars plana (orbicularis ciliaris). The **pars plicata** is the wider, anterior portion containing the **ciliary processes** (see Figure 3-10). Approximately 70 to 80 ciliary processes extend into the posterior chamber, and the regions between them are called **valleys (of Kuhnt)**. A ciliary process measures approximately 2 mm in length, 0.5 mm in width, and 1 mm in height, but there are significant variations in all measurements.¹

The **pars plana** is the flatter region of the ciliary body. It extends from the posterior of the pars plicata to the **ora serrata**, which is the transition between ciliary body and choroid. The ora serrata has a serrated pattern, the forward-pointing apices of which are called **teeth** or **dentate processes**. The rounded portions that lie between the teeth are called **oral bays** (Figure 3-11, A).

The dentate processes are elongations of retinal tissue into the region of the pars plana.

The zonule fibers course from the ciliary body to the lens. Some of these fibers insert into the internal limiting membrane of the pars plana region and travel forward through the valleys between the ciliary processes. Some attach to the internal limiting membrane of the valleys of the pars plicata (Figure 3-11, B). The attachment to the vitreous, the vitreous base, extends forward approximately 2 mm over the posterior pars plana.¹

SUPRACILIARIS (SUPRACILIARY LAMINA)

The **supraciliaris** is the outermost layer of the ciliary body adjacent to the sclera. Its loose connective tissue is arranged in ribbonlike layers containing pig-

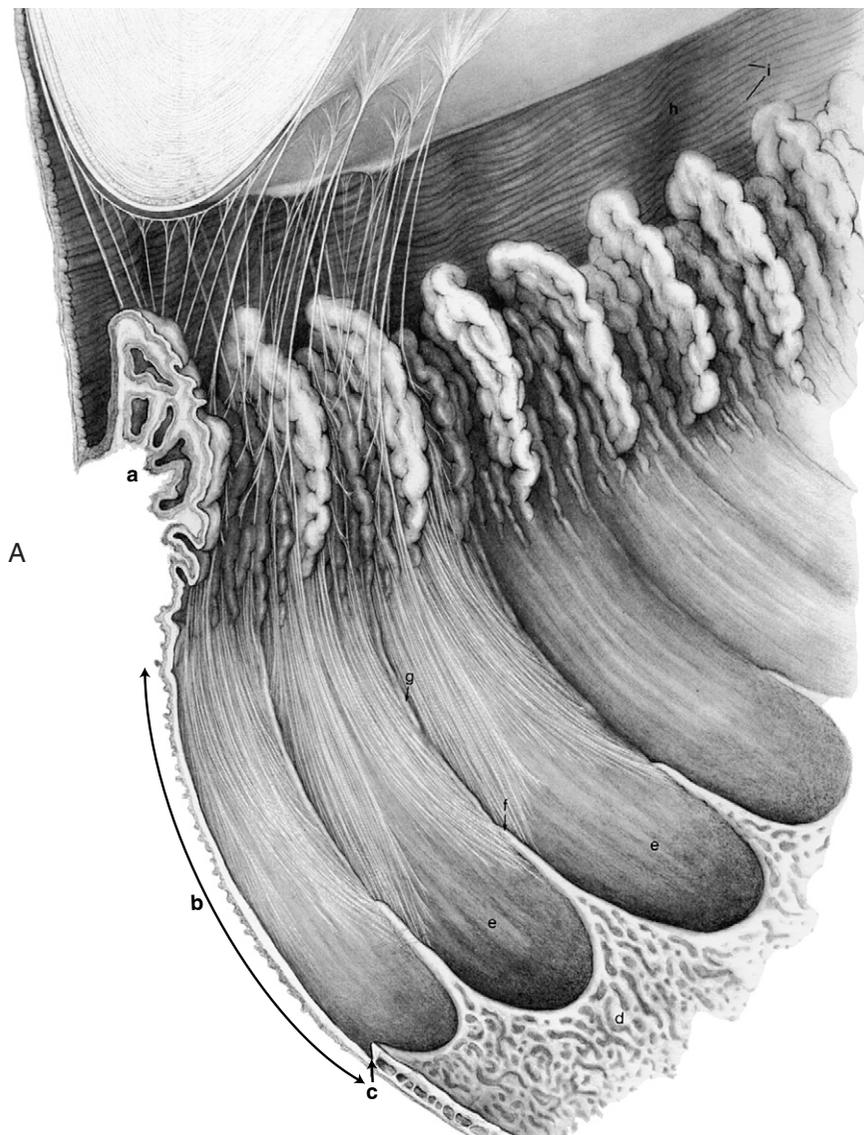


FIGURE 3-11

A, Inner aspect of the ciliary body shows pars plicata (a) and pars plana (b). Ora serrata is at c, and posterior to it, retina exhibits cystoid degeneration (d). Bays (e) and dentate processes (f) of ora are shown; linear ridges or striae (g) project forward from dentate processes across pars plana to enter valleys between ciliary processes. Zonular fibers arise from pars plana beginning 1.5 mm from ora serrata. These fibers curve forward from sides of dentate ridges into ciliary valleys, then from valleys to lens capsule. Zonules coming from the valleys on either side of a ciliary process have a common point of attachment on lens. Zonules attach up to 1 mm from the equator posteriorly and up to 1.5 mm from the equator anteriorly. At equatorial border, attaching zonules give a crenated appearance to lens. Ciliary processes vary in size and shape and often are separated from one another by lesser processes. Radial furrows (h) and circular furrows (i) of peripheral iris are shown. *Continued*

mented melanocytes, fibroblasts, and collagen bands¹ (Figure 3-12). The arrangement of these bands allows the ciliary body to slide against the sclera without detaching from or stretching the tissue. The arrangement of the supraciliary allows for the accumulation of fluid within its spaces, which may cause a displacement of the ciliary body from the sclera. Damage to the layer caused by trauma may result in a ciliary body detachment.

CILIARY MUSCLE

The **ciliary muscle** is composed of smooth muscle fibers oriented in longitudinal, radial, and circular directions. Interweaving occurs between fiber bundles and from layer to layer, such that various amounts of connective tissue are found among the muscle bundles.¹ The **longitudinal muscle fibers (of Brücke)** lie adjacent to

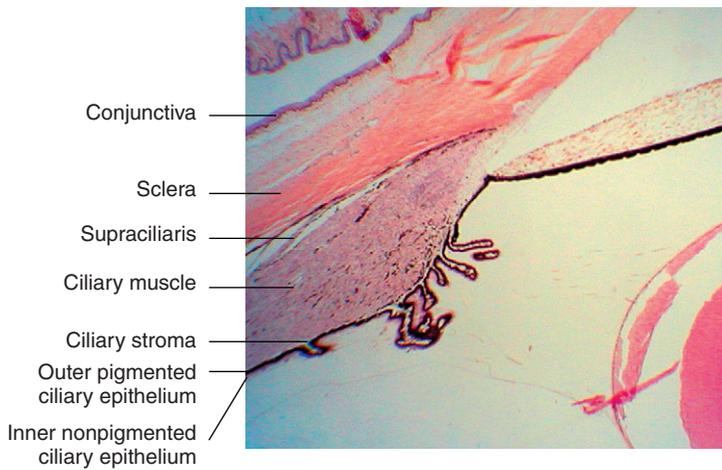
the supraciliary and parallel to the sclera. Each muscle bundle resembles a long narrow V the base of which is at the scleral spur, whereas the apex is in the choroid. The tendon of origin attaches the muscle fibers to the scleral spur and to adjacent trabecular meshwork sheets. The insertion of the ciliary muscle is in the anterior one third of the choroid in the form of stellate-shaped terminations or “muscle stars.”^{1,2} Below the longitudinal muscle fibers, the **radial fibers** form wider, shorter interdigitating Vs that originate at the scleral spur and insert into the connective tissue near the base of the ciliary processes.¹ This layer is a transition from the longitudinally oriented fibers to the circular fibers.

The innermost region of ciliary muscle, (**Müller’s annular muscle**), is formed of circular muscle bundles with a sphincter-type action. These fibers are located near the major circle of the iris. Figure 3-13 shows the relationship between these regions of the ciliary muscle and surrounding structures.



FIGURE 3-11 cont'd

B, Anterior view of the ciliary processes showing zonules attaching to lens. Zonules form columns (a) on either side of ciliary processes (b), which meet on a single site (c) as they attach to lens. These two columns form a triangle, base of which is on ciliary body and apex of which is on lens. Zonules form tentlike structure (d) as they become attached to lens capsule. Equatorial surface of lens is crenated (e) by attachment of zonule. Iris is pulled upward, revealing its posterior surface containing radial folds (f) and circular furrows (g). (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

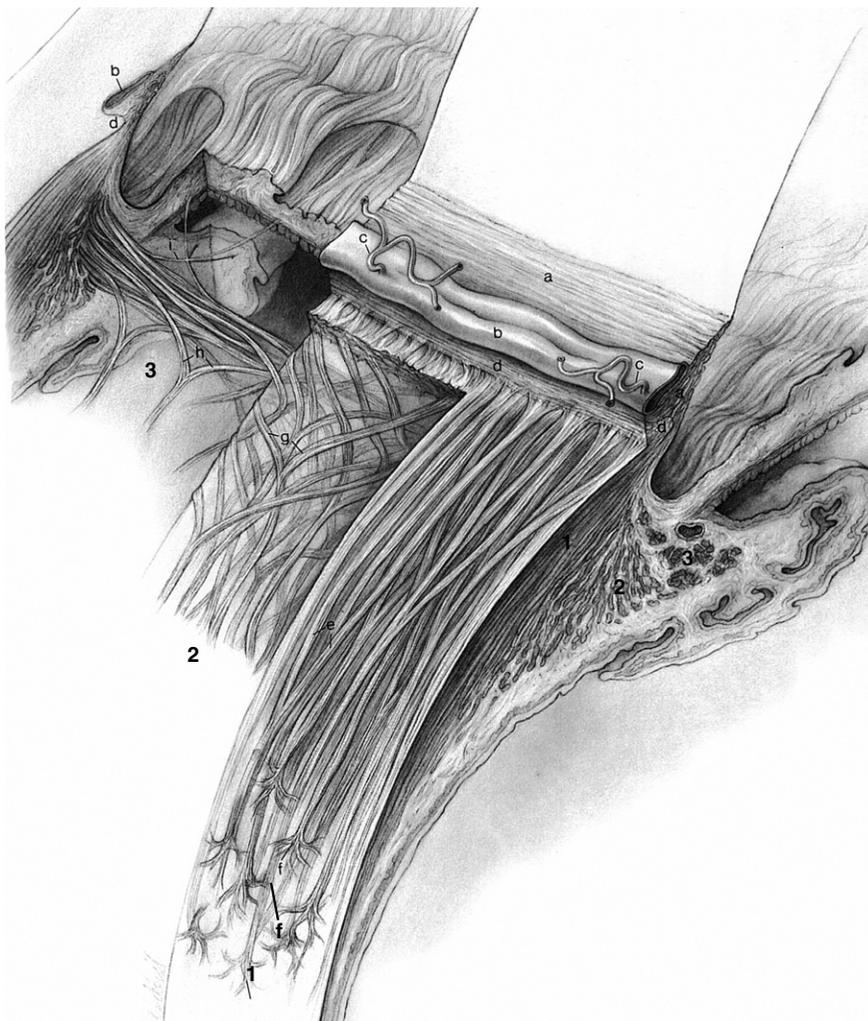
**FIGURE 3-12**

Light micrograph of transverse section of the ciliary body, showing detachment from sclera in region of supraciliaris. Ciliary muscle occupies most of ciliary body, stroma is located in center of each process, zonular remnants are evident in posterior chamber between ciliary body and lens equator.

The ciliary muscle is dually innervated by the autonomic nervous system. Parasympathetic stimulation activates the muscle for contraction, whereas sympathetic innervation likely has an inhibitory effect that is a function of the level of parasympathetic activity.⁸⁻¹⁰

CILIARY STROMA

The highly vascularized, loose connective tissue **stroma** of the ciliary body lies between the muscle and the epithelial layers and forms the core of each of the ciliary processes; it is continuous with the connective tissue that separates the bundles of ciliary muscle. Anteriorly, the stroma is continuous with iris stroma. It thins in the pars plana, where it continues posteriorly as choroidal stroma. The major arterial circle of the iris is located in the ciliary stroma anterior to the circular muscle and near the iris root. This circular artery is formed by the

**FIGURE 3-13**

Ciliary body, including the ciliary muscle and its components. Cornea and sclera have been dissected away, but trabecular meshwork (a), Schlemm's canal (b), and two external collectors (c), as well as scleral spur (d), have been left undisturbed. Three components of ciliary muscle are shown separately, viewed from the outside and sectioned meridionally. Section 1 shows longitudinal ciliary muscle. In section 2, longitudinal ciliary muscle has been dissected away to show radial ciliary muscle. In section 3, only the innermost circular ciliary muscle is shown. Ciliary muscle originates in ciliary tendon, which includes scleral spur (d) and adjacent connective tissue. The cells originate as paired V-shaped bundles. Longitudinal muscle forms long, V-shaped trellises (e) that terminate in epichoroidal stars (f). Arms of V-shaped bundles formed by radial muscle meet at wide angles (g) and terminate in ciliary processes. V-shaped bundles of circular muscle originate at such distant points in ciliary tendon that their arms meet at a very wide angle (h). Iridic portion is shown at (i), joining circular muscle cells. (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

anastomosis of the long posterior ciliary arteries and the anterior ciliary arteries. The stromal capillaries are large and fenestrated, particularly in the ciliary processes, and most are located near the pigmented epithelium.¹

CILIARY EPITHELIUM

Two layers of epithelium, positioned *apex to apex*, cover the ciliary body and line the posterior chamber and part of the vitreous chamber. Both epithelial layers contain cellular components characteristic of cells actively involved in secretion.¹¹

The outer layer (i.e., the one next to the stroma) is pigmented and cuboidal, and the cells are joined by desmosomes and gap junctions.^{1,12-14} Anteriorly, the **pigmented ciliary epithelium** is continuous with the anterior iris epithelium (Figure 3-14). Posteriorly, it is continuous with the retinal pigment epithelium (RPE) (Figure 3-15). A basement membrane attaches the pigment epithelium to the stroma. This basement membrane is continuous anteriorly with the basement membrane of the anterior iris epithelium and posteriorly with the inner basement membrane portion of Bruch's membrane of the choroid.¹

The inner epithelial layer (i.e., the layer lining the posterior chamber) is nonpigmented and is composed of columnar cells in the pars plana and cuboidal cells in the pars plicata.¹ The lateral walls of the cells contain extensive interdigitations and are joined, near their apices, by desmosomes, gap junctions, and zonula occludens, which form one site of the blood-aqueous barrier.^{3,12-17} The **nonpigmented ciliary epithelium** is continuous anteriorly with the posterior iris epithelium (see Figure 3-14). It continues posteriorly at the ora serrata, where it undergoes significant transformation, becoming neural retina (see Figure 3-15). The metabolically active nonpigmented epithelial cells are involved in active secretion of aqueous humor components and serve as a diffusion barrier between blood and aqueous.¹⁸

The two epithelial layers are positioned apex to apex because of invagination of the neural ectoderm in forming the optic cup (see Chapter 7). Intercellular junctions, desmosomes, and tight junctions connect the two layers.¹ Gap junctions between the apical surfaces provide a means of cellular communication between the layers and probably are important in the formation of aqueous.^{12,13,15,19}

The basement membrane covering the nonpigmented epithelium, the internal limiting membrane of the ciliary body, lines the posterior chamber, is continuous with the internal limiting membrane of the retina, and is the attachment site for the zonular fibers as well as the fibers of the vitreous base. The basal aspect of the

nonpigmented cell has numerous infoldings into which the basement membrane extends.^{1,3}

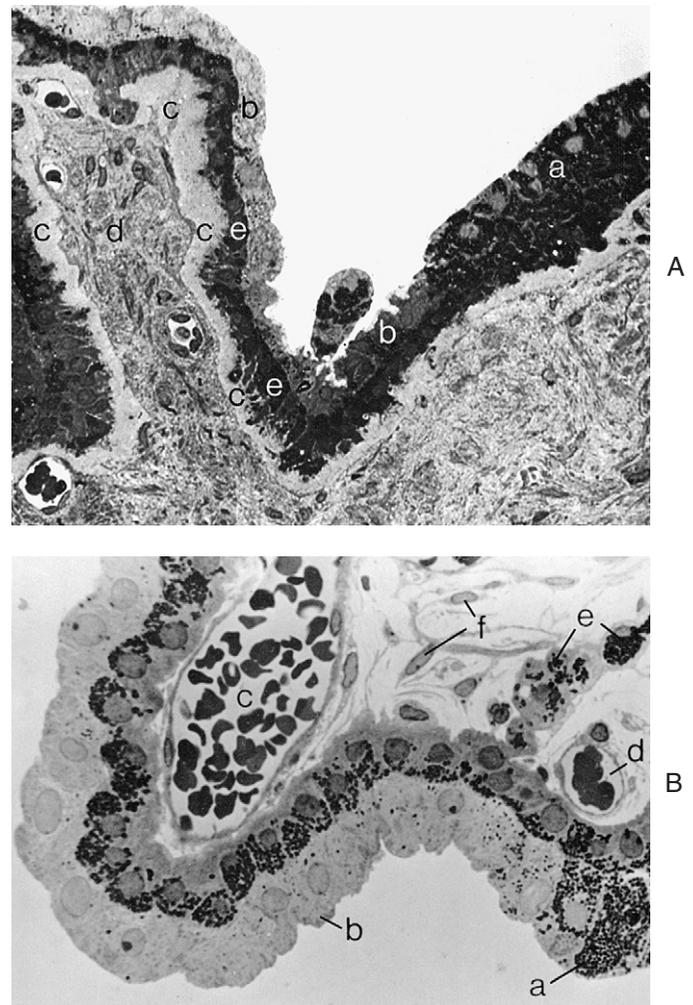


FIGURE 3-14

A, Light micrograph of the ciliary body of an elderly person showing transition of pigmented iris epithelium (a) into nonpigmented ciliary epithelium (b). Note basement membrane–like strip (c) interposed between dense collagenous connective tissue layers of this ciliary process (d) and pigmented epithelium (e). (×500.) **B**, Light micrograph of the ciliary body of a young person showing transition of nonpigmented ciliary body epithelium (b) into pigmented iris epithelium. Epithelium reveals increasing numbers of melanin granules until some of the cells become filled with pigment (a). Large vein (c) and a capillary (d) lie in stroma close to pigmented epithelium. Compare stroma of young eye with that in A. Some melanocytes (e) and fibroblasts (f) are seen. (×640.) (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

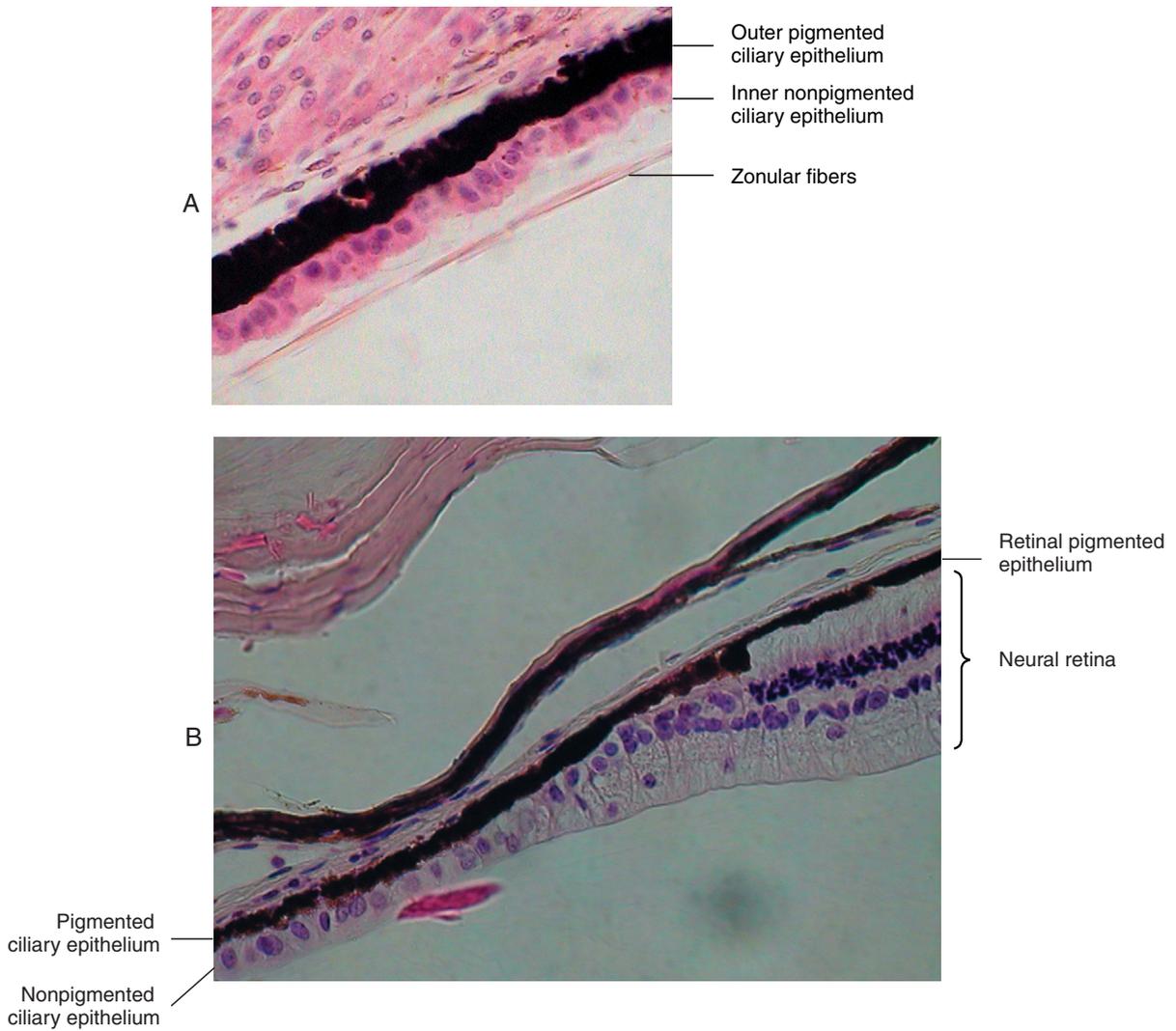


FIGURE 3-15

A, Light micrograph of ciliary epithelial layers in pars plana. **B**, Light micrograph of ora serrata region. Ciliary body at left, retina and choroid at right. Transition from pigmented ciliary epithelium to retinal pigment epithelium and transition from nonpigmented ciliary epithelium to neural retina.

CHOROID

The **choroid** extends from the ora serrata to the optic nerve and is located between the sclera and the retina, providing nutrients to outer retinal layers (Figure 3-16). It consists primarily of blood vessels. However, a thin connective tissue layer lies on each side of the stromal vessel layer.

SUPRACHOROID LAMINA (LAMINA FUSCA)

Thin, pigmented, ribbonlike branching bands of connective tissue—the **suprachoroid lamina**, or **lamina fusca**—traverse a potential space—the **suprachoroidal space**, or “perichoroidal” space—between the sclera and the choroidal vessels.^{1,3} This layer contains components from both sclera (collagen bands and fibroblasts) and choroidal stroma (melanocytes) (Figure 3-17).¹ If the choroid separates from the sclera, part of the suprachoroid will adhere to the sclera and part will remain attached to the choroid.² The looseness of the tissue allows the vascular net to swell without causing detachment. The anterior suprachoroidal lamina is the site of the “muscle–star” insertions of the longitudinal muscle fibers from the ciliary body. The suprachoroidal space carries the long posterior ciliary arteries and nerves from the posterior to the anterior portion of the globe.

CHOROIDAL STROMA

The **choroidal stroma** is a pigmented, vascularized, loose connective tissue layer containing melanocytes, fibroblasts, macrophages, lymphocytes, and mast cells. Collagen fibrils are arranged circularly around the vessels, which are branches of the short posterior ciliary arteries. These vessels are organized into tiers, those with larger lumina occupying the outer layer (**Haller’s layer**). They branch as they pass inward, forming the medium-sized vessels (**Sattler’s layer**), which continue branching to form a capillary bed (Figure 3-18). The venules join to become veins that gather in a characteristic vortex pattern in each quadrant of the eye and exit the choroid as four (occasionally five) large vortex veins. Choroidal veins are unusual in that they contain no valves.²

The choroidal vessels are innervated by the autonomic nervous system. Sympathetic stimulation causes vasoconstriction. The effect of the parasympathetic system is less clear.²⁰

CHORIOCAPILLARIS

The specialized capillary bed is called the **choriocapillaris** (lamina choriocapillaris). It forms a single layer of anastomosing, fenestrated capillaries having wide lumina (see Figure 3-18). In each, the lumen is approximately three to four times that of ordinary

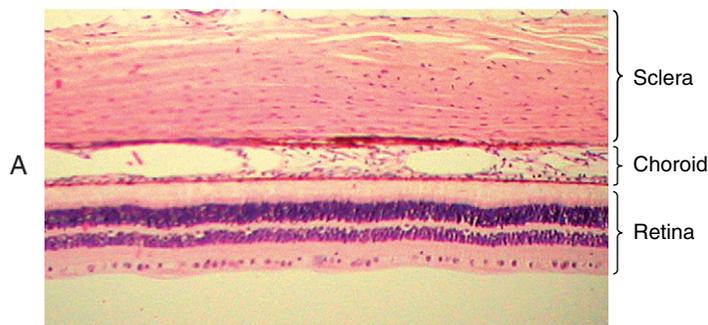
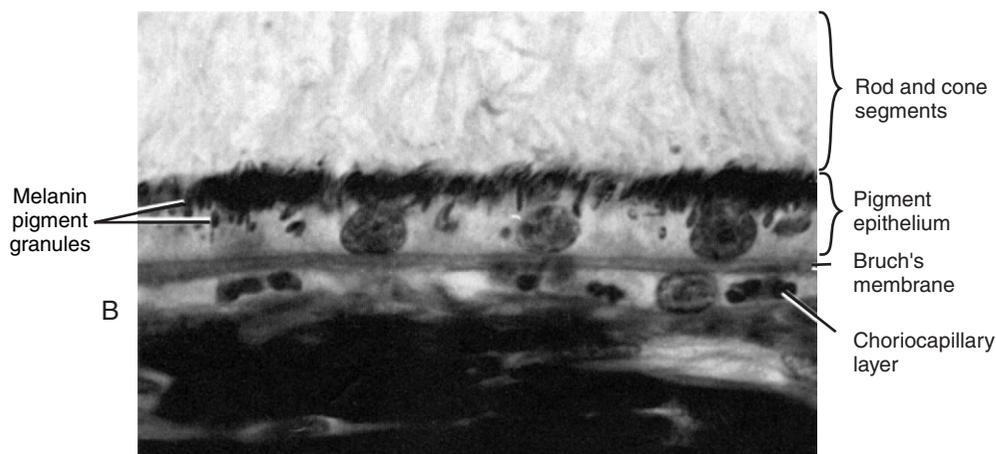


FIGURE 3-16

A, Photomicrograph of section through full thickness of the eye showing retina, choroid, and sclera. **B**, Pigment epithelium. ($\times 1000$). (**B** from Krause WJ, Cutts JH: *Concise text of histology*, Baltimore, 1981, Williams & Wilkins.)



capillaries, such that two or three red blood cells can pass through the capillary abreast, whereas in ordinary capillaries the cells usually course single file¹. The cell membrane is reduced to a single layer at the fenestrations, facilitating the movement of material through the vessel walls.²¹ Occasional **pericytes** (Rouget cells), which may have a contractile function, are found around the capillary wall.^{1,3} Pericytes have the ability to alter local blood flow.²² The choriocapillaris is densest in the macular area, where it is the sole blood supply for a small region of retina. The choriocapillaris is unique to the choroid and does not continue into the ciliary body.

BRUCH'S MEMBRANE (BASAL LAMINA)

The innermost layer of the choroid, **Bruch's membrane**, fuses with the retina. It runs from the optic nerve to the ora serrata, where it undergoes some modification before continuing into the ciliary body.¹ Bruch's membrane (or the basal lamina) is a multilaminated sheet containing a center layer of elastic fibers.²³ As seen through an electron microscope, the membrane components, from outer to inner, are the (1) interrupted basement membrane of the choriocapillaris, (2) outer collagenous zone, (3) elastic layer, (4) inner collagenous zone, and (5) basement membrane of the RPE cells^{1,2} (Figure 3-19). Fine filaments from the basement membrane of the RPE merge with the fibrils of the inner collagenous zone, contributing to the tight adhesion between choroid and the outer, pigmented layer of the retina.

At the ora serrata the basement membrane of the RPE is continuous with the basement membrane of the pigmented epithelium of the ciliary body. The collag-

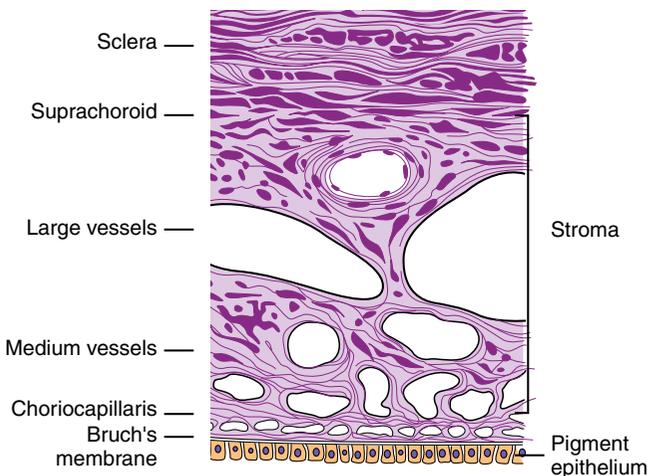


FIGURE 3-17
Histology of choroidal layers.

enous and elastic layers disappear into the ciliary stroma, and the basement membrane of the choriocapillaris continues as the basement membrane of the ciliary body capillaries.

FUNCTIONS OF UVEA

FUNCTIONS OF IRIS

The iris acts as a diaphragm to regulate the amount of light entering the eye. The two iris muscles are innervated separately: The parasympathetically innervated sphincter muscle is responsible for constriction of the pupil, and the sympathetically innervated dilator muscle causes pupillary enlargement.

FUNCTIONS OF CILIARY BODY

The ciliary body produces and secretes the aqueous humor. Its musculature causes accommodation and can affect aqueous outflow.

CLINICAL COMMENT: ACCOMMODATION

*The ability of the eye to change power and bring near objects into focus on the retina is called **accommodation**. It is accomplished by increasing the power of the lens. Contraction of the longitudinal fibers of the ciliary muscle pulls the choroid forward, and contraction of the circular fibers draws the ciliary body closer to the lens, decreasing the diameter of the ring formed by the ciliary body. This releases tension on the zonule fibers and allows the lens capsule to adopt a more spheric shape. The lens thickens, and the anterior surface curve increases. These changes result in an increase in refractive power, or accommodation. When the ciliary muscle is relaxed, the eye is said to be "at rest" and is used for distance vision. During accommodation, the iris sphincter also contracts, restricting incoming light rays and decreasing spheric aberration.*

Ciliary muscle contraction can change the configuration of the trabecular meshwork because some of the longitudinal fibers are attached to trabecular meshwork sheets. This altered configuration can facilitate aqueous movement through the anterior chamber angle structures.²⁴ Accommodation has been found to cause a decrease in IOP²⁵ (accommodation is discussed further in Chapter 5).

CLINICAL COMMENT: PRESBYOPIA

***Presbyopia** is the loss of the ability to accommodate, a normal age-related change and the subject of continuing research. In rhesus monkeys the tendon that attaches the ciliary muscle to the scleral spur shows extensive age-related structural changes: It thickens with age and becomes surrounded by a dense layer of collagen, thus losing its elasticity. This loss of elasticity restricts muscle movement and hampers accommodation.²⁶ A similar mechanism may be a component of human presbyopia, along with changes involving the lens itself (see Chapter 5).*

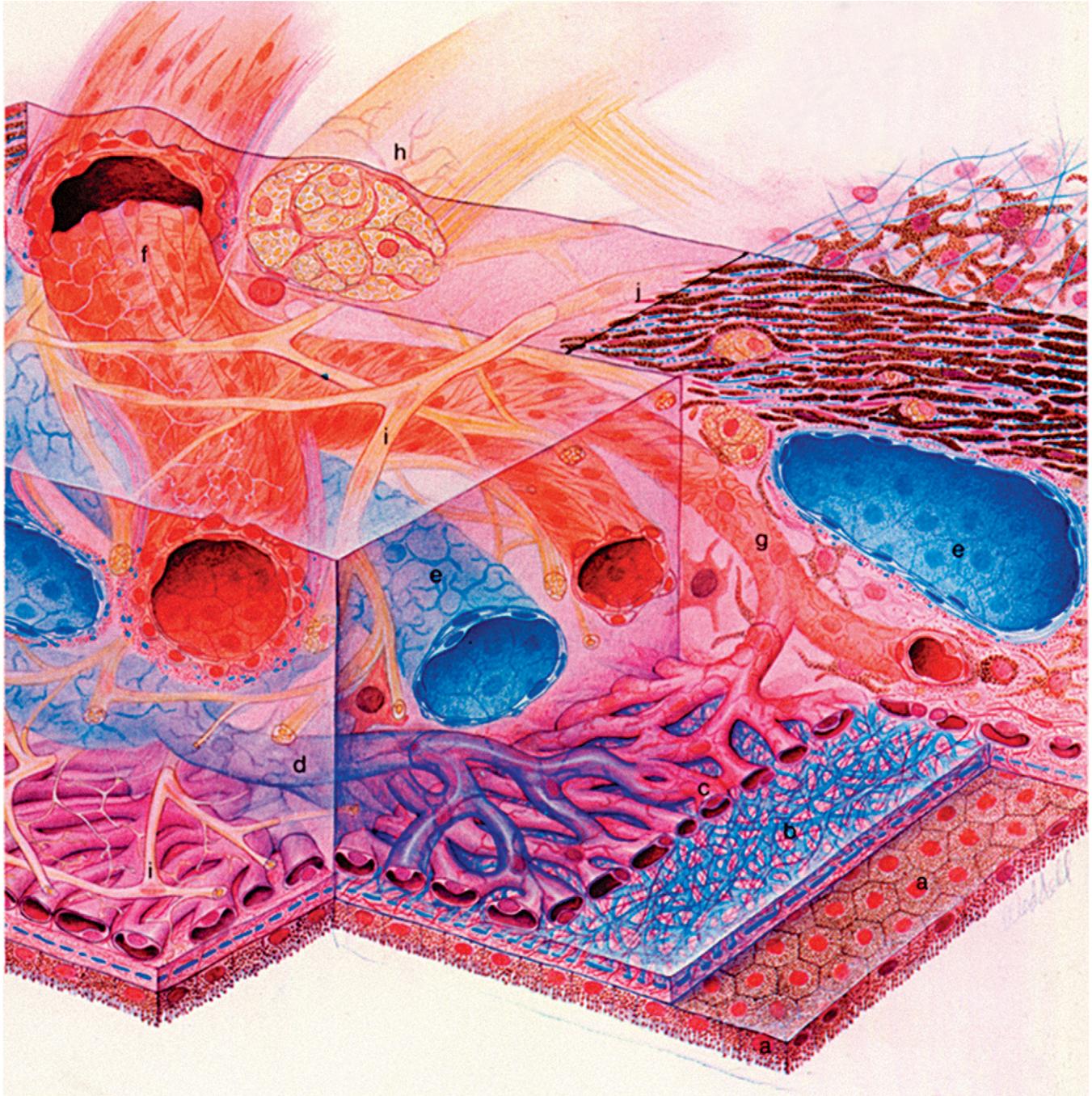


FIGURE 3-18

Drawing of choroidal blood supply and innervation and Bruch's membrane. Pigment epithelium of retina (a) is in close contact with Bruch's membrane (b). Elastica of Bruch's membrane is blue, and meshes contain collagen fibrils. Choriocapillaris (c) forms an intricate network along inner choroid. Venules (d) leave choriocapillaris to join vortex system (e). Short ciliary artery is shown at f, before its branching (g) to form choriocapillaris. Short ciliary nerve enters choroid at h and sends ramifying branches into choroidal stroma (i). Suprachoroidea (suprachoroid lamina), with its star-shaped melanocytes, is at j. (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)



FIGURE 3-19

Layers of Bruch's membrane, delineated on basis of electron microscope studies: 1, Interrupted basement membrane of choriocapillaris; 2, outer collagenous zone; 3, elastic layer; 4, inner collagenous zone; 5, basement membrane of retinal pigment epithelial cells. (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

Aqueous Production

Both the ciliary body capillaries and the epithelial layers are active in the production and secretion of aqueous. The large capillaries of the ciliary body have numerous fenestrations, which facilitate the movement of substances into and out of the blood. Active transport and secretion move substances from the stroma through the epithelium. The nonpigmented epithelium, in particular, actively secretes components of the aqueous humor into the posterior chamber.^{1,2}

Vitreous Production

Investigators recently have suggested that the epithelium of the pars plana region has a significant role in the production and secretion of several connective tissue macromolecules located in the vitreous body.²⁷

Blood-Aqueous Barrier

The blood-aqueous barrier selectively controls the substance that is secreted as the aqueous humor. The fenestrated ciliary body capillaries permit large molecules

to exit the blood. However, the tight zonular junctions of the nonpigmented epithelium prevent the molecules from passing between the cells, forcing them instead to pass through the cell to enter the posterior chamber. One of the substances thus controlled is *protein*. The protein content of aqueous humor is very small compared with that of blood.²⁸ Proteins pass easily out of the ciliary vessels through the fenestrations but do not pass into the posterior chamber because of the tight junction barrier of the nonpigmented epithelium.^{13,29-31}

The iris is freely permeated by the aqueous humor, which readily enters the stroma through the surface crypts.¹ To prevent large molecules from leaking out of the iris blood vessels and altering the content of the aqueous fluid, the iris capillaries have no fenestrations, and their endothelial cells maintain the barrier function through the zonula occludens junctions.^{17,31-33}

FUNCTIONS OF CHOROID

The vascular choroid provides nutrients to the outer retina and is an egress for catabolites from the retina, which diffuse through Bruch's membrane into the choriocapillaris. The darkly pigmented choroid absorbs excess light that passes through the RPE layer. The suprachoroidal space provides a pathway for the posterior vessels and nerves that supply the anterior segment.

With aging, excessive basement membrane (basal lamina) material is deposited in the collagenous zones of Bruch's membrane.³⁴⁻³⁶ These deposits in the inner collagenous zone, called **drusen**, can be seen as small, pinhead-sized, yellow-white spots in the fundus. The drusen, which contain cellular fragments and an accumulation of basal laminar material, are located below the RPE basement membrane and displace the retina inward.³⁷

CLINICAL COMMENT: AGE-RELATED MACULAR DEGENERATION

*Degenerative processes involving the choroid-retina interface in the macular area often are manifested as **age-related macular degeneration (AMD)**. AMD is the most common cause of blindness in Western countries.³⁸ This disease is multifaceted in origin and can involve the presence of multiple or confluent drusen, a thick layer of basal laminar deposit, detachment or atrophy of the RPE, subsequent formation of disciform scars, loss of photoreceptors, and neovascularization.^{37,39}*

Metabolites from the choriocapillaris and waste products from the retina must pass through Bruch's membrane. With age, phospholipids accumulate in this membrane, probably because of defective mechanisms in the dephosphorylation process.^{35,40-43} Free radicals resulting from oxidative stress have been implicated in these cellular metabolic changes.⁴⁴

Continued

The accumulation of lipids in Bruch's membrane with increasing age appears to be greater in the central fundus than in the periphery.⁴⁵ Bruch's membrane becomes hydrophobic and presents a barrier to water movement, thereby inhibiting the passage of metabolites.⁴⁶ If water accumulates between the RPE and Bruch's membrane, displacement and detachment may occur.⁴² This process is represented diagrammatically in Figure 3-20.

Loss of nutrients to the highly metabolic retina can cause (1) atrophy of the RPE, followed by loss of photoreceptors,^{43,47} or (2) development of a neovascular membrane in an attempt to compensate for the loss of nutrients.⁴⁴ The new vessels branch from the choriocapillaris and can remain beneath the RPE or can penetrate Bruch's membrane and enter the retina.⁴⁴ However, these vessels are fragile, leak, and tend to hemorrhage into retinal tissue.^{44,48} Visual loss in AMD results from detachment of the RPE resulting from water accumulation, atrophy of the RPE and photoreceptors, or the presence of a subretinal neovascular membrane.^{35,40}

Risk factors associated with AMD include genetics; age; lighter pigmentation of skin, hair, or iris; skin sun sensitivity; smoking; sun exposure; and cataract surgery.^{44,46,49-53} Although these risk factors have been elucidated, their role in AMD is still not seen as causative. The complex interplay among these factors, however, implicates many if not all of them in AMD.

No definitive treatment for AMD exists as yet, but supplementation with antioxidants or minerals (e.g., high doses of vitamins C and E, beta carotene, zinc, lutein, and zeaxanthin) may provide some protective effect or slow the progression to advanced disease in patients with mild AMD.^{54,55} However, others question the effectiveness of such supplements in AMD.⁵⁶⁻⁶⁰

BLOOD SUPPLY TO UVEAL TRACT

The short posterior ciliary arteries enter the globe in a circle around the optic nerve, and their branches form the choroidal vessels. The long posterior ciliary arteries and the anterior ciliary arteries join to form the major circle of the iris, which supplies vessels to the iris and ciliary body. The venous return for most of the uvea is through the vortex veins (see Chapter 11 for further information on the blood supply).

UVEAL INNERVATION

Sensory innervation of the uvea is provided through the nasociliary branch from the trigeminal nerve. Sympathetic fibers from the superior cervical ganglion via the ophthalmic and short ciliary nerves innervate the choroidal blood vessels, and sympathetic fibers from the superior cervical ganglion via the long ciliary nerves innervate the iris dilator and ciliary muscles. Parasympathetic fibers from the ciliary ganglion innervate the ciliary muscle, the iris sphincter muscle, and the choroidal vessels.

AGING CHANGES IN UVEA IRIS

With age, loss of pigment from the epithelium is evident at the pupillary margin and on transillumination.

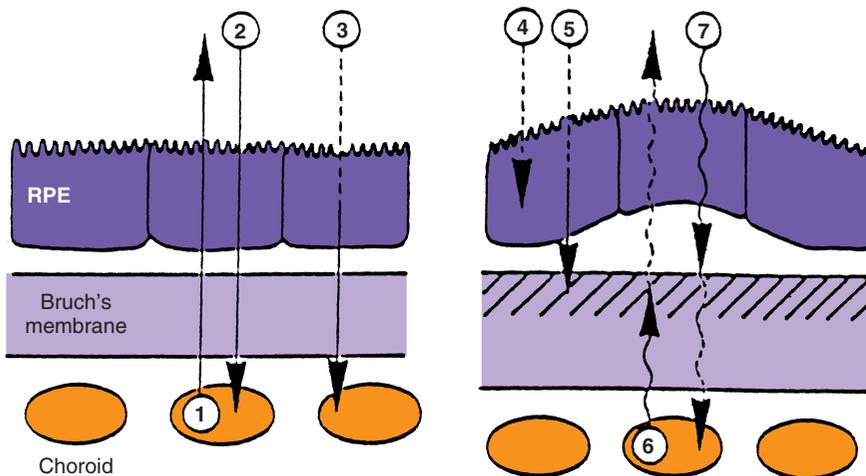


FIGURE 3-20

Summary of implications of lipid accumulation in Bruch's membrane for transport systems operating across retinal pigment epithelium (RPE). In youngest age group: 1, metabolites pass from choroid through Bruch's membrane across RPE to neural retina; 2, water moves predominantly from neural retina to choroid; and 3, progress of catabolism results in accumulation of waste products that are predominantly cleared via the choroid. In older age group: 4, with increasing age, catabolism results in accumulations (lipofuscin) within RPE; 5, waste products rich in lipid begin to accumulate within Bruch's membrane; 6, accumulation of lipid-rich debris within Bruch's membrane may inhibit metabolic input to neural retina; and 7, presence of a hydrophobic barrier within Bruch's membrane impedes passage of water and may result in detachment of RPE. (From Pauleikhoff D, Harper CA, Marshall J et al: *Ophthalmology* 97(2):171, 1990.)

Pigment deposition may be seen on the iris surface, anterior lens surface, posterior cornea, and trabecular meshwork. The dilator muscle becomes atrophic, and the sphincter muscle becomes sclerotic, making it more difficult to dilate the older pupil pharmacologically.⁶¹

CILIARY BODY

Although the amount of connective tissue within the layer of ciliary muscle increases with age,⁶² there is no significant correlation between loss of ciliary muscle contractile ability and age.^{62,63}

CHOROID

The changes that occur in AMD occur throughout the choroid with advancing age. However, only those occurring in the macula significantly affect visual acuity and the patient's daily life. Bruch's membrane increases in thickness with age. Lipid particles accumulate, decreasing the membrane's permeability to serum proteins, and its capacity to facilitate metabolite exchange with the retina decreases.⁶⁴⁻⁶⁶ Calcification and deposits in the inner collagenous layer are responsible for the clinical appearance of drusen, which increase in number with age.⁴⁶ As lysozymal activity in the RPE decreases with age, abnormal material (including lipofuscin) may accumulate in Bruch's membrane.⁴⁴

The choriocapillaris decreases in density and diameter, resulting in a decrease in choroidal blood flow, and choroidal thickness decreases in the normal-aging macula.^{44,67}

REFERENCES

- Hogan MJ, Alvarado JA, Weddell JE, editors: *Histology of the human eye*, Philadelphia, 1971, Saunders, p 202.
- Warwick R: *Wolff's anatomy of the eye and orbit*, ed 7, Philadelphia, 1976, Saunders, p 61.
- Fine BS, Yanoff M: *Ocular histology*, Hagerstown, Md, 1979, Harper & Row, p 195.
- Loewenfeld IE: *The pupil: anatomy, physiology, and clinical applications*, Boston, 1999, Butterworth-Heinemann.
- Bartlett JD, Jaanus SD: *Clinical ocular pharmacology*, ed 3, Boston, 1995, Butterworth-Heinemann, pp 776, 915.
- Imesch PD, Bindley CD, Khademian Z et al: Melanocytes and iris color, *Arch Ophthalmol* 114:443, 1996.
- Catania LJ: *Primary care of the anterior segment*, East Norwalk, Conn, 1988, Appleton & Lange, p 211.
- Gilmartin B: A review of the role of sympathetic innervation of the ciliary muscle in ocular accommodation, *Ophthalmic Physiol Opt* 6(1):23, 1986.
- Rosenfield M, Gilmartin B: Oculomotor consequences of beta-adrenoreceptor antagonism during sustained near vision, *Ophthalmic Physiol Opt* 7(2):127, 1987.
- Gilmartin B, Bullimore MA, Rosenfield M et al: Pharmacological effects on accommodative adaptation, *Optom Vis Sci* 69(4):276, 1992.
- Eichhorn M, Inada K, Lutjen-Drecoll E: Human ciliary body in organ culture, *Curr Eye Res* 19(4):277, 1991.
- Raviola G, Raviola E: Intercellular junctions in the ciliary epithelium, *Invest Ophthalmol Vis Sci* 17:958, 1978.
- Caprioli J: The ciliary epithelia and aqueous humor. In Hart WM Jr, editor: *Adler's physiology of the eye*, ed 9, St Louis, 1992, Mosby, p 228.
- Raviola G: The fine structure of the ciliary zonule and ciliary epithelium, *Invest Ophthalmol* 10(11):851, 1971.
- Raviola G: The structural basis of the blood-ocular barriers, *Exp Eye Res* 25(suppl):27, 1977.
- Noske W, Stamm CC, Hirsch M: Tight junctions of the human ciliary epithelium: regional morphology and implications on transepithelial resistance, *Exp Eye Res* 59:141, 1994.
- Sonsino J, Gong H, Wu P et al: Co-localization of junction-associated proteins of the human blood-aqueous barrier: occludin, ZO-1 and F-actin, *Exp Eye Res* 71:123, 2002 (abstract).
- Shiose Y: Electron microscopic studies on blood-retinal and blood-aqueous barriers, *Jpn J Ophthalmol* 14:73, 1970 (abstract).
- Takats K, Kasahara T, Kasahara M et al: Ultracytochemical localization of the erythrocyte/HepG2-type glucose transporter (GLUT1) in the ciliary body and iris of the rat eye, *Invest Ophthalmol Vis Sci* 32(5):1659, 1991.
- Ruskell G: Facial parasympathetic innervation of the choroidal blood vessels in monkeys, *Exp Eye Res* 12:166, 1971.
- Bernstein MH, Hollenberg MJ: Fine structure of the choriocapillaris and retinal capillaries, *Invest Ophthalmol* 4(6):1016, 1965.
- Chakravarthy U, Gardiner TA: Endothelium-derived agents in pericyte function/dysfunction, *Prog Ret Eye Res* 18(4):511, 1999.
- Alexander RA, Garner A: Elastic and precursor fibres in the normal human eye, *Exp Eye Res* 36:305, 1983.
- Ebersberger A, Flugel C, Lutjen-Drecoll E: Ultrastructural and enzyme histochemical studies of regional structural differences within the ciliary muscle in various species, *Klin Monatsbl Augenheilkd* 203(1):53, 1993 (abstract).
- Mauger RR, Likens CP, Applebaum M: Effects of accommodation and repeated applanation tonometry on intraocular pressure, *Am J Optom Physiol Opt* 61(1):28, 1984.
- Tamm E, Lutjen-Drecoll E, Rohen JW et al: Posterior attachment of ciliary muscle in young, accommodating, old, presbyopic monkeys, *Invest Ophthalmol Vis Sci* 32:1678, 1991.
- Bishop PN, Takanosu M, le Goff M et al: The role of the posterior ciliary body in the biosynthesis of vitreous humour, *Eye* 16:454, 2002.
- Krause U, Raunio V: Proteins of the normal human aqueous humour, *Ophthalmologica* 160:280, 1970.
- Smith RS: Ultrastructural studies of the blood-aqueous barrier. I. Transport of an electron dense tracer in the iris and ciliary body of the mouse, *Am J Ophthalmol* 71:1066, 1971.
- Varma SD, Reddy VN: Phospholipid composition of aqueous humor plasma and lens in normal and alloxan diabetic rabbits, *Exp Eye Res* 13:120, 1972.
- Cunha-Va JG: The blood-ocular barriers: past, present, and future, *Doc Ophthalmol* 93:149, 1997.
- Waizman MB, Jackson RT: Effects of topically administered ouabain on aqueous humor dynamics, *Exp Eye Res* 4:135, 1965.
- Schlingemann RO, Hofman P, Klooster J et al: Ciliary muscle capillaries have blood-tissue barrier characteristics, *Exp Eye Res* 66:747, 1998.
- Sarks SH: Aging and degeneration in the macular region: a clinico-pathological study, *Br J Ophthalmol* 60:324, 1976.
- Van der Schaft TL, Mooy CM, deBruijn WC et al: Histological features of the early stages of age-related macular degeneration: a statistical analysis, *Ophthalmology* 99:278, 1992.

36. Van der Schaft TL, Mooy CM, deBruijn WC et al: Immunohistochemical light and electron microscopy of basal laminar deposit, *Graefes Arch Clin Exp Ophthalmol* 232(1):40, 1994.
37. Ramrattan RS, van der Schaft TL, Mooy CM et al: Morphometric analysis of Bruch's membrane, the choriocapillaris, and the choroid in aging, *Invest Ophthalmol Vis Sci* 35(6):2857, 1994.
38. Leibowitz HM, Krueger DE, Maunder LR et al: The Framingham Eye Study monograph: an ophthalmological and epidemiological study of cataract, glaucoma, diabetic retinopathy, macular degeneration, and visual acuity in a general population of 2631 adults, *Surv Ophthalmol* 24:335, 1980.
39. Bressler NM, Bressler B, Fine SL: Age-related macular degeneration, *Surv Ophthalmol* 32:375, 1988.
40. Sheraidah G, Steinmetz R, Maguire J et al: Correlation between lipids extracted from Bruch's membrane and age, *Ophthalmology* 100(1):47, 1993.
41. Pauleikhoff D: Drusen in Bruch's membrane: their significance for the pathogenesis and therapy of age-associated macular degeneration, *Ophthalmologe* 89(5):363, 1992 (abstract).
42. Pauleikhoff D, Harper CA, Marshall J et al: Aging changes in Bruch's membrane: a histochemical and morphological study, *Ophthalmology* 97(2):171, 1990.
43. Zarbin MA: Age-related macular degeneration: a review of pathogenesis, *Eur J Ophthalmol* 8(4):199, 1998.
44. Ambati J, Ambati BK, Yoo SH et al: Age-related macular degeneration: etiology, pathogenesis, and therapeutic strategies, *Surv Ophthalmol* 48(3):257, 2003.
45. Holz FG, Sheraidah G, Pauleikhoff D et al: Analysis of lipid deposits extracted from human macular and peripheral Bruch's membrane, *Arch Ophthalmol* 112(3):402, 1994.
46. Guymer R, Luthert P, Bird A: Changes in Bruch's membrane and related structures with age, *Prog Ret Eye Res* 18(1):59, 1998.
47. Curcio CA, Millican CL, Bailey T et al: Accumulation of cholesterol with age in human Bruch's membrane, *Invest Ophthalmol Vis Sci* 42:265, 2001.
48. Bailey RN: The surgical removal of a subfoveal choroidal neovascular membrane: an alternative treatment to laser photocoagulation, *J Am Optom Assoc* 64(2):104, 1993.
49. Cruickshanks KJ, Klein R, Klein BE et al: Sunlight and the 5-year incidence of early age-related maculopathy: the Beaver Dam Eye Study, *Arch Ophthalmol* 119(2):246, 2001.
50. McCarty CA, Mukesh BN, Fu CL et al: Risk factors for age-related maculopathy: the Visual Impairment Project, *Arch Ophthalmol* 119(10):1455, 2001.
51. Klein R, Klein BE, Jensen SC et al: The relationship of ocular factors to the incidence and progression of age-related maculopathy: the Beaver Dam Eye Study, *Arch Ophthalmol* 116(4):506, 1998.
52. Mitchell P, Smith W, Wang JJ: Iris color, skin sun sensitivity, and age-related maculopathy: the Blue Mountains Eye Study, *Ophthalmology* 105(8):1359, 1998.
53. Young RW: The family of sunlight-related eye diseases, *Optom Vis Sci* 71(2):125, 1994.
54. Age-related Eye Disease Study Research Group: A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss, *Arch Ophthalmol* 119(10):1417, 2001.
55. Gale CR, Hall NE, Phillips DI et al: Lutein and zeaxanthin status and risk of age-related macular degeneration, *Invest Ophthalmol Vis Sci* 44:2461, 2003.
56. Smith W, Mitchell P, Webb K et al: Dietary antioxidants and age-related maculopathy: the Blue Mountains Eye Study, *Ophthalmology* 106(4):761, 1999.
57. Flood V, Smith W, Wang JJ: Dietary antioxidant intake and incidence of early age-related maculopathy: the Blue Mountains Eye Study, *Ophthalmology* 109(12):227, 2002.
58. Kuzniarz M, Mitchell P, Flood VM et al: Use of vitamin and zinc supplements and age-related maculopathy: the Blue Mountains Eye Study, *Ophthalmic Epidemiol* 9(4):283, 2002.
59. Bone RA, Landrum JT, Guerra LH et al: Lutein and zeaxanthin dietary supplements raise macular pigment density and serum concentrations of these carotenoids in humans, *J Nutr* 133(4):922, 2003.
60. Klein R, Klein BE, Tomany SC et al: Ten-year incidence and progression of age-related maculopathy, *Ophthalmology* 109:1767, 2002.
61. Oates DC, Belcher CD: Aging changes in trabecular meshwork, iris, and ciliary body. In Albert DM, Jakobiec FA, editors: *Principles and practice of ophthalmology*, Philadelphia, 1994, Saunders, p 697.
62. Purdue MT, Sivak JG: Age-related changes in human ciliary muscle, *Optom Vis Sci* 77(4):204, 2000.
63. Strenk SA, Semmlow JL, Strenk LM et al: Age-related changes in human ciliary muscle and lens: a magnetic resonance imaging study, *Invest Ophthalmol Vis Sci* 40(6):1162, 1999.
64. Moore DJ, Clover GM: The effect of age on the macromolecular permeability of human Bruch's membrane, *Invest Ophthalmol Vis Sci* 42:2970, 2001.
65. Moore DJ, Hussain AA, Marshall J: Age-related variation in the hydraulic conductivity of Bruch's membrane, *Invest Ophthalmol Vis Sci* 36(7):1290, 1995.
66. Ruberti JW, Curcio CA, Millican CL et al: Quick-freeze/deep-etch visualization of age-related lipid accumulation in Bruch's membrane, *Invest Ophthalmol Vis Sci* 44:1753, 2003.
67. Ramrattan RS, van der Schaft TL, Mooy CM et al: Morphometric analysis of Bruch's membrane, the choriocapillaris, and the choroid in aging, *Invest Ophthalmol Vis Sci* 35(6):2857, 1994.



The innermost coat of the eye is a neural layer, the retina, located between the choroid and the vitreous. It includes the macula, the area at the posterior pole used for sharpest acuity and color vision. The **retina** extends from the circular edge of the optic disc, where the nerve fibers exit the eye, to the ora serrata. It is continuous with the epithelial layers of the ciliary body, with which it shares embryologic origin. The retina is derived from neural ectoderm and consists of an outer pigmented layer, derived from the outer layer of the optic cup, and the neural retina, derived from the inner layer of the optic cup (see Chapter 7). The pigmented layer is tightly adherent to the choroid throughout, but the neural retina is attached to the pigmented epithelium and thus to the choroid only in a peripapillary ring around the disc and at the ora serrata. Although it contains millions of cell bodies and their processes, the neural retina has the appearance of a thin, transparent membrane.

The retina is the site of transformation of light energy into a neural signal. It contains the first three cells (photoreceptor, bipolar, and ganglion) in the visual pathway, the route by which visual information from the environment reaches the brain for interpretation. Photoreceptor cells transform photons of light into a neural signal through the process of phototransduction, then transfer this signal to bipolar cells, which in turn synapse with ganglion cells, which transmit the signal from the eye. Other retinal cells—horizontal cells, amacrine cells, and interplexiform neurons—modify and integrate the signal before it leaves the eye. This chapter discusses these cells and the detailed anatomy of the retina; the remainder of the visual pathway is described in Chapter 13.

RETINAL HISTOLOGIC FEATURES

Under light microscopy the retina has a laminar appearance in which 10 layers are evident (Figure 4-1). Closer examination reveals that these are not all “layers,” but rather a single layer of pigmented epithelium and three layers of neuronal cell bodies, between which lie their processes and synapses. This section describes the epithelial layer and the types and functions of the neural cells; the next section

discusses the components of each of the 10 so-called retinal layers.

RETINAL PIGMENT EPITHELIUM

The **retinal pigment epithelium (RPE)**, the outermost retinal layer, is a single cell thick and consists of pigmented hexagonal cells. These cells are columnar in the area of the posterior pole and are even longer, narrower, and more densely pigmented in the macular area.¹ The cells become larger and more cuboidal as the layer nears the ora serrata, where the transition to the pigmented epithelium of the ciliary body is located. Because of the orientation of the embryologic cells, the basal aspect of the cells is adjacent to the choroid, and the apical surface faces the neural retina. The basal aspect contains numerous infoldings and is adherent to its basement membrane, which forms a part of Bruch’s membrane of the choroid; therefore its attachment to the choroid is strong. Despite its close association with the choroid, the RPE is considered a part of the retina because it is from the same embryologic germ cell layer—neural ectoderm.

The RPE cells contain numerous *melanosomes*, pigment granules that extend from the apical area into the middle portion of the cell and somewhat obscure the nucleus, which is located in the basal region. Pigment density differs in various parts of the retina and in individual cells, which can give the fundus a mottled appearance when viewed with the ophthalmoscope. In the retina, melanin is densest in the RPE cells located in the macula and at the equator.² Other pigmented bodies, *lipofuscin* granules, contain degradation products of phagocytosis and increase in number with age.^{1,3-7} The cell cytoplasm also contains smooth and rough endoplasmic reticulum, Golgi apparatus, mitochondria, and numerous lysosomes.

The apical portion of an RPE cell consists of microvilli that extend into the layer of photoreceptors, enveloping the specialized outer segment tips (Figure 4-2). However, no intercellular junctions connect the RPE and photoreceptor cells. A potential space separates the epithelial cell and the photoreceptor.¹ This subretinal space⁸ is a remnant of the gap formed between the two layers of the optic cup after invagination of the optic vesicle (see Chapter 7).

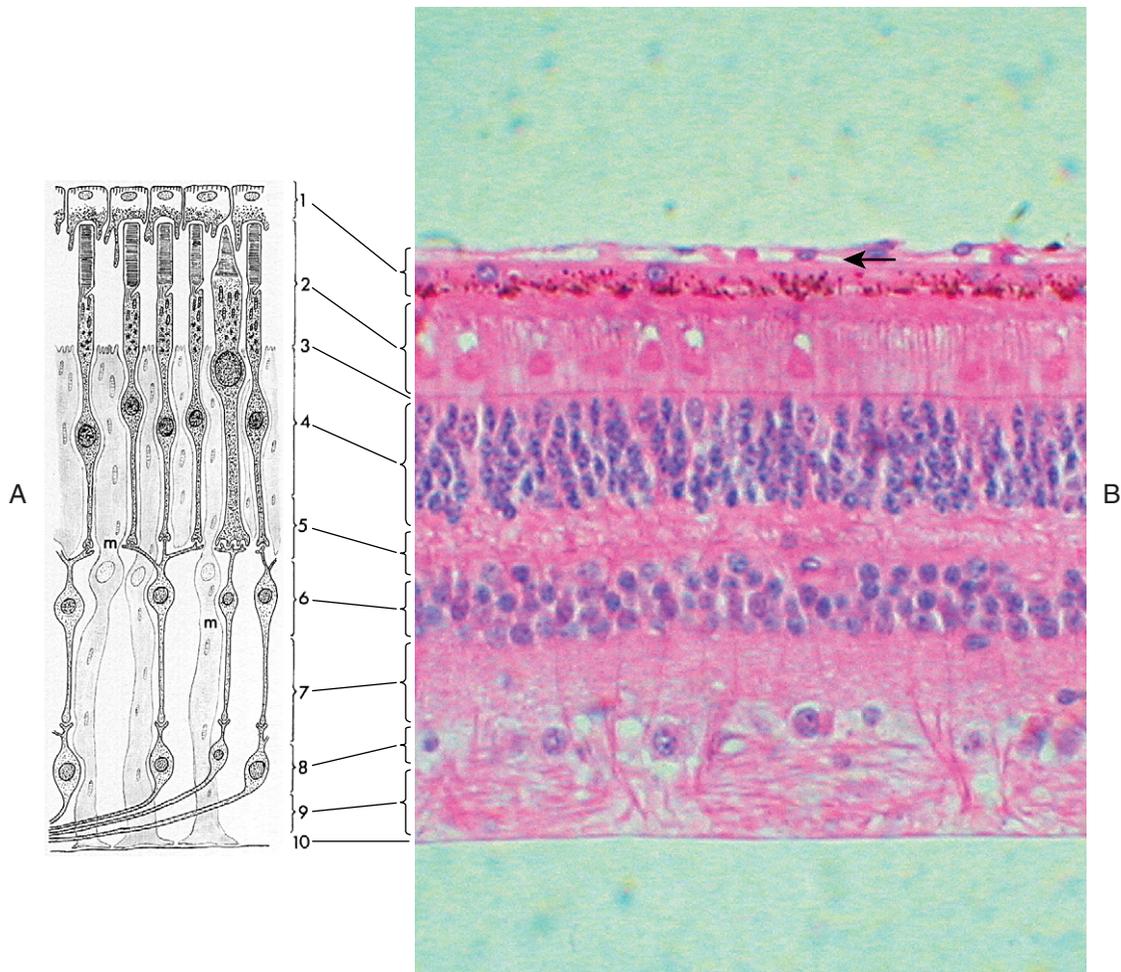


FIGURE 4-1

A, Layers of the retina. 1, Retinal pigment epithelial layer; 2, photoreceptor layer; 3, external limiting membrane; 4, outer nuclear layer; 5, outer plexiform layer; 6, inner nuclear layer; 7, inner plexiform layer; 8, ganglion cell layer; 9, nerve fiber layer; 10, internal limiting membrane. Only photoreceptors (rods and one cone), bipolar cells, ganglion cells, and fibers of Müller cells (*m*) are illustrated. Numbers refer to 10 retinal layers. (From Leeson CR, Leeson S: *Histology*, Philadelphia, 1976, Saunders.) **B**, Photomicrograph of same area. At top is inner portion of choroid with choriocapillaris (*arrow*).

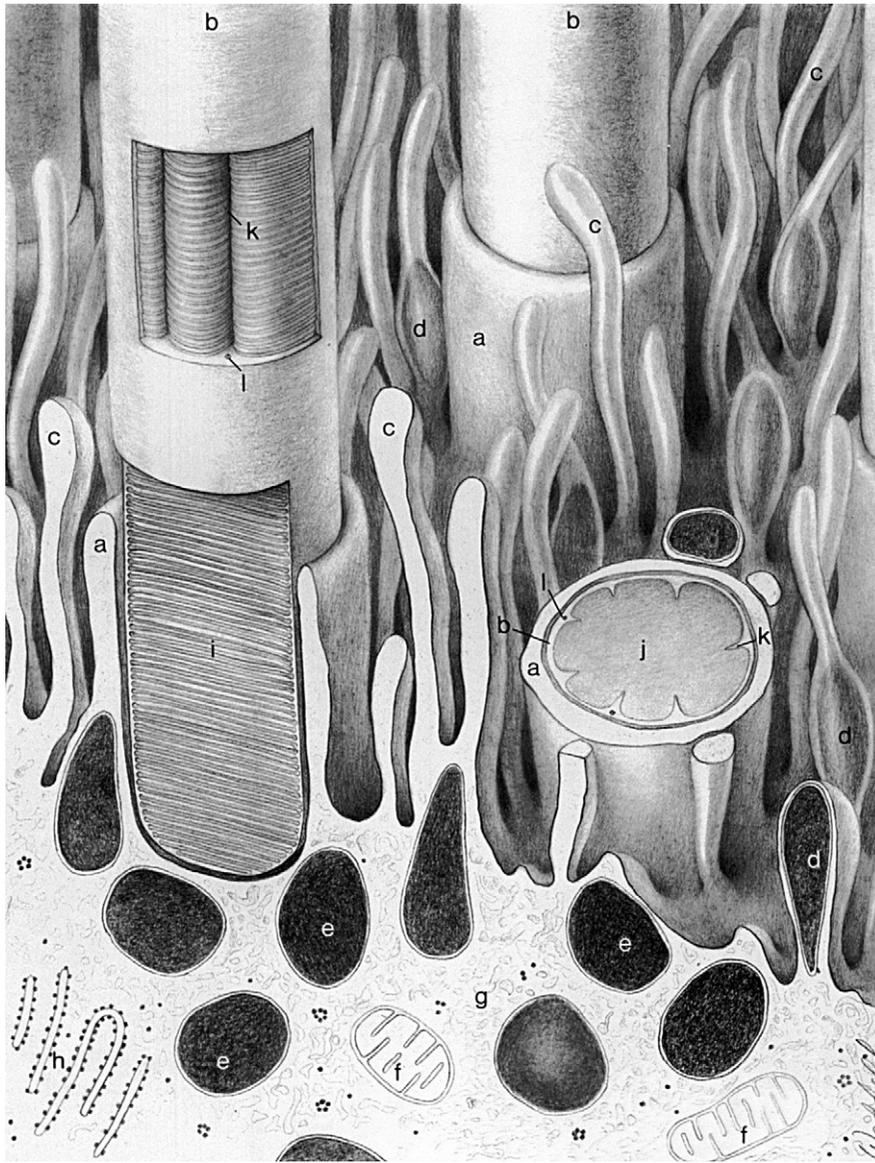


FIGURE 4-2

Three-dimensional drawing of relationship between outer segments of rods and cells of retinal pigment epithelium (RPE). Thick sheaths (*a*) of RPE enclose external portions of rod outer segments (*b*). Numerous fingerlike villous processes (*c*) are found between photoreceptors and contain pigment granules (*d*). Apical portion of RPE layer of cells at bottom contains numerous pigment granules (*e*); mitochondria (*f*); a well-developed, smooth-surfaced endoplasmic reticulum (*g*); a poorly developed, rough-surfaced endoplasmic reticulum (*h*); and scattered free ribosomes. Stacks of rod outer segment discs are depicted in meridional section (*i*) and in cross section (*j*). Periphery of discs shows scalloping (*k*). Microtubules originating in basal body of rod cilium extend externally into outer segment; one such microtubule is shown in cross section (*l*). (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

Terminal bars consisting of zonula occludens and zonula adherens join the RPE cells near their apices.¹ Desmosomes are present throughout the layer, and gap junctions between the cells allow for electrical coupling, providing a low-resistance pathway for the passage of ions and metabolites.⁹

PHOTORECEPTOR CELLS

Photoreceptor cells, the rods and cones, are special sense cells containing photopigments that absorb photons of light. The cells originally were named for their shapes, but the name does not always reflect the shape, particularly in the cone population. More important in the designation of rod or cone is the level of illumination in which each is active. Rods are more active in *dim* illumination, and cones are active in *well-lit* conditions. Visual pigments in the photoreceptors are activated on excitation by light.

Retinal Pigment Epithelium–Neuroretinal Interface

Several factors are involved in maintaining the close approximation between the photoreceptor cell layer and the RPE layer. Passive forces, such as intraocular pressure (IOP), osmotic pressure,¹⁰⁻¹² fluid transport across the RPE,^{13,14} and presence of the vitreous,¹⁵ help preserve the position of the neural retina. Interdigitations between the RPE microvilli and the rod and cone outer segments provide a physical closeness between the two entities,¹ and the material that occupies the extracellular space between the two layers likely provides adhesive forces.¹⁶⁻¹⁸

An unstructured, amorphous material was once thought to occupy the extracellular space between the RPE cells and the photoreceptors and to surround the outer and inner segments of the photoreceptors. More recent studies have described an organized honeycomb-like structure, the **interphotoreceptor matrix (IPM)**.¹⁹ The outer segments are surrounded completely by the IPM and extend through openings in its meshwork. The constituents of the IPM domains around the rods differ from those around the cones; those surrounding the cones are described as a “matrix sheath.”¹⁹⁻²¹ The domains are believed to be bound together laterally, forming a highly coherent structural unit.¹⁹ The IPM constituents are bound tightly to both the epithelial cells and the photoreceptor cells and may exceed the strength of the RPE cells. In laboratory experiments a forceful separation between these two layers often ruptures the RPE cell, leaving remnants of pigment attached to the photoreceptors.^{3,22} The adhesive mechanism is attributed to molecular bonds within this extracellular material.^{16,18,22-24}

The IPM provides a means for the exchange of metabolites²⁵ and for interactions between the two layers.²⁶ In addition, the IPM may be partly responsible for orienting the photoreceptor outer segments for optimal light capture.¹⁷ Despite these apparent forces, the interface between the RPE and the photoreceptor layer is the common location of separation in a retinal detachment.

CLINICAL COMMENT: RETINAL DETACHMENT

*When a **retinal detachment** occurs, the separation usually lies between the RPE cells and the photoreceptors because no intercellular junctions join these cells. The RPE cells remain attached to the choroid and cannot be separated from it without difficulty. Retinal detachment separates the photoreceptors from their blood supply, and if the layers are not repositioned quickly, the affected area of photoreceptor cells will necrose. An argon laser often is used to photocoagulate the edges of the detachment, producing scar tissue. This photocoagulation prevents the detachment from enlarging and facilitates the repositioning of the photoreceptors.*

Composition of Rods and Cones

Rods and cones are composed of several parts, starting nearest the RPE: (1) the outer segment, containing the visual pigment molecules for the conversion of light into a neural signal; (2) a connecting stalk, the cilium; (3) the inner segment, containing the metabolic apparatus; (4) the outer fiber; (5) the cell body; and (6) the inner fiber, which ends in a synaptic terminal (Figure 4-3).

Outer Segment. The **outer segment** is made up of a stack of membranous discs (600 to 1000 per rod)² and is enclosed by the plasmalemma of the cell. Each disc is a flattened membrane sac with a narrow intradisc space; the discs are stacked on top of one another and are separated by an extradisc space. Visual pigment molecules are located within the disc membranes. A biochemical change is initiated within these molecules when they are activated by a photon of light. The tip of the outer segment is oriented toward the RPE, and the base is oriented toward the inner segment.

Cilium. A connecting stalk, or **cilium**, extends from the innermost disc, joining the outer segment with the inner segment and acting as a conduit between them (Figure 4-4). It is a modified cilium consisting of a series of nine pairs of tubules from which the central pair, usually present in motile cilia, is missing. The plasmalemma around the outer segment is continuous across the cilium with that of the inner segment.

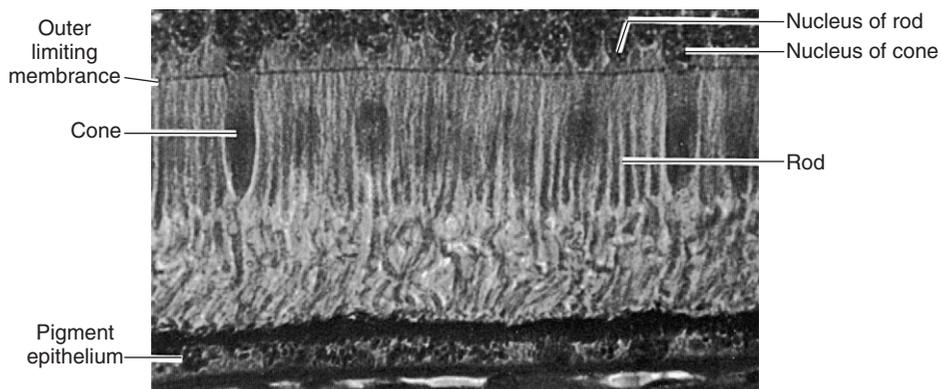
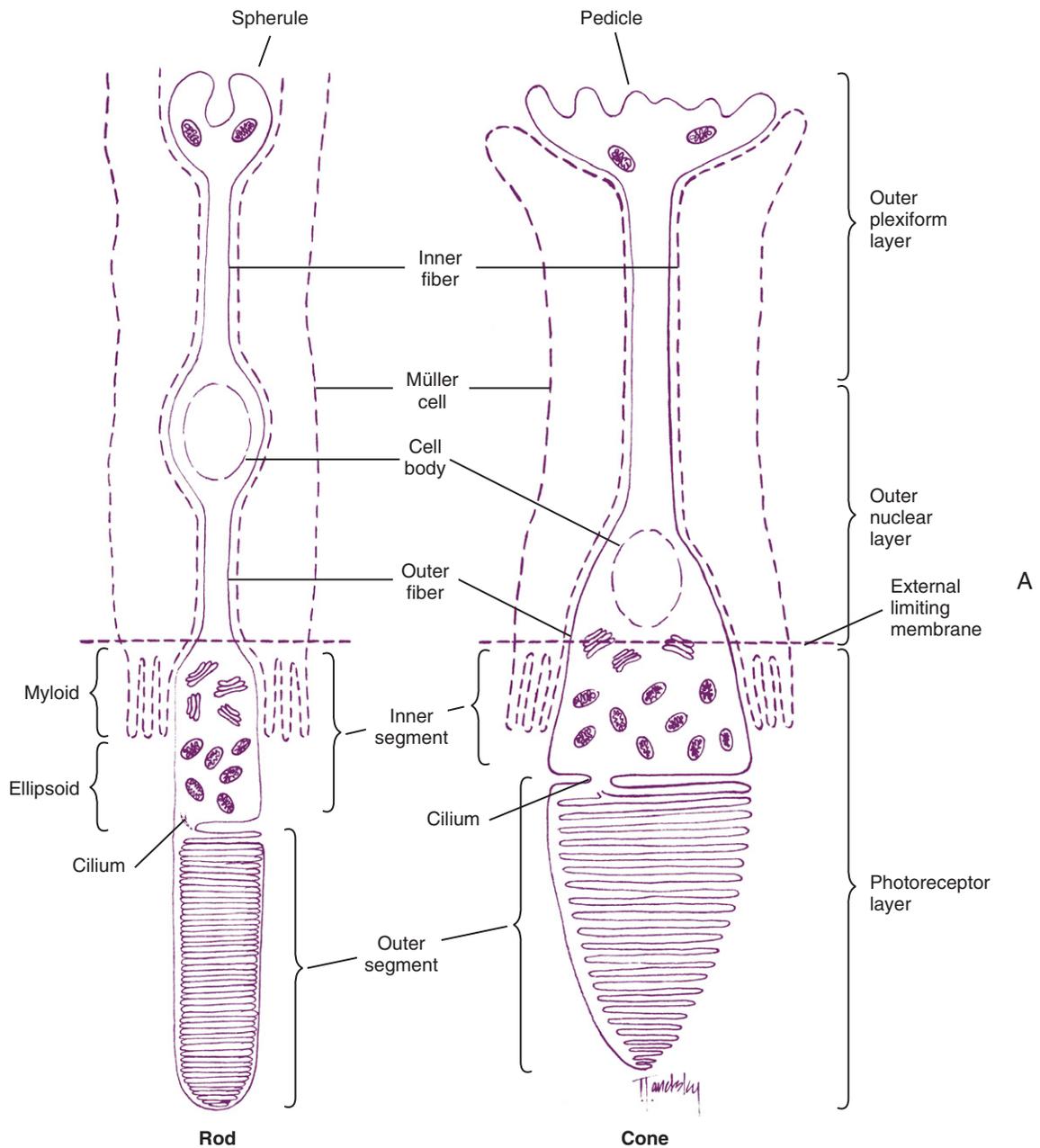
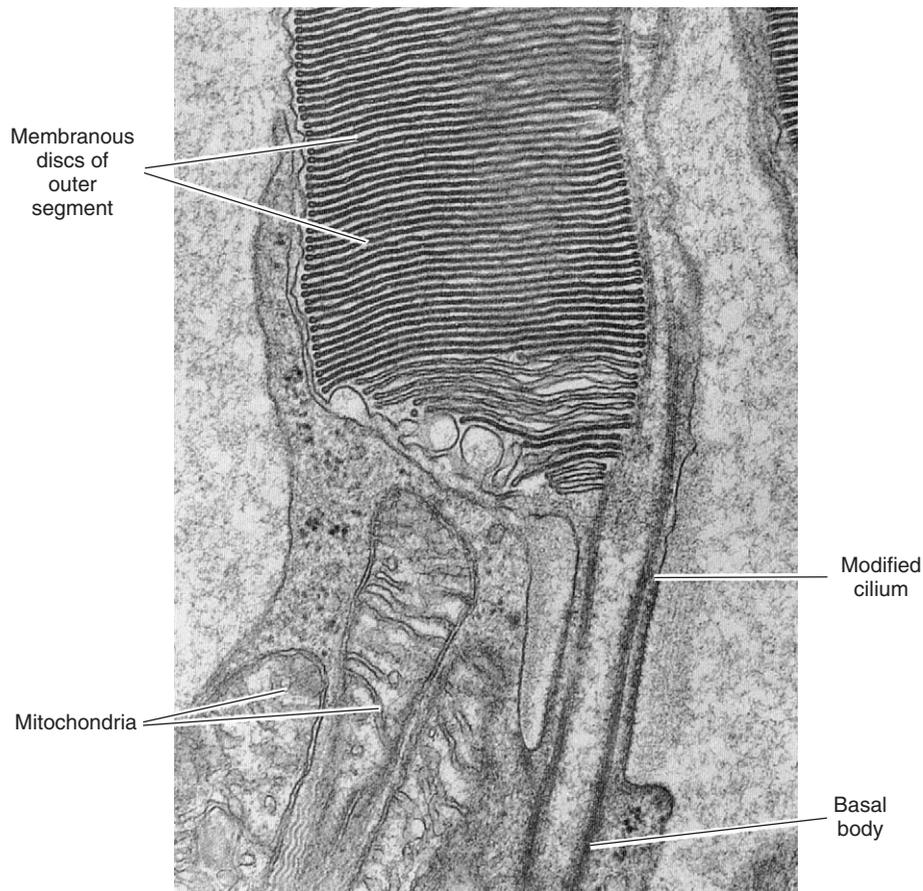


FIGURE 4-3

A, Photoreceptor cells. Portions of Müller cells (*dotted lines*) are shown adjoining the rods and cones. **B**, Retina. ($\times 1000$.) (**B** from Krause WJ, Cutts JH: *Concise text of histology*, Baltimore, 1981, Williams & Wilkins.)

**FIGURE 4-4**

Junction of outer and inner segment of rod. (Transmission electron microscope; $\times 45,000$.)
(From Krause WJ, Cutts JH: *Concise text of histology*, Baltimore, 1981, Williams & Wilkins.)

Inner Segment. The **inner segment** contains cellular structures and can be divided into two parts. The **ellipsoid** is nearer the outer segment and contains numerous mitochondria. The part closer to the cell body, which is sometimes called the **myoid**, contains other cellular organelles, such as the endoplasmic reticulum and Golgi apparatus; protein synthesis is concentrated in this area.²⁷ The term “myoid,” however, is derived from a similar area in amphibians that contains a contractile structure that produces orientational movements of the outer segments of cones.²⁸ The human myoid does not have contractile properties,²⁹ although the axis of the inner and outer segments is oriented toward the exit pupil of the eye, maximizing the ability of the photoreceptor to capture light. The radial orientation becomes more evident in cells located farther from the macula.^{8,30,31}

Outer Fiber, Cell Body, and Inner Fiber. The **outer fiber** extends from the inner segment to the **cell body**, the portion containing the nucleus. The **inner fiber**

is an axonal process containing microtubules and runs inward from the cell body, ending in specialized synaptic terminals that contain synaptic vesicles. The photoreceptor nerve endings synapse with bipolar and horizontal cells.

Rod and Cone Morphology

Rods. The plasmalemma, enclosing the rod outer segment, is separate from the disc membrane except for a small region at the base where invaginations of the plasmalemma form discs, the intradisc space of which is continuous with the extracellular space (see Figure 4-3, A). The remainder of the discs form sacs that are closed at both ends and are free of attachment to the surrounding membrane and adjacent discs.^{8,32} The discs are fairly uniform in width, and the photosensitive pigment rhodopsin is located within the disc membrane.

Young²⁷ applied a pulse of radiolabeled amino acids which were incorporated into disc components. He observed that the band of radioactivity moved from the

inner segment, where protein is synthesized, into newly assembled discs in the outer segment. The labeled discs moved from the base to the tip, and the label was finally seen in phagosomes of the RPE cells. This study established that components of disc membranes are produced in the inner segment and move along the connecting stalk to be incorporated into discs at the outer segment base.²⁷ The discs gradually are displaced outward by the formation of new discs and, as they reach the tip, are sloughed off, taken up by the RPE cells, and phagocytosed.^{33,34} This process, the *rod outer segment renewal system*, appears to involve active processes in both the RPE and the outer segment.^{27,35} The discs apparently are shed regularly, with most of the shedding occurring in the early morning.³⁶⁻³⁹

The rod inner and outer segments are approximately the same width. The inner segment is joined to the cell body by the relatively long and narrow outer fiber. The inner fiber extends from the cell body and terminates in a rounded, pear-shaped structure called a spherule (see Figure 4-3, A). The internal surface of the spherule is invaginated,⁴⁰ forming a synaptic complex that contains bipolar dendrites and horizontal cell processes. Each rod spherule synapses with one to four bipolar cells.⁴¹

Rods release the neurotransmitter glutamate.

Cones. As in the rod, the outer segment of the cone is enclosed by a plasmalemma, but in this case the plasma membrane is continuous with the membranes forming most of the discs, and the discs are not separated easily from one another⁴² (Figure 4-5). In many cones the discs at the base are wider than those at the tip, giving the characteristic cone shape, although some cone outer segments have a shape similar to the rod.

The cone outer segment is shorter than that of the rod and may not reach the RPE layer. However, tubular processes protrude from the apical surface of the epithelial cell to surround the cone outer segment.⁴³ One of three visual pigment molecules is contained within the disc membrane, and each pigment molecule is activated by the absorption of light in a specific range in the color spectrum. The absorptions occur at 420 nm (blue), 531 nm (green), and 588 nm (red).

Early studies of cone outer segment renewal theorized that the formation of discs at the cone base was not uniform and sequential because radiolabeled protein appeared to be distributed throughout the outer segment membrane, not merely in the disc membranes.^{34,44} More recently, electron-microscope studies suggest that formation of new discs does occur at the base, but because of the more extensive connections with the surrounding plasmalemma, the labeled molecules are able to diffuse throughout the cone outer segment membrane rather than being confined to discs, as occurs in the rods.⁴² Investigations continue into the mechanism by which the discs become narrower as they approach the tip.⁴⁵ Cone discs too are shed periodically, often at the end of the day, and are phagocytosed by the RPE.^{39,42,46,47} The factors that regulate the cycle of disc shedding are still under investigation.

The shape of the inner segment also contributes to the cone shape. The ellipsoid area of the cone is wider and contains more mitochondria than the rod.¹ The outer fiber is short and stout and may even be absent in the cone; thus, cone nuclei lie outer to rod nuclei. The inner fiber terminates in a broad, flattened structure called a **pedicle**, which has several invaginated areas

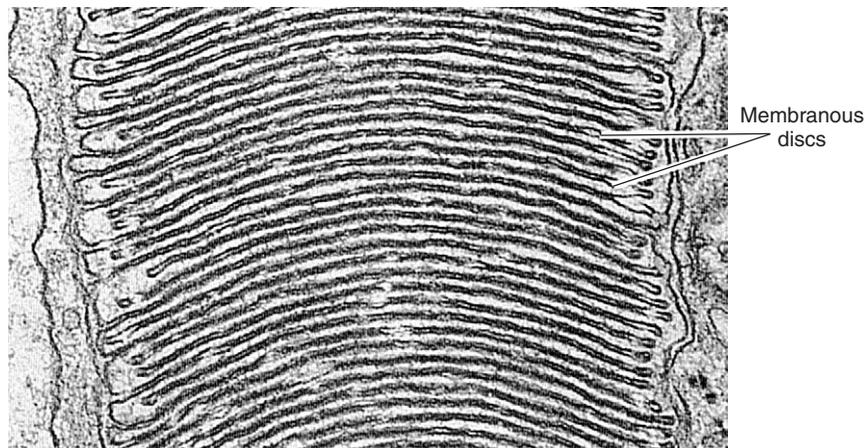


FIGURE 4-5

Cone outer segment. (Transmission electron microscope; $\times 56,000$.) (From Krause WJ, Cutts JH: *Concise text of histology*, Baltimore, 1981, Williams & Wilkins.)

within its flattened surface (see Figure 4-3, A). Cone pedicles have three types of synaptic contacts. Triads are found within the invaginations; contacts with bipolar cells occur on the flat surfaces; and gap junctions are located on the lateral expansions (telodendria) of the pedicle and permit electrical communication between adjacent rods or cones.^{8,48}

As with rods, cones use glutamate for a neurotransmitter.

BIPOLAR CELLS

The **bipolar cell** is the second-order neuron in the visual pathway. The nucleus of the bipolar cell is large and contains minimal cell body cytoplasm. Its *dendrite* synapses with photoreceptor and horizontal cells, and its *axon* synapses with ganglion and amacrine cells; glutamate is its neurotransmitter. Bipolar cells relay information from photoreceptors to horizontal, amacrine, and ganglion cells and receive extensive synaptic feedback from amacrine cells.⁴⁹ Eleven types of bipolar cells have been classified on the basis of morphology, physiology, and dendritic contacts with photoreceptors;⁵⁰ all types except the rod bipolar cell are associated with the cone.

Only one type of **rod bipolar cell** has been identified. It has a relatively large body and several spiky dendrites, usually arising from a single, thick process. Rod bipolar cells begin to appear 1 mm from the fovea and continue into the periphery. These are the only bipolar cells that contact rods.^{1,50} The expanse of the dendritic tree widens and the reach of the axonal terminals increases in the rod bipolar cells located in peripheral retina compared with those in central retina. The dendrites of a single rod bipolar cell contact 15 to 20 rods in central retina and up to 80 rods in the periphery, improving light sensitivity.^{50,51} These dendritic processes are the central element in a specific synapse called a triad. A **triad** consists of processes from two horizontal cells flanking a bipolar dendrite within an invagination in a photoreceptor; there is usually one triad per rod.² The rod bipolar axon is large and unbranched and rarely synapses directly with ganglion cells but instead synapses with amacrine processes, which then signal ganglion cells.⁵² This synaptic arrangement allows one set of ganglion cells to carry information from either rod or cone pathways.⁵²

The **midget bipolar cell** has a relatively small body and can be either flat or invaginating. Dendritic terminals of the **flat midget bipolar cell** end in a flat expansion and make contact only with the flat area of the cone pedicle. In central retina, each flat midget bipolar cell contacts only one cone so its dendritic "bouquet" is small, the size of a single cone pedicle. In

peripheral retina, each flat midget bipolar cell has two or three dendritic clusters and thus each cell contacts two or three neighboring cones.^{50,53} A single cone pedicle may have as many as 500 contacts on its flat surface.² The axon of the flat midget bipolar cell has many endings and synapses with ganglion cells of all types.¹

The **invaginating midget bipolar cell** is similar to the flat midget bipolar cell. The dendritic process of the invaginating midget bipolar cell, as the central element in a triad, is flanked by two horizontal cell processes within an invagination in the cone pedicle (Figure 4-6). In central retina the dendritic bouquet of an invaginating midget bipolar cell is the size of a single cone pedicle, implying that each cone is innervated by only one invaginating bipolar cell. Each pedicle can have 12 to 25 triads.² In peripheral retina each bipolar cell may have up to three such dendritic expansions, with the capacity to contact several pedicles.⁵⁰ The axon of the invaginating midget bipolar cell synapses with the dendrite of a single midget ganglion cell and with amacrine processes.¹

The two types of **diffuse cone bipolar cells** are designated type a and type b, called "flat bipolars" and "brush bipolars" by Polyak.⁵⁴ In central retina the diffuse cone bipolar cell contacts approximately five neighboring cones, and in the periphery, each contacts 10 to 15 neighboring cones. The location of the axon terminal differentiates the two types.⁵⁰

The **blue cone bipolar cell** synapses with up to three cone pedicles.⁵⁵ It differs from diffuse cone bipolar cells in that it contacts widely spaced rather than neighboring cones.⁵⁰

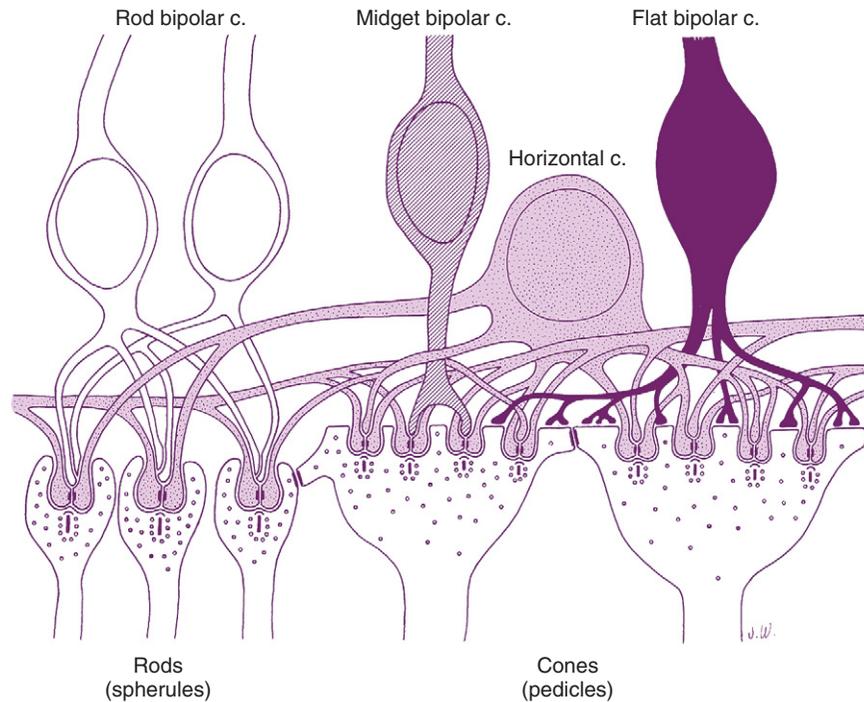
The **giant cone bipolar cell** derives its name from the extent of its dendritic tree. The major dendrite branches into three trees, and then clusters of processes branch from these, each group being the size of a cone pedicle. The two types, designated *diffuse* and *bistratified*, differ only in the location of their axon terminations.^{50,56}

Figure 4-7 shows several of the bipolar cell types.

GANGLION CELLS

The next cell in the visual pathway, the third-order neuron, is the **ganglion cell**. Ganglion cells can be *bipolar* (e.g., a single axon and a single dendrite) or *multipolar* (a single axon and more than one dendrite).⁵⁷ Cell size varies greatly, with some large cells 28 to 36 μm .⁵⁰ The various methods used to classify ganglion cells make classification rather confusing.

An older, broad classification groups ganglion cells into three types. *W cells* project to the midbrain, carrying information for the pupillary response and reflexive eye movements. *Y cells* project to the lateral

**FIGURE 4-6**

Rod spherule and cone pedicle and their synapses. Rod and cone bipolar cells show extensive contacts. Horizontal cells also make synapses with both rods and cones. Interconnections are shown between rod spherules and cone pedicles. (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

geniculate body, with some having collateral branches that travel to the midbrain, perhaps with pupillary information. *X cells* primarily respond in visual discrimination and project to the lateral geniculate body.²

Ganglion cells have also been classified on the basis of cell body size, branching characteristics, termination of dendrites, and diameter of fiber and dendritic tree.⁵⁰ Figure 4-8 shows several types of ganglion cells, both central and peripheral. These ganglion cell types are designated G3 to G23 (not all numbers are represented).

Another designation classifies ganglion cells based on the lateral geniculate body layer in which they terminate. P cells terminate in the parvocellular layers. The **P1 ganglion cell**, also called the **midget ganglion cell**, is the most common P cell. This relatively small cell has a single dendrite and can be differentiated into two types, according to the stratification of the dendritic branching.⁵⁰ Certain P1 midget cells are connected to only one midget bipolar cell, invaginating or flat, which in turn might be linked to a single cone receptor,⁵⁸ providing a channel that processes high-contrast detail and color resolution. This situation is likely to occur in

the fovea. A convergent pathway occurs in a number of P1 cells that receive input from two bipolar axons.

The **P2 ganglion cell** also terminates in the parvocellular layers but has a densely branched, compact dendritic tree that spreads horizontally. These cells can be differentiated into two types depending on the location of the dendrite termination.⁵⁰

The **M-type ganglion cell** projects to the magnocellular layers of the lateral geniculate body. The M cell has coarse dendrites with spiny features, and the dendritic tree enlarges from central to peripheral retina.⁵⁰

Each ganglion cell has a single axon, which emerges from the cell body and turns to run parallel to the inner surface of the retina; the axon uses glutamate as its neurotransmitter. The axons come together at the optic disc and leave the eye as the optic nerve. The termination for approximately 90% of these axons is the lateral geniculate body; others project to subthalamic areas involved in processes such as the pupillary reflexes and the circadian rhythm.^{2,50}

The photoreceptor cells, bipolar cells, and ganglion cells carry the neural signal in a three-step pathway through the retina. The neural signal is modified within

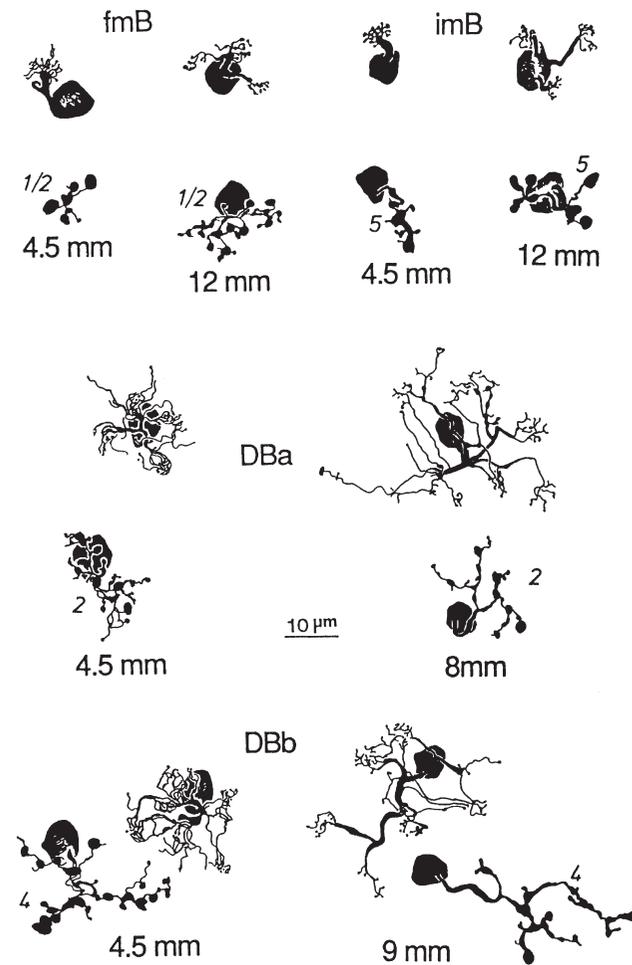


FIGURE 4-7

Camera lucida drawings of cone bipolar cells of the human retina as seen in whole-mount Golgi preparations (scale bar = 10 μ m). Each cell is drawn at two levels: dendritic tree in outer plexiform layer (OPL) (*top*) and axon terminal in inner plexiform layer (IPL) (*bottom*). Stratification of axon terminal according to five strata of IPL is given by adjacent italicized number. Positions on retina in millimeters of eccentricity are indicated for each cell illustrated. Midget bipolar cells, fmB and imB varieties, are indicated above diffuse small-field bipolar types, DBa and DBb. See text for further details. (From Kolb H, Linberg KA, Fisher SK: *J Comp Neurol* 318:150, 1992.)

the retina by other cells that create intraretinal cross-connections, provide feedback information, or integrate retinal function.¹

HORIZONTAL CELLS

The **horizontal** cell transfers information in a horizontal direction parallel to the retinal surface. It has one long process, or axon, and several short dendrites with branching terminals; the processes spread out parallel

to the retinal surface, and all terminate in the outer plexiform layer (Figure 4-9). Horizontal cells synapse with photoreceptors, bipolar cells, and other horizontal cells. One type of horizontal cell synapses only within a cone pedicle in the special triad junction. Horizontal cells are thought to contact bipolar cells lying some distance from the photoreceptor that activated the horizontal cell. Horizontal cells can release an inhibitory transmitter, thus playing a role in the complex process of visual integration.^{56,59}

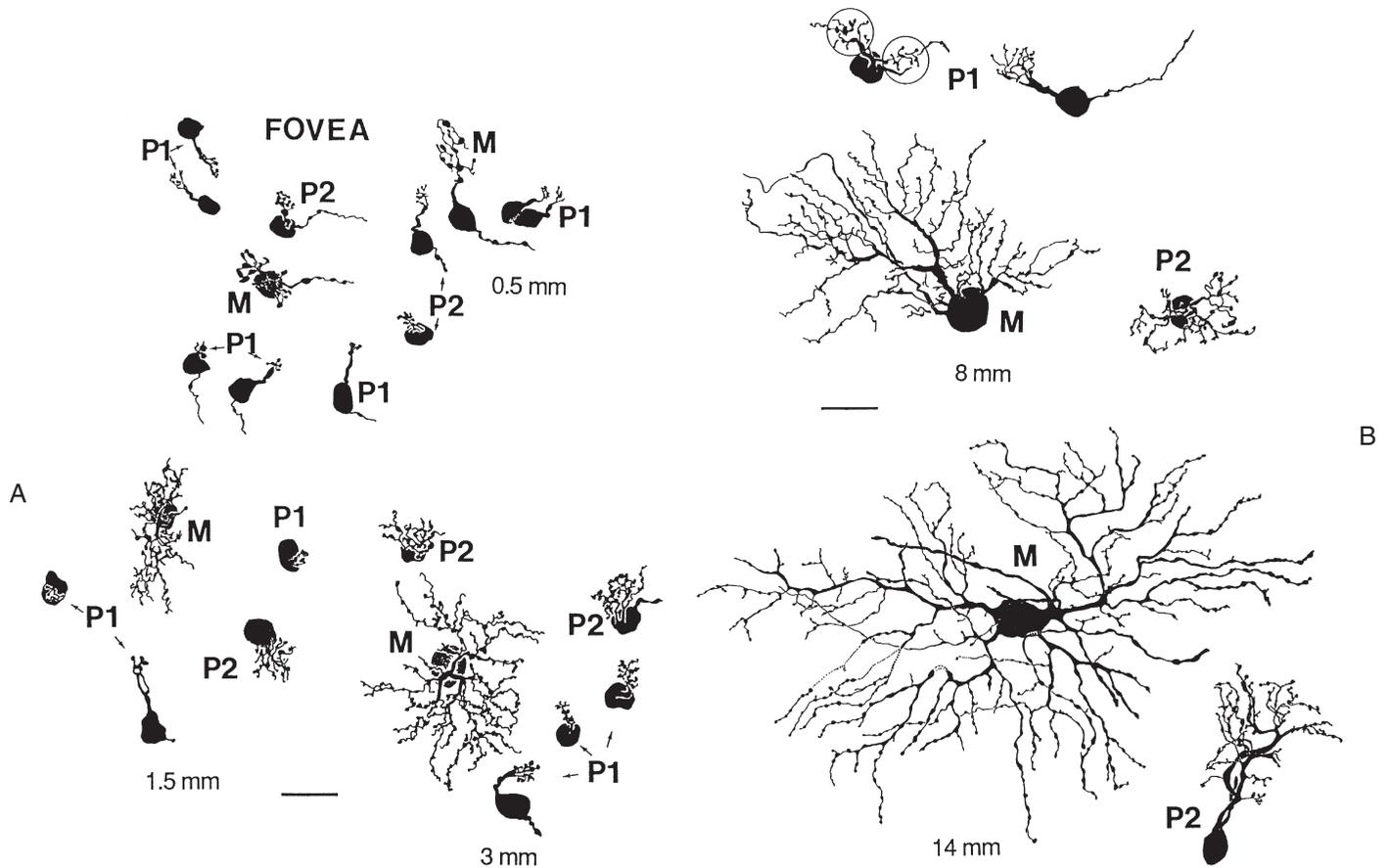
Three types of horizontal cells have been differentiated: HI, HII, and HIII. HI cells have dendrites that synapse with 7 to 18 cones and a large, thick axon ending in a fan-shaped expanse of terminals that end in rod spherules more than 1 mm away.⁶⁰ All the HII processes apparently contact cones and might be specific for blue cones.⁵⁰ HIII cells have a large dendritic tree that synapses with many cones, not all of which are neighboring; evidence suggests that these horizontal cells avoid blue cones, thus being selective for red and green.^{50,61} The termination of the HIII axon has not yet been determined. Horizontal cells provide inhibitory feedback to photoreceptors or inhibitory feed forward to bipolar cells.⁶⁰ Horizontal cells can modulate the cone response but are not thought to influence that of the rod.^{52,60}

AMACRINE CELLS

The **amacrine cell** has a large cell body, a lobulated nucleus, and a single process with extensive branches that extend into the inner plexiform layer. The process, which has both dendritic and axonal characteristics and carries information horizontally, forms complex synapses with axons of bipolar cells, dendrites and soma of ganglion cells; with processes of interplexiform neurons; and with other amacrine processes.^{1,62} Because of the extremely broad spread of its process, the amacrine cell plays an important role in modulating the information that reaches the ganglion cells.⁵⁶

As many as 30 to 40 different amacrine cell types may be described as *stratified* or *diffuse*. They can also be classified into four groups—narrow field, small field, medium field, and large field—according to the extent of coverage by their intertwined branching processes. Each of these groups can be subdivided into different types according to the level of the retinal layer in which their nerve endings terminate.^{50,63}

One of the most widely studied amacrine types is the AII cell, a narrow-field type (Figure 4-10). The AII cells are the conduit by which the rod signal reaches ganglion cells.⁶³ An AII cell may receive input from as many as 30 rods through rod bipolar cells.² The AII cell then synapses with a ganglion cell and may also relay information from the rod pathway to the cone pathway.

**FIGURE 4-8**

A, Ganglion cells (P1, P2, and M) of foveal and central human retina (scale bar = 25 μm). Three types can be distinguished on dendritic tree size when they occur adjacent to one another. P1 ganglion cells have a minute dendritic tree at the fovea, which expands to be no more than a small bouquet of varicosities 9 to 12 μm across ×3 mm of eccentricity. P2 ganglion cells have dendritic trees approximately double the size of P1 cells. M ganglion cells average three times the size of P2 cells in dendritic extent. All three types occur as "a" and "b" subtypes, dependent on levels of their dendritic trees in sublamina *a* or sublamina *b* of inner plexiform layer. **B**, Ganglion cells (P1, P2, and M) of middle and far peripheral retina (scale bar = 25 μm). These cells exhibit continuation (in relation to part **A**) of their increasing dendritic tree sizes at greater eccentricities. Many P1 cells in this region have two dendritic heads (circled). Others are normal, single-headed P1 cells, reaching a maximum dendritic tree size of 25 μm. P2 and M cells occur into far periphery and are distinguished clearly by both cell body size and dendritic tree size. (From Kolb H, Linberg KA, Fisher SK: *J Comp Neurol* 318:147, 1992.)

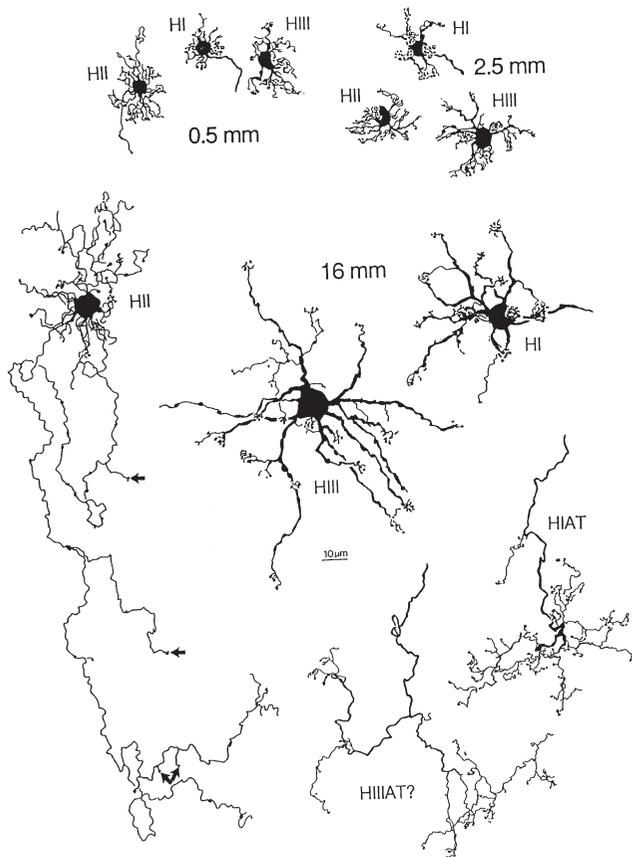


FIGURE 4-9

Whole-mount views of horizontal cells of human retina (scale bar = 10 μ m). Cells of fovea (0.5 mm) are small and difficult to distinguish into the three types but still recognizable to the trained eye. By 2.5 mm of eccentricity, HI, HII, and HIII cell types are discernible from one another. In peripheral retina (16 mm), HIII is clearly larger than HI and has an asymmetric dendritic field. HII cells have a “woolly” appearance that distinguishes them readily from HI and HIII cells. Short, curled axon of HII type gives rise to occasional terminals (*arrows*). HI axon terminal ends as fan-shaped structure with many “lollipop” terminals (*HIAT*), whereas a finer, more loosely clustered terminal is putatively assigned to HIII horizontal cell type *HIIIAT*. (From Kolb H, Linberg KA, Fisher SK: *J Comp Neurol* 318:147, 1992.)

Wide-field amacrine cells form reciprocal synapses with rod bipolar cells and modify the signal transmitted from rod bipolar to AII cells. These reciprocal connections occur at rod dyad synapses.² Most amacrine cells contain the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) or glycine and have both presynaptic and postsynaptic endings.^{2,63} Amacrine cells are joined to one another via gap junctions,⁶³ and some cells have been found to combine information from rod and cone pathways before innervating a ganglion cell.⁵⁸

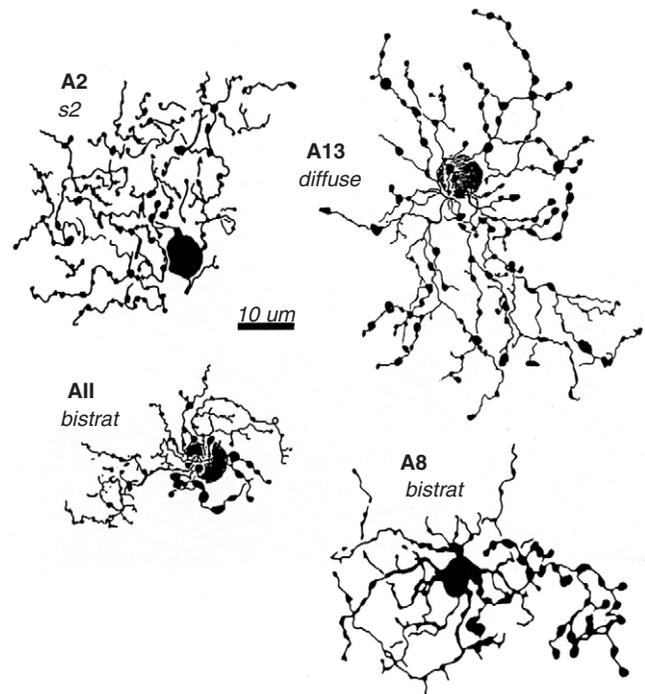


FIGURE 4-10

Whole-mount view of amacrine AII cell. (From Kolb H: *Eye* 11:904, 1997.)

INTERPLEXIFORM NEURONS

The **interplexiform neuron** has a large cell body and is found among the layer of amacrine cells. The processes extend into both synaptic layers and convey information between these layers (Figure 4-11), apparently providing feedback from inner to outer retinal layers.^{50,56} The nerve endings are both presynaptic and postsynaptic to amacrine processes or amacrine cell bodies in the inner plexiform layer. Interplexiform neurons are presynaptic to rod or cone bipolar cells in the outer plexiform layer.^{2,8,64}

NEUROGLIAL CELLS

Neuroglial cells, although not actively involved in the transfer of neural signals, provide structure and support and play a role in the neural tissue reaction to injury or infection. Types of neuroglial cells found in the retina include Müller cells, microglial cells, and astrocytes.

Müller Cells

Müller cells are large neuroglial cells that extend throughout much of the retina. They play a supportive role, providing structure. The apex of the Müller cell is

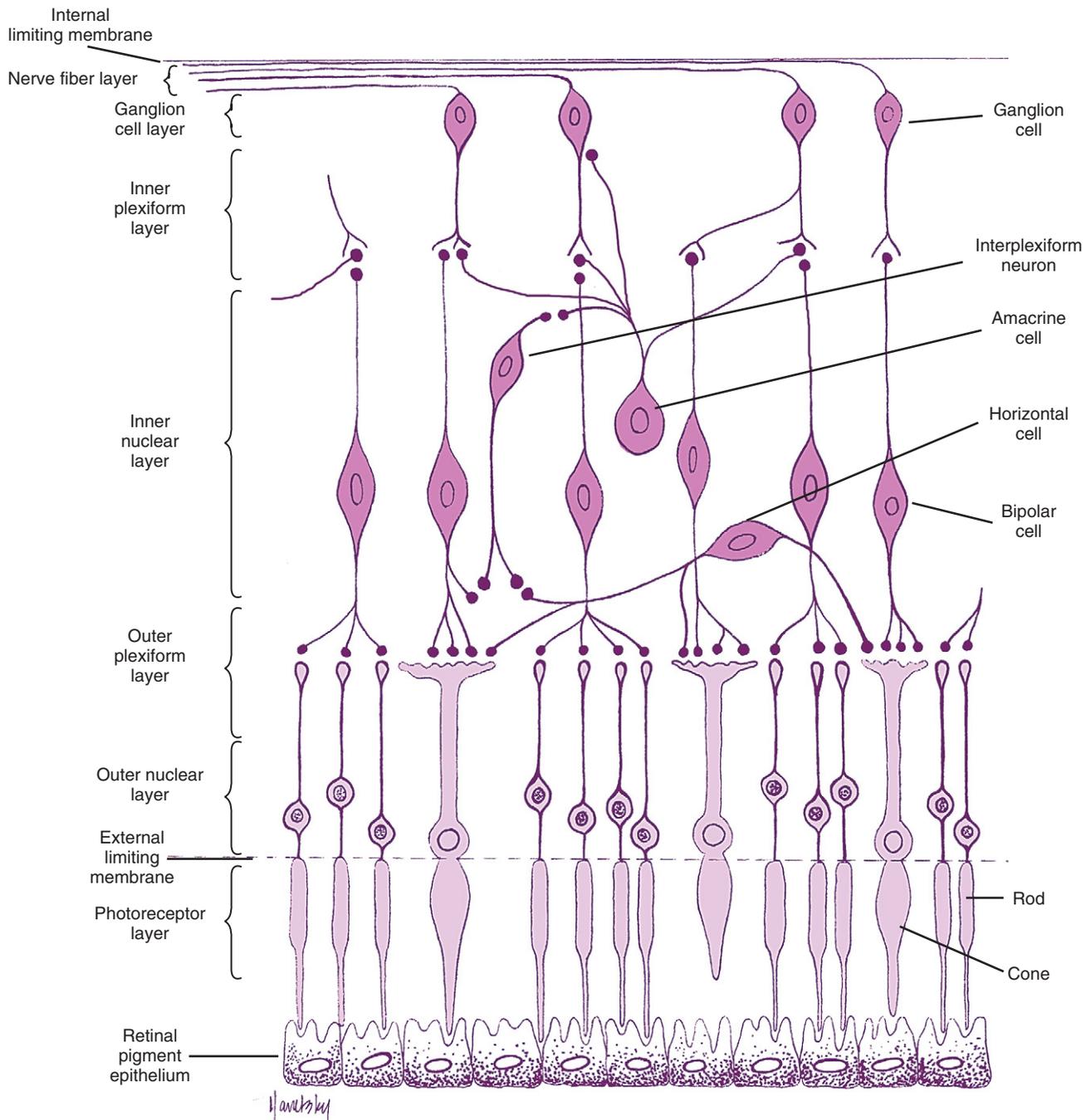


FIGURE 4-11

Retinal cells and synapses. The 10 retinal layers are indicated.

in the photoreceptor layer, whereas the basal aspect is at the inner retinal surface. Cellular processes form a reticulum among the retinal cell bodies and fill in most of the space of the retina not occupied by neuronal elements (Figure 4-12). Müller cells ensheath dendritic processes within the synaptic layers, providing insulation

from electrical and chemical activation, and their processes cover most ganglion axons.⁶⁵

The neuronal cell bodies and their processes appear to reside in tunnels within the Müller cell.⁵¹ Delicate apical villi, **fiber baskets (of Schultze)**, terminate between the inner segments of the photoreceptors.^{1,28}

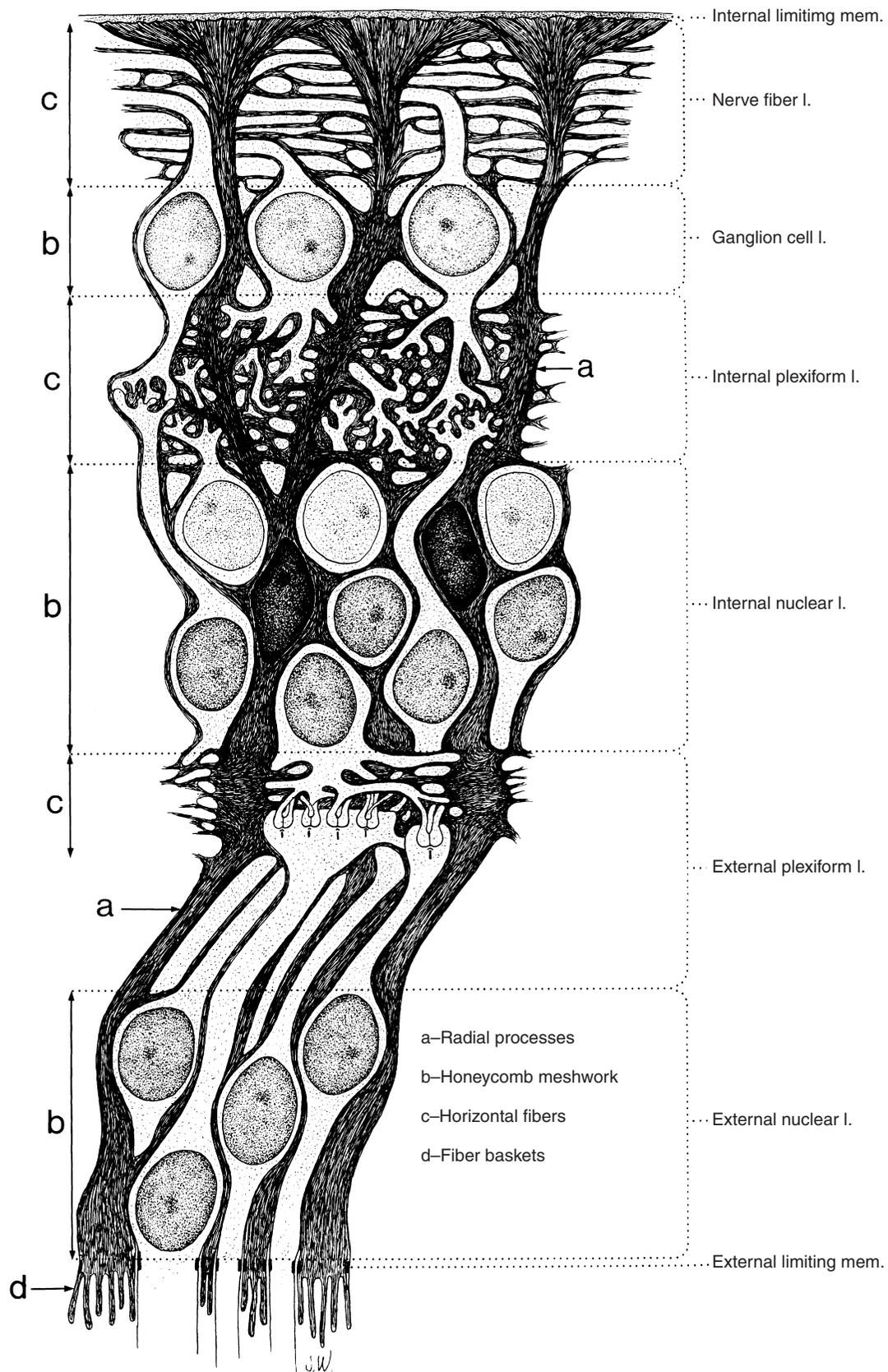


FIGURE 4-12

Structure of the Müller cell. *mem.*, membrane; *l.*, layer. (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

On light microscopy, Müller cell processes can be seen passing through the layer containing the nerve fibers of the ganglion cells, perpendicular to the retinal surface. An expanded process, called the *endfoot*, along the basal aspect of the Müller cell contributes to the membrane separating the retina from the vitreous, and extensions of Müller cells wrap around blood vessels.¹ The pervasiveness of the Müller cell results in very little extracellular space in the retina (see Figure 4-12). Besides providing structure, the Müller cell acts as a buffer in regulating concentrations of potassium ions (K^+), GABA, and glutamate in the extracellular space.⁶⁶ It is also involved in glucose metabolism by synthesizing and storing glycogen.⁶⁷⁻⁶⁹

Microglial Cells and Astrocytes

Microglial cells are wandering phagocytic cells and might be found anywhere in the retina. Their number increases in response to tissue inflammation and injury.

Astrocytes are star-shaped fibrous cells found in inner retina, usually in the nerve fiber and ganglion cell layers. These perivascular cells form an irregular supportive network that encircles nerve fibers and retinal capillaries.¹ They may contribute to the internal limiting membrane as well as perform some of the same functions as the Müller cells.⁷⁰

TEN RETINAL LAYERS

The “10-layered” arrangement of the retina is actually a remarkable organization of alternate groupings of the retinal neurons just described and their processes. Traditionally, descriptive names were given to these so-called layers, and these designations are still in use today (Figure 4-13).

1. Retinal pigment epithelium
2. Photoreceptor cell layer
3. External limiting membrane
4. Outer nuclear layer

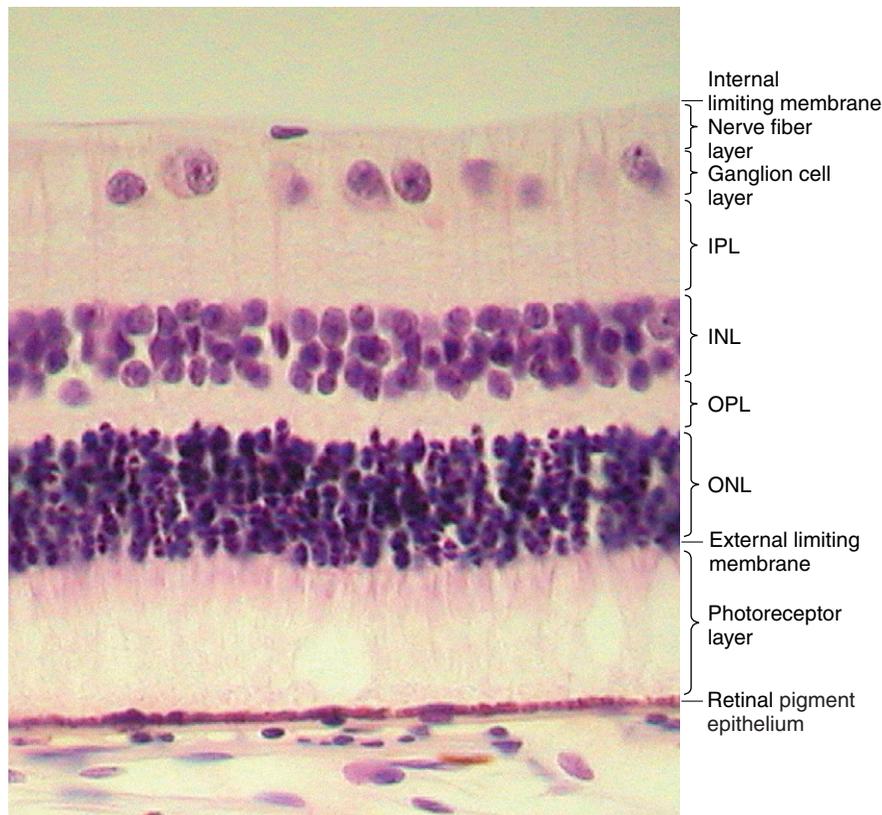


FIGURE 4-13

Light micrograph of full-thickness view of the retina.

5. Outer plexiform layer
6. Inner nuclear layer
7. Inner plexiform layer
8. Ganglion cell layer
9. Nerve fiber layer
10. Internal limiting membrane

RETINAL PIGMENT EPITHELIUM

The RPE consists of a single layer of pigmented cells, as previously discussed. There are 4 to 6 million RPE cells, and each cell interacts with 30 to 40 photoreceptors.^{36,71,72} The RPE is an active area with several functions. First, the zonula occludens of the RPE are an important part of the blood-retinal barrier, which selectively controls movement of substances from the choriocapillaris into the retina.⁷³ (In this regard, the RPE is analogous to the epithelium of the choroid plexus, in the ventricles of the brain.) Second, cellular lysosomes within the cells enable the cells to phagocytose fragments from the continual shedding of the photoreceptor outer segment discs. Third, the RPE metabolizes and stores vitamin A, which is used in the formation of photopigment molecules,^{74,75} and is the site for some of the biochemical processes necessary for renewal of these molecules.⁸ Fourth, the pigment granules within the cells absorb light, thereby reducing excess scattering. Fifth, the cells contribute to the formation of the intercellular complex between the RPE layer and the photoreceptors.^{76,77}

PHOTORECEPTOR LAYER

The **photoreceptor layer** is composed of the outer and inner segments of rods and cones. Projections from the apical surface of Müller cells separate the inner segments.

EXTERNAL LIMITING MEMBRANE

The **external limiting membrane** is not a true membrane but actually consists of intercellular junctions between photoreceptor cells and between photoreceptor and Müller cells at the level of the inner segments. On light microscopy the so-called membrane appears as a series of dashes, resembling a fenestrated sheet through which processes of the rods and cones pass. This band of zonula adherens has the potential to act as a metabolic barrier restricting the passage of some large molecules.^{8,76}

OUTER NUCLEAR LAYER

The **outer nuclear layer (ONL)** contains the rod and cone cell bodies; the cone cell body and nucleus are larger than those of the rod. Cone outer fibers are very

short, and therefore the cone nuclei lie in a single layer close to the external limiting membrane; cell bodies of the rods are arranged in several rows inner to the cone cell bodies. The ONL is thickest in the fovea, where it contains approximately 10 layers of cone nuclei.²

OUTER PLEXIFORM LAYER

The **outer plexiform layer (OPL; also outer synaptic layer)** has a wide *external band* composed of inner fibers of rods and cones and a narrower *inner band* consisting of synapses between photoreceptor cells and cells from the inner nuclear layer. Rod spherules and cone pedicles synapse with bipolar and horizontal cells in the OPL. Many of these synapses consist of invaginations in the photoreceptor terminal; the invaginations are deep in the spherule but more superficial in the pedicle.⁸ In these junctures the photoreceptor element contains a membranous plate, the synaptic ribbon^{8,58} (Figure 4-14). The invaginating synapse within rods can have multiple postsynaptic elements (sometimes more than three). Invaginating synapses in cone pedicles that consist of two postsynaptic horizontal cell processes flanking a bipolar dendrite are usually triads (see Figure 4-6). Invaginating midjet bipolar cells are involved in cone triads, and all cones have at least one invaginating midjet bipolar and one flat midjet bipolar contact.⁸

Synaptic contacts also occur outside invaginating synapses in the OPL. Horizontal cells make synaptic contact with bipolar dendrites and contact other horizontal cell processes via gap junctions.^{60,78} Bipolar dendrites synapse with photoreceptor cell endings; a single photoreceptor can have contact with more than one bipolar dendrite. The relatively long axon of the interplexiform neuron makes numerous synaptic connections with processes entering photoreceptor terminals.^{64,79}

Desmosome-like attachments called *synaptic densities* are located within the arrangement of interwoven, branching, bipolar dendrites and horizontal cell processes in the OPL. These synaptic densities are seen as a series of dashed lines on light microscopy and resemble a discontinuous membrane, termed the **middle limiting membrane**. This “membrane” demarcates the extent of the retinal vasculature²⁸ and may prevent exudates and hemorrhages from spreading into the outer retinal layers.⁵¹

INNER NUCLEAR LAYER

The **inner nuclear layer (INL)** consists of the cell bodies of horizontal cells, bipolar cells, amacrine cells, interplexiform neurons, Müller cells, and some displaced ganglion cells. The nuclei of the horizontal cells are located next to the outer plexiform layer, where

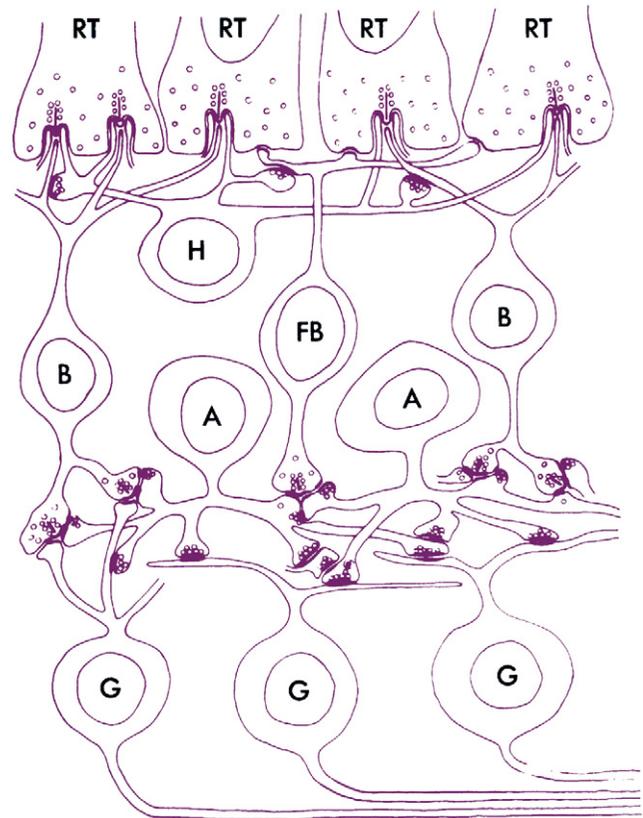
**FIGURE 4-14**

Electron micrograph of cone pedicle. Note dark linear bodies (synaptic ribbons) in pedicle. ($\times 20,000$.) (From Leeson CR, Leeson ST: *Histology*, Philadelphia, 1976, Saunders.)

their processes synapse. The nuclei of the amacrine cells are located next to the inner plexiform layer, where their processes terminate. The bipolar cell has its dendrite in the outer plexiform layer and its axon in the inner plexiform layer (Figure 4-15). The interplexiform neuron also has processes in both synaptic layers and is thought to receive input in the inner plexiform layer and project it to the outer plexiform layer.⁶⁴ The retinal vasculature of the deep capillary network is located in the inner nuclear layer.

INNER PLEXIFORM LAYER

The inner plexiform layer (IPL; also **inner synaptic layer**) consists of synaptic connections between *axons* of bipolar cells and *dendrites* of ganglion cells. The IPL

**FIGURE 4-15**

Arrangements of synaptic contacts found in vertebrate retinas. In outer synaptic layer, processes from bipolar (B) and horizontal cells (H) penetrate into invaginations in receptor terminals (RT) and terminate near synaptic ribbons (lamellae) of receptor. Processes of flat bipolar cells (FB) make superficial contacts on bases of some receptor terminals. Horizontal cells make conventional synaptic contacts onto bipolar dendrites and other horizontal cell processes (not shown). Because horizontal cells usually extend farther laterally in outer synaptic layer than do bipolar dendrites, distant receptors presumably can influence bipolar cells via horizontal cells. In the inner synaptic layer, two basic synaptic pathways are suggested. Bipolar terminals may contact one ganglion cell dendrite and one amacrine process at ribbon synapses (*left side*) or two amacrine cell (A) processes (*right side*). When the latter arrangement predominates in a retina, numerous conventional synapses between amacrine processes (serial synapses) are observed, and ganglion cells (G) are contacted mainly by amacrine processes (*right*). Amacrine processes in all retinas make synapses of conventional type back onto bipolar terminals (reciprocal synapses). (From Dowling JE: *Invest Ophthalmol* 9:655, 1970.)

contains the synapse between the second-order and third-order neuron in the visual pathway (see Figure 4-15). Generally, the axon of the invaginating midganglion bipolar cell ends in the inner half of the IPL, and the axon of the flat midganglion bipolar cell ends in the outer half of the IPL.^{50,53} Synapses also occur between (1) amacrine

processes and bipolar axons, (2) amacrine processes and ganglion cell bodies and dendrites, (3) amacrine cells, and (4) amacrine cells and interplexiform neurons (Figure 4-16).

Ribbon synapses in the IPL involve contact among a bipolar axon and a pair of postsynaptic processes, which may be amacrine or ganglion.^{8,80} A reciprocal synapse, thought to be inhibitory, involves the second contact of an amacrine process with a bipolar axon, providing negative feedback.⁵¹ Gap junctions between amacrine cells are also located in the IPL. Some displaced amacrine and ganglion cell bodies may also be seen.

GANGLION CELL LAYER

The **ganglion cell layer** is generally a single cell thick except near the macula, where it might be 8 to 10 cells thick, and at the temporal side of the optic disc, where it is two cells thick. Although lying side by side, ganglion cells are separated by glial processes from Müller cells.⁷⁰ Displaced amacrine cells, which send their processes outward, may be found in the ganglion cell layer, as may some displaced Müller cell bodies and astroglial cells.⁸ Toward the ora serrata, the number of ganglion cells diminishes, and the nerve fiber layer thins.

NERVE FIBER LAYER

The **nerve fiber layer (NFL; also stratum opticum)** consists of the ganglion cell axons. Their course runs parallel to the retinal surface; the fibers proceed to the optic disc, turn at a right angle, and exit the eye through the lamina cribrosa as the optic nerve. The fibers generally are unmyelinated within the retina. The NFL is thickest at the margins of the optic disc, where all the fibers accumulate. The group of fibers that radiate to the disc from the macular area is called the papillomacular bundle. This important grouping of fibers carries the information that determines visual acuity.

The retinal vessels, including the superficial capillary network, are located primarily in the NFL but may lie partly in the ganglion cell layer. Processes of Müller cells are common in the NFL, where they ensheath vessels and nerve fibers.

CLINICAL COMMENT: RETINAL HEMORRHAGES

Hemorrhages from retinal vasculature have a characteristic appearance. Because of the arrangement of the nerve fibers, the blood pools in a feathered pattern called a flame-shaped hemorrhage indicative of the NFL location. Hemorrhages in the inner nuclear layer usually appear rounded and often are called dot or blot hemorrhages (Figure 4-17).

INTERNAL LIMITING MEMBRANE

The **internal limiting membrane** forms the innermost boundary of the retina. The outer retinal surface of this membrane is uneven and is composed of extensive, expanded terminations of Müller cells (often called footplates) covered by a basement membrane. The inner or vitreal surface is smooth. The connection between this membrane and the vitreous is still under investigation and may actually occur at a biochemical level (see Chapter 6); only in the periphery are vitreal fibers incorporated into the internal limiting membrane.⁵¹

Anteriorly, the internal limiting membrane of the retina is continuous with the internal limiting membrane of the ciliary body. It is present over the macula but undergoes modification at the optic disc, where processes from astrocytes replace those of the Müller cells.⁵⁷

CLINICAL COMMENT: FUNDUS VIEW OF THE INTERNAL LIMITING MEMBRANE

Reflections from the internal limiting membrane produce the retinal sheen seen with the ophthalmoscope. In younger persons this membrane gives off many reflections and appears glistening; the sheen is less evident in older individuals.

RETINAL FUNCTION

Light passes through most of the retinal layers before reaching and stimulating the photoreceptor outer segment discs. The neural flow then proceeds back through the retinal elements in the opposite direction of the incident light. The efficient and accurate performance of the retina is not hampered by this seemingly reversed situation.

SCOTOPIC AND PHOTOPIC VISION

The visual system is highly specialized for the detection and analysis of patterns of light and, by visual adaptation, can modify its capacity to respond to light at both high and low levels of illumination. Rods are extremely sensitive in poorly lit conditions (scotopic vision), when cones are least responsive. In **scotopic vision** the light-sensitive retina allows detection of objects at low levels of illumination. Its ability to recognize fine detail is poor, however, and color vision is absent; objects are seen in shades of gray.⁵⁹

Cone activity dominates in **photopic vision**, when the retina is responsive to a broader range of light wavelengths. Bright illumination is necessary for the sharp visual acuity and color discrimination of photopic vision. Cones are designated, depending on the wave-



FIGURE 4-16

Synaptic contacts among bipolar, amacrine, and ganglion cells in inner plexiform layer. Bipolar axonal endings: *A*, axodendritic endings at a dyad; *B*, axosomatic ending on ganglion cell; *C*, bipolar axon–amacrine soma contact. Amacrine cell contacts with other cells: *D*, axoaxonal contact between bipolar and amacrine cell processes; *E*, axodendritic contact between amacrine and ganglion cell; *F*, axosomatic contact between amacrine cell process and soma of ganglion cell. (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)



FIGURE 4-17
Fundus photo, OD, from patient with nonproliferative diabetic retinopathy exhibiting scattered dot and blot hemorrhages. (Courtesy Pacific University Family Vision Center, Forest Grove, Ore.)

length that they absorb, as red (588nm), green (531nm), or blue (420nm).⁸¹

NEURAL SIGNALS

The neural signal generated by the photoreceptors is modified and processed by the complex synaptic pathway through which it passes. There is a greater convergence of rods than of cones onto a ganglion cell. In most retinal regions there is a high ratio of rods to ganglion cells, resulting in high sensitivity for the detection of light and motion. It is estimated that 75,000 rods drive 5000 rod bipolar cells and 250 AII amacrine cells before converging onto a single ganglion cell.⁸² A relatively small number of cones drive the cone bipolar cell, and a small number of cone bipolar cells drive a single ganglion cell. In some situations there is a 1:1 ratio between ganglion and cone cells, reflecting the enormous amount of detail that the cone population can discriminate.¹ A single midganglion bipolar dendrite may contact only one cone pedicle, and its axon then synapses on a single midganglion ganglion cell.⁸² The cone pathway involves a three-neuron chain, whereas the rod

pathway involves a four-neuron chain because of the amacrine cell inclusion.²

Ganglion cell axons can be thought of as “carrying information in processing streams,” such that certain types of information are directed toward specific destinations.⁸ One major target is the lateral geniculate body, wherein some axons terminate in the parvocellular layers, which process wavelength, shape, fine detail, and resolution of contrast. Other axons end in the magnocellular layers, which discern movements and flickering light but have poor wavelength sensitivity.⁸³ Visual information terminating in the midbrain is important in the autonomic control of the ciliary and iris muscles. Other centers that receive visual information can influence motor pathways that control eye, head, and neck movements.

NUMBER AND DISTRIBUTION OF NEURAL CELLS

In 1935, Østerberg⁸⁴ estimated the cell count in the retina at 110 to 125 million rods and 6.3 to 6.8 million cones. More recent research indicates that there are 80

Rights were not granted to include this figure in electronic media.
Please refer to the printed publication.

FIGURE 4-18

Distribution of rods and cones in human retina. Instead of retinal distances, Østerberg's values⁸⁴ for corresponding perimetric angles are given. Although approximate only, especially at higher angles, such values are more useful in practice than are distances on the retina. Note that distribution of rods and cones on nasal side in and near the fovea, not given on this graph, would be approximately the same as distribution on temporal side of retina, which is seen to the left of vertical, passing through 0 degrees on the angle scale. (From Pirenne M: *Vision and the eye*, London, 1948, Pilot Press.)

to 110 million rods and 4 to 5 million cones.^{85,86} The density of rods is greater than that of cones except in the macular region, where cones are concentrated; rods are absent from the fovea,¹⁵ the macular center (Figure 4-18). Rod density is greatest in an area concentric with the fovea, beginning approximately 3 mm (7 degrees) from it.^{51,59} The number of both types of photoreceptors diminishes toward the ora serrata.

There are approximately 35.68 million bipolar cells⁸⁷ and 1.12 to 2.22 million ganglion cells.⁸⁸ The signals from numerous photoreceptors converge at one ganglion cell, indicating integration and refinement of the initial response of the photoreceptor cells.

RETINAL SYNAPSES

There are two types of synapses in the retina, electrical and chemical. The gap junction is an electrical synapse, allowing current to pass directly between cells; that is, no chemical mediator is necessary. This ensures a rapid rate of signal transmission. Gap junctions are found between photoreceptor and horizontal cells and occasionally between a bipolar terminal and an amacrine process.⁸

Chemical synapses contain synaptic vesicles that release a neurotransmitter from the presynaptic terminal

into the synaptic cleft. The transmitter binds to specific sites on the postsynaptic membrane, eliciting an excitatory or inhibitory change in that neuron. There are three types of chemical synapses in the retina—conventional, ribbon, and flat. Junctions containing a ribbonlike protein structure in the presynaptic terminal are called ribbon junctions. Triads are ribbon junctions that have three postsynaptic processes, whereas dyads have two. Flat junctions are found only at the cone pedicles.⁸

The extremely complex processing of neural signals in excitatory and inhibitory circuits within the retina is beyond the scope of this book. The reader is referred to any of several works on this subject (see References).

REGIONS OF RETINA

The retina is often described as consisting of two regions, peripheral and central. The peripheral retina is designated for detecting gross form and motion, whereas the central area is specialized for visual acuity. In area, the periphery makes up most of the retina, and rods dominate. The central retina is rich in cones, has more ganglion cells per area than elsewhere, and is a relatively small portion of the entire retina.

CLINICAL COMMENT: PERIPHERAL VISION

When the eyes are looking straight ahead, the object of interest is imaged on the macular area in the central retina, and the rest of the field that is in view, sometimes described as that seen "out of the corner of one's eye," is focused on more peripheral retinal regions. Detail and color of those objects in the central area of vision are evident but the objects in the periphery are less clear. Even slight movement in the more peripheral areas often stimulates the retina and frequently elicits a turning of the eye or head toward the motion.

CENTRAL RETINA

Macula Lutea

The **macula lutea** appears as a darkened region in the central retina and may seem to have a yellow hue because of the xanthophyll pigments lutein and zeaxanthin.^{51,89} These pigments have been found throughout the retina, with the greatest concentration in the plexiform layers of the macula.⁹⁰ The newborn has little if any of these pigments, but they gradually accumulate from dietary sources. These pigments apparently act as filters to reduce chromatic aberration but may also have an antioxidant effect, suggesting a protective role against UV radiation damage.⁸⁹ The macula lutea is approximately 5.5 mm in diameter; its center is approximately 3.5 mm lateral to the edge of the disc and approximately 1 mm inferior to the center of the disc. The pigment epithelial cells are taller and contain more pigment than cells elsewhere in the retina, which contributes to the darkness of this area. However, the intensity of the pigment varies greatly from person to person.⁵⁷ The choroidal capillary bed also is thicker in the macula lutea than elsewhere.

Useful color vision occupies an area approximately 9 mm in diameter, the center of which is the macula lutea.⁸ The entire macular region consists of the foveola, the fovea, and the parafoveal area and perifoveal area (annular regions) (Figure 4-19). These areas are described and delineated on the basis of histologic findings, with consideration given to the number and rows of cells in the nuclear layers. However, these areas are not easily differentiated on viewing the living retina.

CLINICAL COMMENT: TERMINOLOGY

*The terms used to describe the macular areas differ between the histologist and the clinician. The histologist uses the word fovea to describe what a clinician would label macula, and the histologist calls the foveola that which a clinician would label the fovea. The term **macula** is purely a clinical one and usually refers to the area of darker coloration that is approximately the same size as the optic disc; clinically the term **fovea** then refers to the very center of this area. The **posterior pole** is another term used in clinical descriptions of the fundus. There is no universal agreement regarding its definition, and its usage varies from clinician to clinician.²⁸*

Fovea (Fovea Centralis)

The shallow depression in the center of the macular region is the **fovea**, or central fovea of the retina (fovea centralis retinae). This depression is formed because the retinal cells are displaced, leaving only photoreceptors in the center. The fovea has a horizontal diameter of approximately 1.5 mm. The curved wall of the depression is known as the **clivus**, which gradually slopes to the floor, the **foveola**. The fovea has the highest concentration of cones in the retina; estimates vary from 199,000 to 300,000 cones per square millimeter.^{86,91} The number falls off rapidly as one moves away from the fovea in all directions. In this area of the retina, specialized for discrimination of detail and color vision, the ratio between cone cells and ganglion cells approaches 1:1.⁸ In more peripheral areas of the retina, which are sensitive to light detection but have poor form discrimination, there is a high ratio of rods to ganglion cells.

Within the fovea is a capillary-free zone 0.4 to 0.5 mm in diameter⁹² (Figure 4-20). The lack of blood vessels in this region allows light to pass unobstructed into the photoreceptor's outer segment.

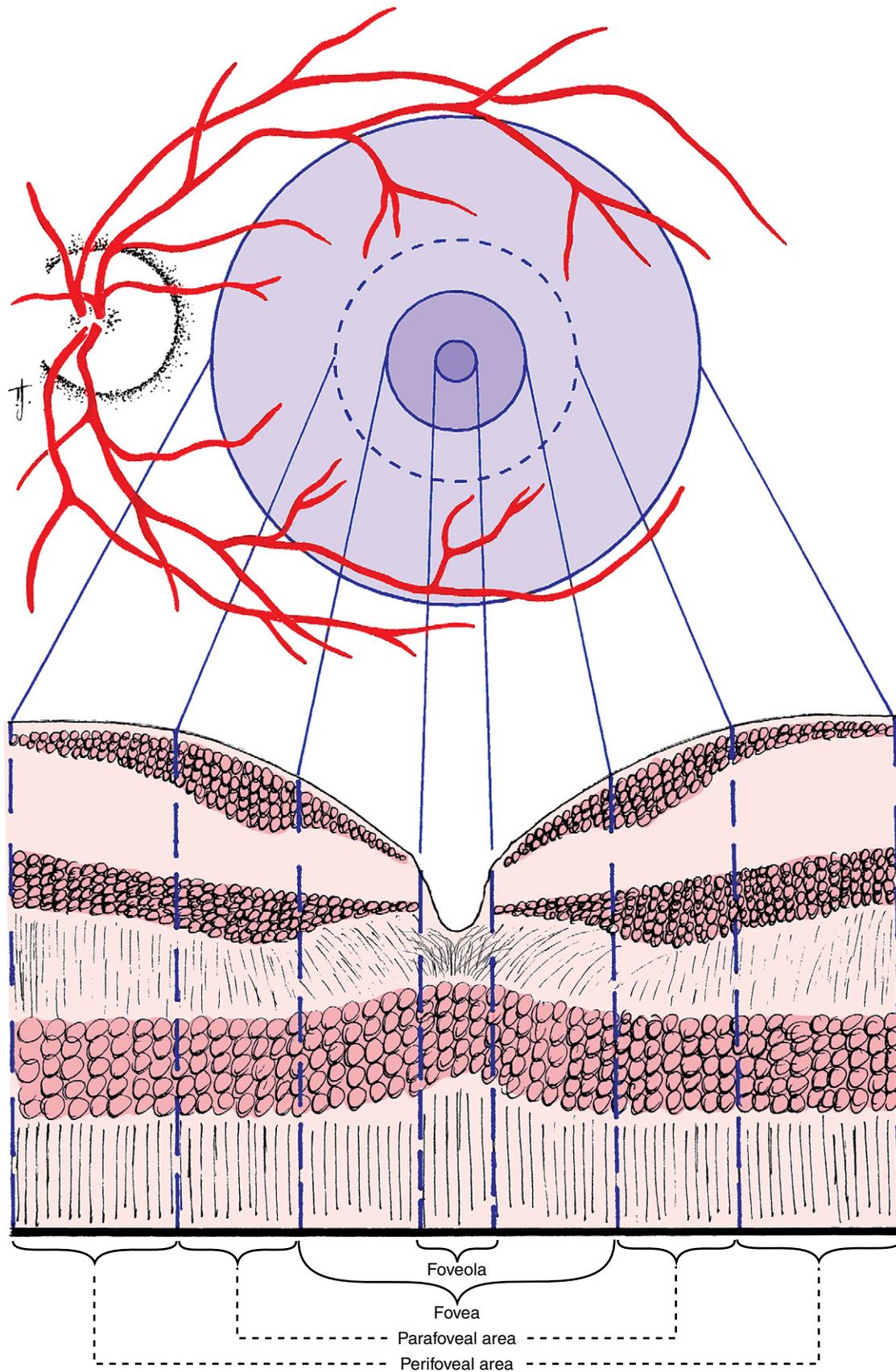
The only photoreceptors located in the center of the fovea are cones. These are tightly packed, and the outer segments are elongated, appearing rodlike in shape yet containing the visual pigments of the cone population. The external limiting membrane is displaced vitreally because of the lengthening of the outer segments. This rod-free region has a diameter of approximately 0.57 mm¹ and represents approximately 1 degree of visual field.⁹¹ Most of the other retinal elements are displaced, allowing light to reach the photoreceptors directly without interference of other retinal cells (Figure 4-21).

The cells of the inner nuclear layer and ganglion cell layer are displaced laterally and accumulate on the walls of the fovea. The photoreceptor axons become longer as they deviate away from the center; these fibers are called **Henle's fibers**. They must take an oblique course to reach the displaced bipolar and horizontal cells (Figure 4-22). This region of the OPL is known as **Henle's fiber layer**.¹

Foveola

The diameter of the **foveola** is approximately 0.35 mm. At the foveola the retina is approximately 0.13 mm thick, compared to 0.18 mm at the equator and 0.11 mm at the ora serrata.¹ The foveola contains the densest population of cones that have the smallest cross-sectional diameters of all the photoreceptors.⁸

The layers present in the foveola are the RPE, photoreceptor layer, external limiting membrane, ONL (which contains about 10 rows of cone nuclei), Henle's fiber layer, and internal limiting membrane. Moving

**FIGURE 4-19**

Regions of retina and corresponding histologic architecture.

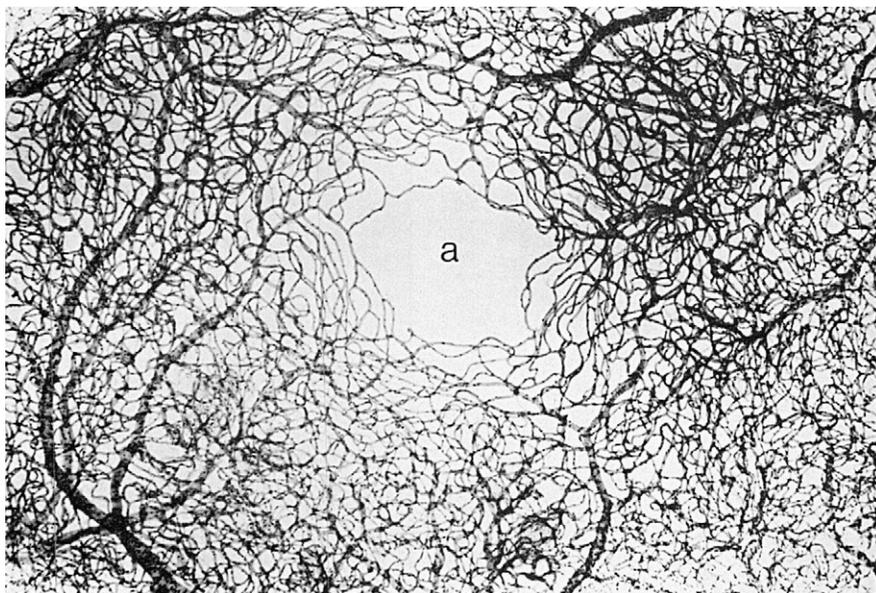


FIGURE 4-20
Capillary bed of macular region, with capillary-free zone (*a*) in its center. (×42.5.) (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

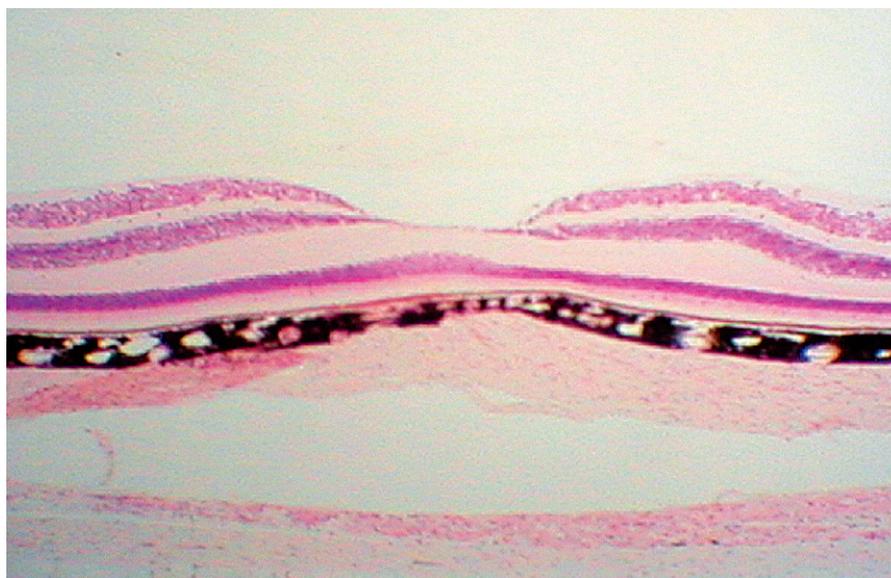
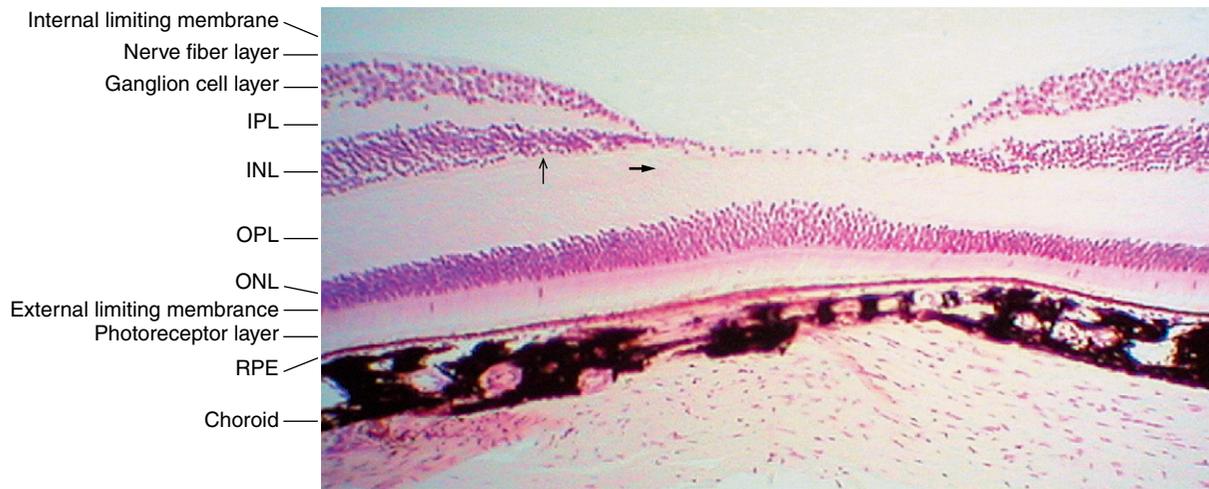


FIGURE 4-21
Light micrograph of the foveal region. The indentation caused by the absence of several retinal layers is evident.

**FIGURE 4-22**

Light micrograph of foveal region. Layers present in the center of the foveal area are RPE, photoreceptor layer, external limiting membrane, outer nuclear layer, Henle's fiber layer (note oblique orientation of fibers at heavy arrow), a few scattered nuclei from inner nuclear layer, internal limiting membrane. Light arrow shows middle limiting membrane within outer plexiform layer.

laterally along the sides of the fovea, the other layers of the retina are increasingly represented. Müller cell processes are found throughout the macular, foveal, and foveolar areas.

CLINICAL COMMENT: CENTRAL FOVEAL REFLEX

When the ophthalmoscope light shines directly into the fovea, it reflects a pinpoint of light called the **central foveal reflex**. This pinpoint reflection is caused by the parabolic shape formed by the *clivus*. Because the shape of the fovea is not always exactly parabolic, the reflection may vary in sharpness and regularity from person to person. The fovea is the site at which the object of interest is imaged. In younger persons the sheen from the internal limiting membrane sometimes is seen as a circular macular reflex (Figure 4-23).

CLINICAL COMMENT: METAMORPHOPSIA

The axis of the photoreceptor outer segment is oriented to accomplish capture of incident light rays. If a disruption occurs so that the outer segment is no longer oriented toward the exit pupil, vision may be altered. With macular edema, the orientation of the photoreceptors is changed, and **metamorphopsia** can often be elicited with an Amsler grid.⁹³

Parafoveal and Perifoveal Areas

The annular zone surrounding the fovea can be divided into an inner parafoveal area and an outer perifoveal area (see Figure 4-19). The **parafoveal zone** contains the

largest accumulation of retinal bipolar and ganglion cells. The inner nuclear layer can be 12 cells thick and the ganglion cell layer 7 cells thick.^{51,57} The **perifoveal area** begins where the ganglion cell layer is four cells thick and ends where it is one cell thick. Within the perifoveal area, the fibers of Henle's fiber layer revert to the usual orientation seen in the outer plexiform layer. The width of the parafoveal area is 0.5 mm and of the perifoveal area, 1.5 mm.¹

PERIPHERAL RETINA

Near the periphery, rods disappear and are replaced by malformed cones, the nuclear layers merge with the plexiform layers, and finally, neural retina becomes a single layer of irregular columnar cells that continue as the nonpigmented epithelium of the ciliary body. The RPE is continuous with the outer pigmented epithelium of the ciliary body, and the internal limiting membrane continues as the internal limiting membrane of the ciliary body. There are few blood vessels in the peripheral retina.

The **ora serrata** is the peripheral termination of the retina and lies approximately 5 mm anterior to the equator of the eye.⁵¹ Its name derives from the scalloped pattern of bays and dentate processes (see Chapter 3); the retina extends further anteriorly on the medial side of the eye. The ora serrata is approximately 2 mm wide and is the site of transition from the complex, multilayered neural retina to the single, nonpigmented layer of ciliary epithelium.⁹⁴ A firm attachment between the retina and vitreous, the *vitreous base*, extends several millimeters posterior to the ora serrata.

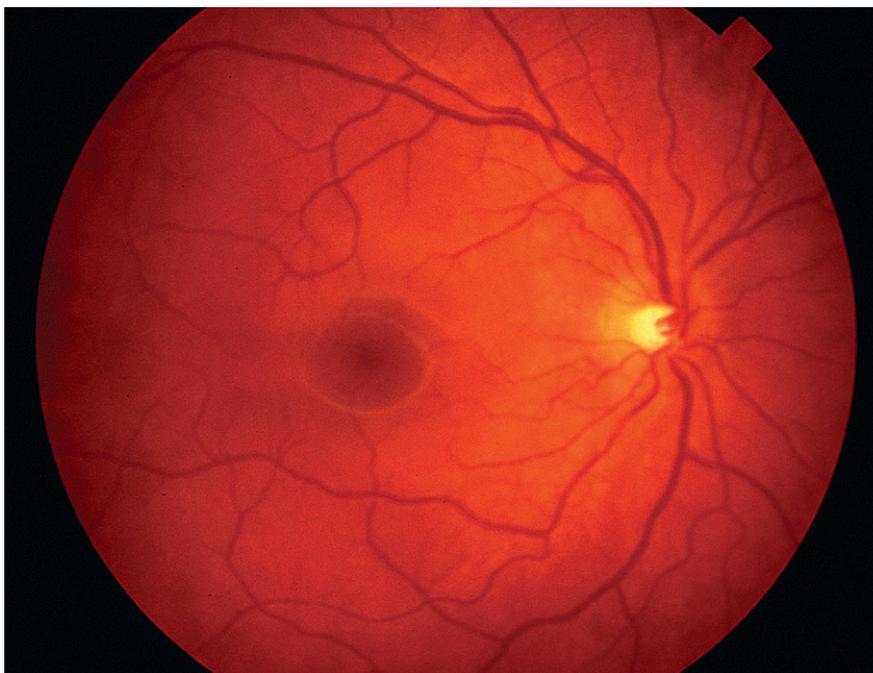


FIGURE 4-23

Normal fundus of the right eye of a teenager. The sheen from the internal limiting membrane is visible as a macular reflection. (Courtesy Pacific University Family Vision Center, Forest Grove, Ore.)

CLINICAL COMMENT: PERIPHERAL RETINAL DEGENERATION

Cystic spaces and atrophied areas often are found in peripheral retina, and their incidence increases with age. One cause for these changes is the poor blood supply in the extreme retinal periphery.^{51,57} Some conditions affecting the peripheral retina are normal, age-related changes, and others might predispose the affected individual to more serious conditions, necessitating periodic, routine, dilated-fundus examinations.

OPTIC DISC

The **optic disc**, or **optic nerve head**, is the site where ganglion cell axons accumulate and exit the eye. It is slightly elongated vertically. The horizontal diameter of the disc is approximately 1.7 mm and the vertical diameter approximately 1.9 mm.⁹⁵ The number of nerve fibers appears to be positively correlated with the size of the optic nerve head; larger discs have relatively more fibers than smaller discs. Smaller discs may demonstrate optic nerve head crowding.^{95,96} Fiber number decreases with age.⁸⁸

The optic disc lacks all retinal elements except the nerve fiber layer and an internal limiting membrane. It is paler than the surrounding retina because there is no

RPE. The pale-yellow or salmon color of the optic disc is a combination of the scleral lamina cribrosa and the capillary network. In some individuals the openings of the lamina cribrosa may be visible through the transparent nerve fibers.

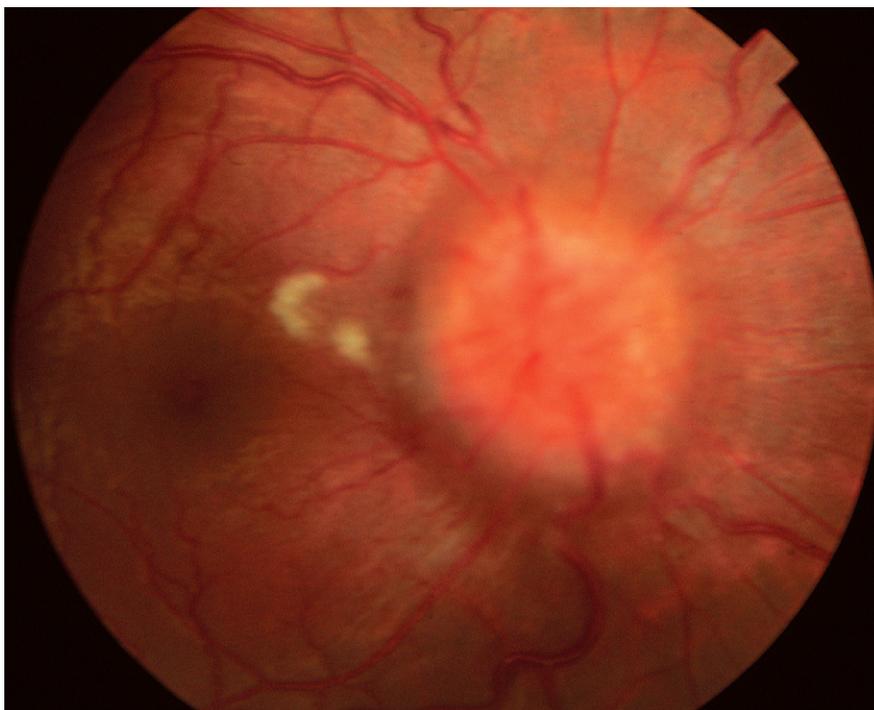
Because the disc contains no photoreceptor cells, light incident on the disc does not elicit a response; thus it represents the **physiologic blind spot**. A depression in the surface of the disc, the **physiologic cup**, varies greatly in size and depth, according to embryologic development (Figure 4-24).

Normally, the disc margins are flat and in the same plane as the retina, swelling only toward the vitreous in optic nerve head edema. Various types of crescents or rings are observed around the optic disc margin. In almost all individuals the disc edges are emphasized by a white rim of scleral tissue, where the sclera separates the optic nerve from the choroid. Different configurations in the anatomic arrangement at the disc border produce the pigmented crescent often seen outer to the scleral crescent. The RPE may not extend to the edge of the disc, and the darkly pigmented choroid might be evident. Irregular areas of hypopigmentation and hyperpigmentation of the RPE are common near the disc.^{97,98}

The optic disc serves as the site of entry for the central retinal artery and the exit site for the central retinal vein.

**FIGURE 4-24**

Variability in the normal cup-to-disc ratios. **A**, Normal fundus of right eye of young adult. Cup is small and shallow, reflection from internal limiting membrane is evident. **B**, Normal fundus of right eye showing large deep normal cup. (Courtesy Pacific University Family Vision Center, Forest Grove, Ore.)

**FIGURE 4-25**

Papilledema of right eye. Note obvious elevation of the optic nerve head. (Courtesy Pacific University Family Vision Center, Forest Grove, Ore.)

CLINICAL COMMENT: OPTIC DISC ASSESSMENT

The color of the disc, configuration and depth of the physiologic cup, cup-to-disc ratio, and appearance of the rim tissue and disc borders are assessed during an ocular health examination.

CLINICAL COMMENT: PAPILLEDEMA

Papilledema is edema of the optic disc secondary to an increase in intracranial pressure (ICP).⁹⁹ As ICP increases, pressure within the meningeal sheaths around the optic nerve slows axoplasmic flow in the ganglion fibers, causing fluid to accumulate within the fibers so that they swell.^{100,101} This accumulation of fluid is seen at the disc as an elevation of the nerve head with blurring of the disc margins (Figure 4-25). This condition is or will become bilateral. The central retinal vein may also be compromised, with hemorrhages becoming evident in the nerve fiber layer in the vicinity of the disc.

Edema of the optic disc from any other cause is referred to as simply “edema of the optic disc.”

RETINAL BLOOD SUPPLY

The outer retinal layers receive nutrition from the choroidal capillary bed; metabolites diffuse through Bruch’s membrane and the RPE into neural retina. The **central retinal artery** provides nutrients to the inner retinal layers. The artery enters the retina through the optic disc, usually slightly nasal of center, and branches into a superior and inferior retinal artery, each of which divides further into nasal and temporal branches, and these vessels continue to bifurcate (see Figure 4-24). The nasal branches run a relatively straight course toward the ora serrata, but the temporal vessels arch around the macular area en route to the periphery. The vessels are located in the nerve fiber layer just below the transparent internal limiting membrane.

Two capillary networks are formed. The *deep* capillary network lies in the inner nuclear layer near the outer plexiform layer, and the *superficial* capillary network is in the nerve fiber layer or ganglion cell layer.⁵⁷ The retina outer to the outer plexiform layer is avascular, and the outer plexiform layer is thought to receive its nutrients from both retinal and choroidal vessels. The middle limiting membrane usually is regarded as the border between the choroidal and retinal supplies.



FIGURE 4-26

Fundus of left eye. Choroidal vessels are evident as lightly colored bands deeper than the retinal vessels. (Courtesy Pacific University Family Vision Center, Forest Grove, Ore.)

A capillary-free zone directly surrounds the retinal vessels, and in the fovea, as mentioned, an area approximately 0.5 mm in diameter is free of all retinal vessels.^{1,28} Retinal vessels are said to be “end vessels” because they do not anastomose with any other system of blood vessels.⁵⁷ Retinal vessels terminate in delicate capillary arcades approximately 1 mm from the ora serrata.²⁸ The retinal capillaries are made up of a single layer of unfenestrated endothelium surrounded by a basement membrane and an interrupted layer of pericytes.^{28,57,102} Pericytes are cells with a contractile function that facilitate blood flow.¹⁰³ The endothelial cells are one part of the blood-retinal barrier because they are joined by zonula occludens.^{1,73,104,105}

A dense peripapillary network of capillaries, radially arranged around the optic nerve head, follows the arcuate course of the nerve fibers as they enter the disc.¹⁰⁶

A **cilioretinal artery** is a vessel that enters the retina from the edge of the disc but has its origin in the choroidal vasculature. Such a vessel, which nourishes the macular area, is found in approximately 15% to 20% of the population¹⁰⁷ (see Figure 11-5). A cilioretinal artery can maintain the viability of the macula if blockage of the central retinal artery occurs. Smaller, less significant cilioretinal vessels can be found in 25% of the population.¹⁰⁷

CLINICAL COMMENT: FUNDUS VIEW OF VESSELS

The retinal blood vessels are readily visible with the ophthalmoscope, and because the vessel walls are transparent, the clinician actually is seeing the column of blood within the vessel. The lighter-colored blood is the oxygenated blood of the artery, whereas the venous deoxygenated blood is slightly darker. The artery generally lies superficial to the vein. With aging and some disease processes, such as hypertension, the arterial wall may thicken and constrict the vein; this is called arteriovenous nicking.

In some individuals the pigmented choroid and its vessels are visible through the retina, and the choroidal vessels appear as flattened ribbons (Figure 4-26).

AGING CHANGES IN RETINA

Normal aging is a slow, continuous process that may predispose to pathologic changes. It is unclear, however, where normal aging changes stop and disease processes begin. The changes that occur in retinal tissue with age can be divided into several categories.

Because an estimated 33% to 50% of the central nervous system (CNS) neurons are lost during a

lifetime, the number of retinal neurons will decrease, but no reliable numbers are available. The number of nerve fibers in the optic nerve decreases, and the fibers are replaced with connective tissue as they degenerate.¹⁰⁸⁻¹¹⁰ Some studies report a decrease in foveal cones with age¹¹¹; others do not.¹¹² Rod density declines with age,¹¹² but no decrease is evident in scotopic sensitivity.¹¹³ The number of astroglial cells is reduced.¹¹⁴

The changes seen in RPE cells include pleomorphism, atrophy, depigmentation, and hyperplasia.^{2,115} Lipofuscin accumulates throughout life in the RPE and the cone inner segments and may be linked to a decrease in the lysosomal activity of enzymes in the metabolically active RPE.^{2,115,116}

Peripapillary chorioretinal atrophy, usually evident as a pale, temporal crescent, is an age-related degeneration of RPE and Bruch's membrane and may be caused by the attenuation of the peripapillary circulation.¹¹⁷ With age there is a decrease in neuroretinal rim tissue and the vertical optic cup diameter and the area of the optic cup both increase; these factors need to be considered when assessing the optic nerve head for glaucoma.¹¹⁸

Müller cells become hypertrophic with age.^{108,109}

Degenerative processes, such as "paving stone," peripheral reticular, and cystoid degeneration, occur in peripheral retina, probably linked to a decrease in blood supply. Retinal vessels become narrower, which may diminish blood flow.

CLINICAL COMMENT: VISIBLE CHANGES

Aging changes in the retina are often clinically observable. The foveal reflex dims because the internal limiting membrane thickens. The fundus color fades because RPE melanin and choroidal pigmentation are lost, making the choroidal vessels more prominent and giving the fundus a tigroid (striped) or tessellated appearance. The accumulations of debris in drusen are located in Bruch's membrane of the choroid but are observed as pinpoint deposits in the retina.

CLINICAL COMMENT: ALZHEIMER'S DISEASE

Some speculate that early changes in the retina might be diagnostic in patients with Alzheimer's disease. Some investigators report a reduction in NFL thickness related to retinal dysfunction,¹¹⁹⁻¹²¹ with the greatest reduction in the foveal region.¹²¹ Others have not found a reduction in NFL thickness.¹²² Evaluating the nerve fiber layer can be difficult but will become more accurate as technology improves. An extensive loss of neurons throughout the retina, particularly ganglion cells and glial cells, has been histologically documented in specimens from patients with Alzheimer's disease.¹²³ An increased cup-to-disc ratio and decreased rim tissue have also been observed in these patients.¹²⁴

REFERENCES

- Hogan MJ, Alvarado JA: Retina. In Hogan MJ, Alvarado JA, Weddell JE, editors: *Histology of the human eye*, Philadelphia, 1971, Saunders, p 393.
- Sharma RK, Ehinger BEJ: Development and structure of the retina. In Kaufman PL, Alm A, editors: *Adler's physiology of the eye*, ed 10, St Louis, 2003, Mosby, p 319.
- Young RW: Pathophysiology of age-related macular degeneration, *Surv Ophthalmol* 31:291, 1987.
- Ko MK, Lee WR, McKechnie NM et al: Post-traumatic hyperlipofuscinosis in the human retinal pigment epithelium, *Br J Ophthalmol* 75(1):54, 1991.
- Feeney-Burns L, Hildebrand ES, Eldridge S: Aging human RPE: morphometric analysis of macular, equatorial, and peripheral cells, *Invest Ophthalmol Vis Sci* 25:195, 1984.
- Weiter JJ, Delori FC, Wing GL et al: Retinal pigment epithelial lipofuscin and melanin and choroidal melanin in human eyes, *Invest Ophthalmol Vis Sci* 27:145, 1986.
- Guymer R, Luthert P, Bird A: Changes in Bruch's membrane and related structures with age, *Prog Ret Eye Res* 18(1):59, 1998.
- Cohen AI: The retina. In Hart MJ Jr, editor: *Adler's physiology of the eye*, ed 9, St Louis, 1992, Mosby, p 579.
- Hudspeth AJ, Yee AG: The intercellular junctional complexes of retinal pigment epithelia, *Invest Ophthalmol* 12:354, 1973.
- Fatt I, Shantinath K: Flow conductivity of retina and its role in retinal adhesion, *Exp Eye Res* 12:218, 1971.
- Kita M, Marmor MF: Systemic mannitol increases the retinal adhesive force in vivo, *Arch Ophthalmol* 109:1449, 1991.
- Yao XY, Moore KT, Marmor MF: Systemic mannitol increases retinal adhesiveness measured in vitro, *Arch Ophthalmol* 109:275, 1991.
- Marmor FM, Abdul-Rahim AS, Cohen DS: The effect of metabolic inhibitors on retinal adhesion and subretinal fluid resorption, *Invest Ophthalmol Vis Sci* 19:893, 1980.
- Kita M, Marmor MF: Effects on retinal adhesive force in vivo of metabolically active agents in the subretinal space, *Invest Ophthalmol Vis Sci* 33:1883, 1992.
- Foulds WS: The vitreous in retinal detachment, *Trans Ophthalmol Soc UK* 95:412, 1975.
- DeGuillebon H, Zanberman H: Experimental retinal detachment: biophysical aspects of retinal peeling and stretching, *Arch Ophthalmol* 87:545, 1972.
- Hollyfield JG, Varner HH, Rayborn ME et al: Retinal attachment to the pigment epithelium, *Retina* 9:59, 1989.
- Hageman GS, Marmor MF, Yao XY et al: The interphotoreceptor matrix mediates primate retinal adhesion, *Arch Ophthalmol* 113(5):655, 1995.
- Hollyfield JG, Varner HH, Rayborn ME: Regional variation within the interphotoreceptor matrix from fovea to the retinal periphery, *Eye* 4:333, 1990.
- Hollyfield JG, Rayborn ME, Landers RA et al: Insoluble interphotoreceptor matrix domains surround rod photoreceptors in the human retina, *Exp Eye Res* 51:107, 1990.
- Miezewska K: The interphotoreceptor matrix, a space in sight, *Microsc Res Tech* 35(6):463, 1996.
- Marmor MF, Yao XY, Hageman GS: Retinal adhesiveness in surgically enucleated human eyes, *Retina* 14(2):181, 1994.
- Nicolaisson B Jr: Connections between the sensory retina and the retinal pigment epithelium, *Acta Ophthalmol (Copenh)* 63:68, 1985.
- Lazarus HS, Hageman GS: Xyloside-induced disruption of interphotoreceptor matrix proteoglycans results in retinal detachment, *Invest Ophthalmol Vis Sci* 33:364, 1992.
- Sigleman J, Ozanics V: Retina. In Jakobiec FA, editor: *Ocular anatomy, embryology, and teratology*, Philadelphia, 1982, Harper & Row, p 441.

26. Tombran-Tink J, Shivaram SM, Chader GJ et al: Expression, secretion, and age-related downregulation of pigment epithelium-derived factor, a serpin with neurotrophic activity, *J Neurosci* 15(7, pt 1):4992, 1995.
27. Young RW: The renewal of the photoreceptor cell outer segments, *J Cell Biol* 33:61, 1967.
28. Fine BS, Yanoff M: The retina. In Fine BS, Yanoff M, editors: *Ocular histology*, ed 2, Hagerstown, Md, 1979, Harper & Row, p 59.
29. Fine BS, Zimmerman LE: Observations on the rod and cone layer of the retina, *Invest Ophthalmol* 2:446, 1963.
30. Laties A, Liebman P, Campbell C: Photoreceptor orientation in the primate eye, *Nature* 218:172, 1968.
31. Laties A, Enoch J: An analysis of retinal receptor orientation. I. Angular relationship of neighboring photoreceptors, *Invest Ophthalmol* 10:69, 1971.
32. Arikawa K, Molday LL, Molday RS et al: Localization of peripherin/rds in the disk membranes of cone and rod photoreceptors: relationship to disk membrane morphogenesis and retinal degeneration, *J Cell Biol* 116(3):659, 1992.
33. Young RW, Bok D: Participation of the retinal pigment epithelium in the rod outer segment process, *J Cell Biol* 42:392, 1969.
34. Young RW: The renewal of rod and cone outer segments in rhesus monkey, *J Cell Biol* 49:303, 1971.
35. Bok D: Retinal photoreceptor-pigment epithelium interactions, *Invest Ophthalmol Vis Sci* 26:1659, 1985.
36. Young RW: Shedding of discs from rod outer segments in the rhesus monkey, *J Ultrastruct Res* 34:190, 1971.
37. LaVail MM: Rod outer segment disk shedding in rat retina, *Science* 194:1071, 1976.
38. Basinger S, Hoffman R, Matthews M: Photoreceptor shedding is initiated by light in the frog retina, *Science* 194:1074, 1978.
39. Young RW: The daily rhythm of shedding and degradation of rod and cone outer segment membranes in the chick retina, *Invest Ophthalmol Vis Sci* 17:105, 1978.
40. Migdale K, Herr S, Klug K et al: Two ribbon synaptic units in rod photoreceptors of macaque, human, and cat, *J Comp Neurol* 455(1):100, 2003 (abstract).
41. Kolb H, Famiglietti EV: Rod and cone pathways in retina of cat, *Invest Ophthalmol Vis Sci* 15:935, 1976.
42. Anderson DH, Fisher SK, Steinberg RH: Mammalian cones: disc shedding, phagocytosis, and renewal, *Invest Ophthalmol Vis Sci* 17:117, 1978.
43. Walls GL: Human rods and cones, *Arch Ophthalmol* 12:914, 1934.
44. Young RW: A difference between rods and cones in the renewal of outer segment protein, *Invest Ophthalmol* 8:222, 1969.
45. Eckmiller MS: Distal invaginations and the renewal of cone outer segments in anuran and monkey retinas, *Cell Tissue Res* 260:19, 1990.
46. Hogan MJ, Wood I, Steinberg RH: Phagocytosis by pigment epithelium of human retinal cones, *Nature* 25:305, 1974.
47. O'Day WT, Young RW: Rhythmic daily shedding of outer segment membranes by visual cells in the goldfish, *J Cell Biol* 76:593, 1978.
48. Raviola E, Gilula NB: Intramembrane organization of specialized contacts in the outer plexiform layer of the retina: a freeze-fracture study in monkey and rabbits, *J Cell Biol* 65:192, 1975.
49. Ayoub GS, Matthews G: Substance P modulates calcium current in retinal bipolar neurons, *Vis Neurosci* 8(6):539, 1992.
50. Kolb H, Linberg KA, Fisher SK: Neurons of the human retina: a Golgi study, *J Comp Neurol* 318(2):147, 1992.
51. Park SS, Sigelman J, Gragoudas ES: The anatomy and cell biology of the retina. In Tasman W, Jaeger EA, editors: *Duane's foundations of clinical ophthalmology*, vol 1, Philadelphia, 1994, Lippincott.
52. Bloomfield SA, Dacheux RF: Rod vision: pathways and processing in the mammalian retina, *Prog Ret Eye Res* 20(3):384, 2001.
53. Boycott BB, Hopkins JM: Cone bipolar cells and cone synapses in the primate retina, *Vis Neurosci* 7(1-2):49, 1991.
54. Polyak SL: *The retina*, Chicago, 1941, Chicago University Press.
55. Mariani AP: Bipolar cells in the monkey retina selective for cones likely to be blue sensitive, *Nature* 308:184, 1984.
56. Witkorsky P: Functional anatomy of the retina. In Tasman W, Jaeger EA, editors: *Duane's foundations of clinical ophthalmology*, vol 1, Philadelphia, 1994, Lippincott.
57. Warwick R: The eyeball. In Warwick R, editor: *Eugene Wolff's anatomy of the eye and orbit*, ed 7, Philadelphia, 1976, Saunders, p 99.
58. Kolb H, Dekorvar L: Midget ganglion cells of the parafovea of the human retina: a study by electron microscopy and serial section reconstructions, *J Comp Neurol* 303(4):617, 1991.
59. Hart M: Visual adaptation. In Hart WM Jr, editor: *Adler's physiology of the eye*, ed 9, St Louis, 1992, Mosby, p 523.
60. Kolb H, Fernandez E, Nelson R: The organization of the vertebrate retina, September 2003, Webvision.med.utah.edu/
61. Kolb H, Ahuelt P, Fisher SK et al: Chromatic connectivity of the three horizontal cell types in the human retina, *Invest Ophthalmol Vis Sci* 30(suppl):348, 1989.
62. Dowling JE, Boycott BB: Neural connections of the retina: fine structure of the inner plexiform layer, *Cold Spring Harb Symp Quant Biol* 30:383, 1965.
63. Kolb H: Amacrine cells of the mammalian retina: neurocircuitry and functional roles, *Eye* 11:904, 1997.
64. Linberg KA, Fisher SK: Ultrastructure of the interplexiform cell of the human retina, *Invest Ophthalmol Vis Sci* 24(suppl):259, 1983.
65. Ogden TE: Nerve fiber layer of the primate retina: thickness and glial contents, *Vis Res* 23:581, 1983.
66. Newman E, Reichenbach A: The Müller cell: a functional element of the retina, *Trends Neurosci* 19(8):307, 1996.
67. Kuwabara T, Cogan D: Retinal glycogen, *Arch Ophthalmol* 66:680, 1961.
68. Newman EA: Membrane physiology of retina glial (Müller) cells, *J Neurosci* 5:2225, 1985.
69. Reichenbach A, Stolzenburg JU, Eberhardt W et al: What do retinal Müller (glial) cells do for their neuronal "small siblings"? *J Chem Neuroanat* 6(4):210, 1993.
70. Ramirez JM, Triviño A, Ramírez AI et al: Structural specializations of human retinal glial cells, *Vis Res* 36(14):2029, 1996.
71. LaCour M: The retinal pigment epithelium. In Kaufman PL, Alm A, editors: *Adler's physiology of the eye*, ed 10, St Louis, 2003, Mosby, p 348.
72. Panda-Jonas S, Jonas JB, Jakobczyk-Zmija M: Retinal pigment epithelial cell count, distribution, and correlations in normal human eyes, *Am J Ophthalmol* 121:181, 1996.
73. Cunha-Va JG: The blood-ocular barriers: past, present, and future, *Doc Ophthalmol* 93:149, 1997.
74. Bok D: The retinal epithelium: a versatile partner in vision, *J Cell Sci Suppl* 17:189, 1993.
75. Grierson I, Hiscott P, Hogg P, et al: Development, repair and regeneration of the retinal pigment epithelium, *Eye* 8(pt 2):255, 1994.
76. Zinn KM, Benjamin-Henkind J: Retinal pigment epithelium. In Jakobiec FA, editor: *Ocular anatomy, embryology, and teratology*, Philadelphia, 1982, Harper & Row, p 533.
77. Martini B, Pandey R, Ogden TE et al: Cultures of human retinal pigment epithelium: modulation of extracellular matrix, *Invest Ophthalmol Vis Sci* 33(3):516, 1992.
78. Usui S, Kamiyama Y, Ishii H et al: Reconstruction of retinal horizontal cell responses by the ionic current model, *Vis Res* 35(12):1711, 1996 (abstract).
79. Kolb H: Organization of the outer plexiform layer of the primate retina: electron microscopy of Golgi-impregnated cells, *Philos Trans R Soc Lond B Biol* 258:261, 1970.

80. Dowling JE, Boycott BB: Organization of the primate retina: electron microscopy, *Proc R Soc Lond B Biol* 166:80, 1966.
81. Marks WB, Dobelle WH, MacNichol EF Jr: Visual pigments of single primate cones, *Science* 43:1181, 1964.
82. Kolb H: The architecture of functional neural circuits in the vertebrate retina, *Invest Ophthalmol* 35(5):2385, 1994.
83. Horton JC: The central visual pathways. In Hart WM Jr, editor: *Adler's physiology of the eye*, ed 9, St Louis, 1992, Mosby, p 728.
84. Østerberg GA: Topography of the layer of rods and cones in the human retina, *Acta Ophthalmol (Copenh)* 6:1, 1935.
85. Farber DB, Flannery JG, Lolley RN et al: Distribution patterns of photoreceptors, protein, and cyclic nucleotides in the human retina, *Invest Ophthalmol Vis Sci* 26:1558, 1985.
86. Curcio CA, Sloan KR, Kalina RE et al: Human photoreceptor topography, *J Comp Neurol* 292:497, 1990.
87. Oettel O: Untersuchungen Über Die Retinaganglien und Optikusfasern. In Rohen JW, editor: *The structure of the eye*, vol 2, Stuttgart, 1965, Verlag, p 97.
88. Jonas JB, Gusek GC, Naumann GO: Optic disc, cup, and neuroretinal rim size, configuration and correlations in normal eyes, *Invest Ophthalmol Vis Sci* 29:1151, 1988.
89. Rapp LM, Maple SS, Choi JH: Lutein and zeaxanthin concentrations in rod outer segment membranes from perifoveal and peripheral human retina, *Invest Ophthalmol Vis Sci* 41:1200, 2000.
90. Nussbaum JJ, Pruett RC, Delori FC: Historic perspectives: macular yellow pigment—the first 200 years, *Retina* 1(14):296, 1981.
91. Ahnelt PK: The photoreceptor mosaic, *Eye* 12:531, 1998.
92. Yamada E: Some structural features of the fovea centralis in the human retina, *Arch Ophthalmol* 82:151, 1969.
93. Kanski JJ: *Clinical ophthalmology*, ed 3, London, 1994, Butterworth-Heinemann, p 383.
94. Pei TF, Smelser GK: Some fine structural features of the ora serrata region in primate eyes, *Invest Ophthalmol Vis Sci* 7:672, 1968.
95. Jonas JB, Schmidt AM, Müller-Bergh JA et al: Human optic nerve fiber count and optic disc size, *Invest Ophthalmol Vis Sci* 33(6):2012, 1992.
96. Quigley HA, Brown AE, Morrison JD et al: The size and shape of the optic disc in normal human eyes, *Arch Ophthalmol* 108(1):51, 1990.
97. Hogan MJ, Alvarado JA, Weddell JE, editors: *Histology of the human eye*, Philadelphia, Saunders, 1971, p 523.
98. Fantes FE, Anderson DR: Clinical histologic correlation of human peripapillary anatomy, *Ophthalmology* 96(1):20, 1989.
99. Alexander LJ: Diseases of the optic nerve. In Bartlett JD, Jaanus SD, editors: *Clinical ocular pharmacology*, ed 2, Boston, 1989, Butterworth, p 690.
100. Hayreh SS: Optic disc edema in raised intracranial pressure, *Arch Ophthalmol* 95:1566, 1977.
101. Wirtschafter JD, Rizzo FJ, Smiley BC: Optic nerve axoplasm and papilledema, *Surv Ophthalmol* 20:157, 1977.
102. Cogan DG, Kuwabara T: The mural cell in perspective, *Arch Ophthalmol* 78:133, 1967.
103. Chakravarthy U, Gardiner TA: Endothelium-derived agents in pericyte function/dysfunction, *Prog Ret Eye Res* 18(4):511, 1999.
104. Shakib M, Cunha-Vaz JH: Studies on the permeability of the blood-retinal barrier. IV. Junctional complexes of the retinal vessels and their role in the permeability of the blood-retinal barrier, *Exp Eye Res* 5:229, 1966.
105. Bernstein MH, Hollenberg MJ: Fine structure of the chorio-capillaris and retinal capillaries, *Invest Ophthalmol* 4(6):1016, 1965.
106. Henkind P: Radial peripapillary capillaries of the retina: anatomy—human and comparative, *Br J Ophthalmol* 51:115, 1967.
107. Hayreh SS: The central artery of the retina: its role in the blood supply of the optic nerve, *Br J Ophthalmol* 47:651, 1963.
108. Paasche G, Gartner U, Germer A et al: Mitochondria of retina Müller (glial) cells: the effect of aging and of application of free radical scavengers, *Ophthalmic Res* 32:229, 2000.
109. Bringmann A, Biedermann B, Schnurbusch U et al: Age- and disease-related changes of calcium channel-mediated currents in human Müller glial cells, *Invest Ophthalmol Vis Sci* 14:2791, 2000.
110. Dohlman CL, McCormick AQ, Drance SM: Aging of the optic nerve, *Arch Ophthalmol* 98:2053, 1980.
111. Yuodelis C, Hendrickson A: A qualitative and quantitative analysis of the human fovea during development, *Vis Res* 26:847, 1986.
112. Curcio CA: Photoreceptor topography in ageing and age-related maculopathy, *Eye* 15(3):376, 2001.
113. Jackson GR, Owsley C, Cordle EP et al: Aging and scotopic sensitivity, *Vis Res* 38:3655, 1998.
114. Ramirez JM, Ramirez AI, Salazar JJ et al: Changes of astrocytes in retinal ageing and age-related macular degeneration, *Exp Eye Res* 73:601, 2001.
115. Yoo SH, Adammis AP: Retinal manifestations of aging, *Int Ophthalmol Clin* 38(1):95, 1998.
116. Boulton M, Dayhaw-Barker P: The role of the retinal pigment epithelium: topographical variation and ageing changes, *Eye* 15:384, 2001.
117. Curcio CA, Saunders PL, Younger PW et al: Peripapillary chorioretinal atrophy, *Ophthalmology* 107:334, 2000.
118. Garway-Heath DF, Wollstein G, Hitchings RA: Aging changes of the optic nerve head in relation to open angle glaucoma, *Br J Ophthalmol* 81(10):840, 1997.
119. Parisi V, Restuccia R, Fattapposta F et al: Morphological and functional retinal impairment in Alzheimer's disease patients, *Clin Neurophysiol* 112(10):1860, 2001.
120. Hedges TR III, Perez GR, Speigelman D et al: Retinal nerve fiber layer abnormalities in Alzheimer's disease, *Acta Ophthalmol Scand* 74(3):217, 1996.
121. Blanks JC, Schmidt SY, Torigoe Y et al: Retinal pathology in Alzheimer's disease. II. Regional neuron loss and glial changes in GCL, *Neurobiol Aging* 17(3):385, 1996.
122. Justino L, Kergoat M, Bergman H et al: Neuroretinal function is normal in early dementia of the Alzheimer type, *Neurobiol Aging* 22(4):691, 2001.
123. Blanks JC, Torigoe Y, Hinton DR et al: Retinal pathology in Alzheimer's disease. I. Ganglion cell loss in foveal/parafoveal retina, *Neurobiol Aging* 17(3):377, 1996.
124. Tsai CS, Ritch R, Schwartz B et al: Optic nerve head and nerve fiber layer in Alzheimer's disease, *Arch Ophthalmol* 109:199, 1991.

5 Crystalline Lens

The **crystalline lens** is an avascular, transparent elliptic structure that aids in focusing light rays on the retina. The lens is located within the posterior chamber, anterior to the vitreous chamber and posterior to the iris (Figure 5-1). The lens is suspended from the surrounding ciliary body by zonular fibers. It is malleable, and ciliary muscle contraction can cause a change in lens shape, increasing the dioptric power of the eye. This mechanism that causes an increase in lens power is **accommodation**, which allows near objects to be focused on the retina.

The posterior lens surface is attached to the anterior vitreous face by the **hyaloid capsular ligament**, a circular ring adhesion. Within this ring is a potential space, the **retrolental space (of Berger)**, an area of non-adhesion between vitreous and lens (see Figure 6-12).

LENS DIMENSIONS

The lens is biconvex, with the posterior surface having the steeper curve. The anterior radius of curvature measures 8 to 14 μm , and the posterior surface radius of curvature measures 5 to 8 μm . The centers of the anterior and posterior surfaces are called the **poles**, and the **lens thickness** is the distance from anterior to posterior pole. The thickness of the unaccommodated lens is 3.5 to 5 mm and it increases 0.02 mm each year throughout life.^{1,2} The **lens diameter** is the nasal-to-temporal measurement and in the infant is 6.5 mm; the diameter reaches 9 mm during the teenage years and does not change significantly from that.^{3,4} The **equator** is the largest circumference of the lens at a location between the two poles.

The refractive power of the unaccommodated lens is approximately 20 diopters (D) and depends on the (1) surface curvatures, (2) refractive index, (3) change in index between the lens and surrounding environment, and (4) length of the optical path. The lens has a *gradient* refractive index because of changes in optical density throughout the lens; the index increases from the anterior to the center of the lens and decreases toward the posterior surface. The refractive index is a factor of protein concentration within the lens fibers.⁵ The variations in index provide additional refractive power.^{6,7} The power of the lens increases in accommo-

modation, with the maximum accommodative amplitude, 14 D, reached between ages 8 and 12 years.⁸ Accommodation decreases with age, approaching zero after 50 years.⁹

EMBRYOLOGIC DEVELOPMENT

The structure of the adult lens is determined during embryologic development. The **lens vesicle**, the first lenslike structure observable in the developing embryo, is composed of a layer of epithelial cells that form a hollow sphere. The cells are positioned so that the apical surface lines the lumen of this sphere. The posterior cells differentiate and elongate, forming the **primary lens fibers**. As these fibers grow and reach the anterior cells (Figure 5-2), the center of the sphere fills. Thus the adult lens has no posterior epithelium because it was used to form these first lens fibers. During the rest of the life of the lens, cell division occurs in the germinative zone of the epithelium just anterior to the lens equator, and the cells thus formed elongate to form secondary lens fibers that are laid down outer to all earlier fibers. With age the lens continues to grow as it forms new fibers (see Chapter 7).

HISTOLOGY

LENS CAPSULE

The **lens capsule** is a transparent envelope that surrounds the entire lens. Its thickness varies with location, being thinnest at the poles and equator and thickest in an annular area around the anterior pole. The capsule is a basement membrane and with time becomes the thickest in the body.¹⁰ The capsule consists primarily of collagen; it contains no elastic fibers but is highly elastic because of the lamellar arrangement of the fibers.^{3,11} It encloses all lens components and helps to mold the shape of the lens. The capsule would prefer to take a more spheric shape, but this tendency is counteracted by the pull from the zonular fibers. The zonular fibers insert into the capsule, merging with it in an area from the equator to near both poles. This outer superficial zone of the capsule is called the *zonular lamella*.³ The lens capsule provides some barrier function preventing

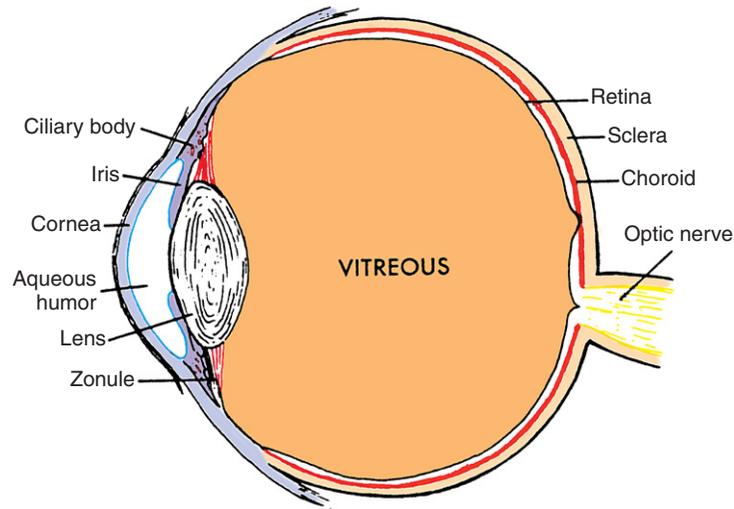


FIGURE 5-1
Diagram showing relationship of the lens and zonule to other ocular structures. (From Paterson CA, Delamere NA: The lens. In Hart WM Jr, editor: *Adler's physiology of the eye*, ed 9, St Louis, 1992, Mosby.)

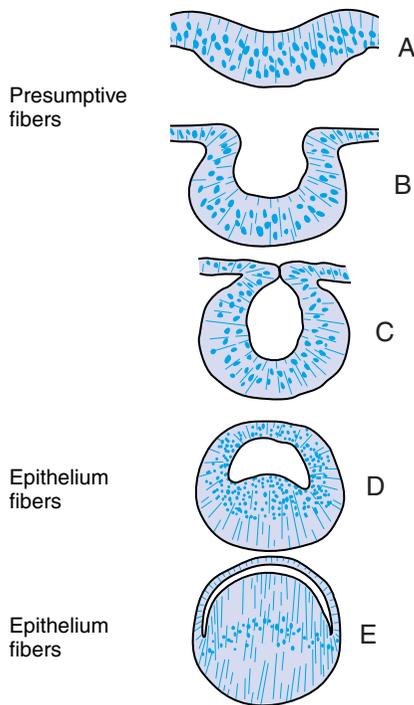


FIGURE 5-2
Development of embryonic nucleus. **A**, Formation of lens placode, precursor of lens. **B**, Invagination forming lens vesicle. **C**, Hollow lens vesicle lined with epithelium. **D**, Posterior cells elongate, becoming primary lens fibers. **E**, Primary lens fibers fill lumen, forming embryonic nucleus. Curved line formed by cell nuclei is lens bow. Anterior epithelium remains in place.

large molecules, such as albumin and hemoglobin,³ from entering the lens. The *anterior lens capsule* is produced by the anterior epithelium and thickens with age. The *posterior lens capsule* may receive some contribution from the basal membrane of lens fibers, but the thickness of the posterior capsule changes minimally throughout life¹²⁻¹⁴ (Figure 5-3).

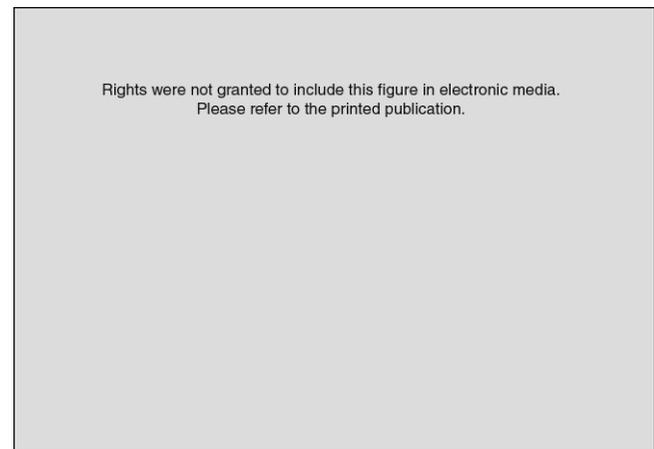
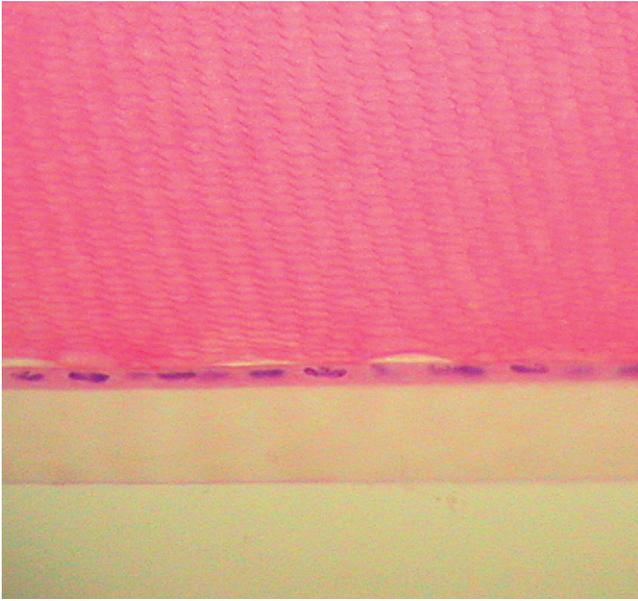


FIGURE 5-3
Thickness of the anterior and posterior lens capsule in relation to age. (From Krag S, Andreassen TT: *Invest Ophthalmol Vis Sci* 44(2):691, 2003.)

**FIGURE 5-4**

Light micrograph of anterior lens epithelium and capsule. Honeycomb appearance of lens fibers above epithelium.

LENS EPITHELIUM

Adjacent to the anterior lens capsule is a layer of cuboidal epithelium, the **anterior lens epithelium** (Figure 5-4). These cells secrete the anterior capsule throughout life and are the site of metabolic transport mechanisms. As noted, no posterior epithelium is present because it was used during embryologic development to form the primary lens fibers. The basal aspect of the epithelial cell is adjacent to the capsule, and the apical portion is oriented inward toward the center of the lens. The lateral membranes of the epithelial cells are joined by desmosomes and gap junctions.^{13,15-18} Although zonula occludens were once thought to join the epithelial cells,¹⁹ more recent studies report few, if any, tight junctions.¹⁴

The band of cells in the preequatorial region that lies just anterior to the equator is called the **germinal zone**, the location of cell mitosis. As cell division continues throughout life, each newly formed cell elongates; the basal aspect stretches toward the posterior pole and the apical aspect toward the anterior pole (Figure 5-5). This process occurs all around the equator, with fibers stretching toward the poles from all aspects of the lens periphery. As the cells in each layer elongate, the cellular nuclei move with the cytoplasm. A line drawn to connect the dots of these nuclei would have an arcuate shape toward the anterior aspect, a configuration called the **lens bow** (see Figure 5-2). Eventually, as it loses all cellular organelles, the elongated cell becomes a lens

fiber. The anterior end of the lens fiber (the apical surface) insinuates itself between the epithelial layer and the underlying lens fibers. The new fibers are laid down outer to the older fibers; the more superficial fibers are longer than deeper fibers, and the youngest cells lie directly below the epithelium and the capsule. All fibers formed from mitosis in the generative zone are called **secondary lens fibers**. Once it loses its nucleus, the mature lens fiber has lost its attachment to the basement membrane.¹³

LENS FIBERS

Lens fiber production continues throughout life, with the new lens fibers being laid down outer to the older fibers; growth results in concentric layers of secondary lens fibers. The structure of the lens is similar to an onion; each layer of fibers approximates a layer of an onion, but then each layer is made up of adjacent fibers. A section through the equator of the lens shows that the fibers cut in cross section are hexagonal in shape and arranged in concentric rings (Figure 5-6). Lens fiber length is approximately 8 to 10 nm.¹⁰ Each fiber has a long crescent shape, with the broad sides parallel to the lens surface and the narrow sides at an angle to the surface and located near the lens poles.

Lens fiber cytoplasm contains a high concentration of proteins, known as **crystallins**, which account for approximately 40% of the net weight of the fiber. The distribution and concentration of crystallins contribute to the gradient refractive index.²⁰ The crystallin concentration varies from approximately 15% in the cortex to 70% in the nucleus.²¹ A cytoskeletal network of microtubules and filaments provides structure and also provides stability by being anchored to the plasma membrane.^{14,20} The lateral membranes have numerous and elaborate interdigitations along the fiber length that take various shapes, such as ball-and-socket and tongue-in-groove junctions, and allow for sliding between fibers^{3,13,14} (Figure 5-7). The fibers also are joined by desmosomes.

Because the lens has no vascular supply and the fibers lose their cellular organelles as they age, some cell-to-fiber and fiber-to-fiber mechanism of communication is necessary. Investigators had assumed an extensive network of gap junctions throughout the lens to account for the facility with which nutrients and ions move within the lens,^{13,22} but recent investigations have questioned this premise. The junctions present along the lens fiber lateral membranes have a distinct morphology that is comparable to gap junctions seen in other epithelial tissue, but there is some reluctance to call them "gap junctions."^{14,17} The lens fiber junctions have a different packing arrangement than the typical gap junction, as well as a different protein connexon

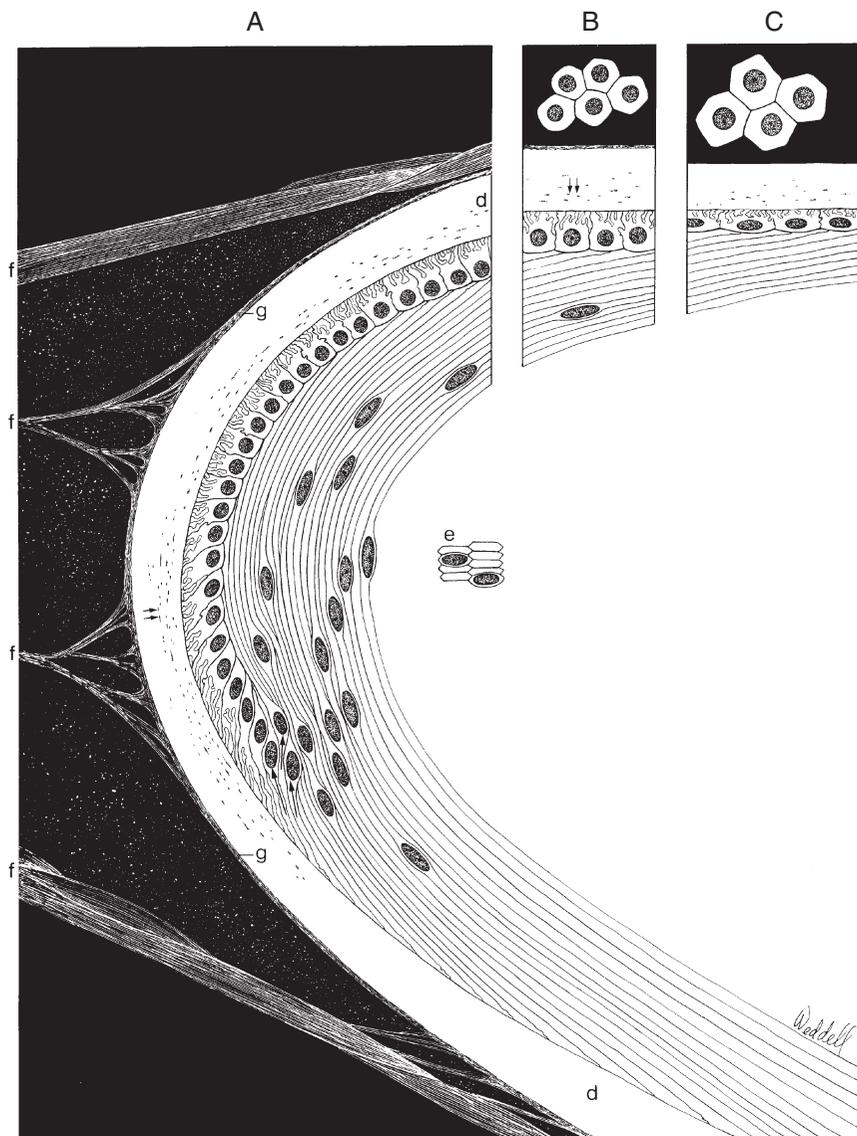


FIGURE 5-5

Composite drawing of crystalline lens, cortex, epithelium, capsule, and zonular attachments. **A**, Anterior central lens epithelium, seen in flat section and cross section. Size and shape of these cells can be compared with those of cells in **B**, intermediate zone, and **C**, equatorial zone. At equator, dividing cells are elongating (*arrows*) to form lens cortical cells. As they elongate, cells send processes anteriorly and posteriorly toward sutures, and their nuclei migrate somewhat anterior to equator to form lens bow. At the same time, nuclei become more and more displaced into lens as new cells are formed at equator. Lens capsule (*d*) is thicker anterior and posterior to equator than at equator itself. Anterior and equatorial capsule contains fine filamentous inclusions (*double arrows*); these are not present posteriorly. Lens fibers elongate into flattened hexagons (*e*) in cross section. Zonular fibers (*f*) attach to anterior and posterior capsule and to equatorial capsule, forming pericapsular or zonular lamella of lens (*g*). (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

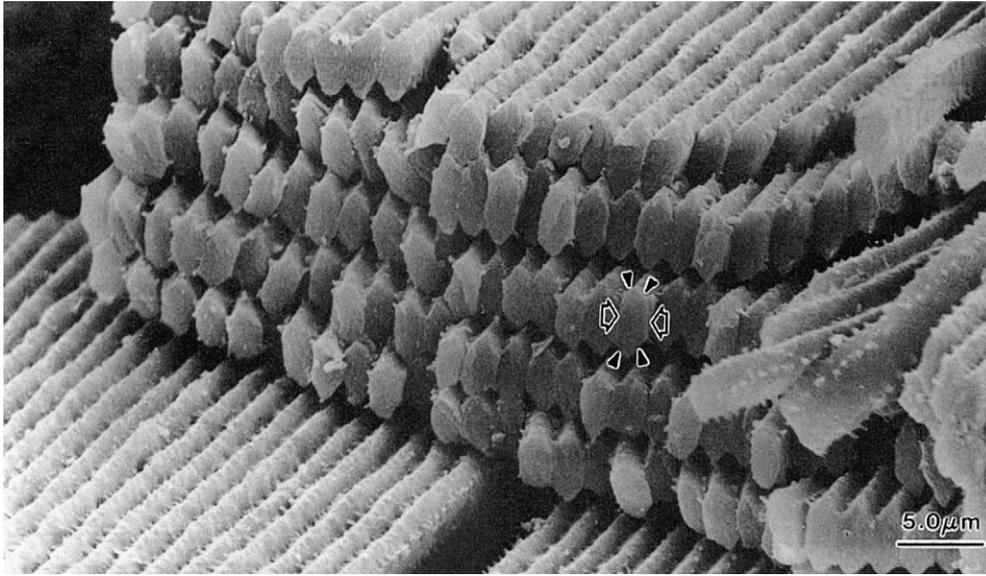


FIGURE 5-6

Scanning electron micrograph shows characteristic hexagonal cross-sectional profiles of lens fiber cells. (From Paterson CA, Delamere NA: *The lens*. In Hart WM Jr, editor: *Adler's physiology of the eye*, ed 9, St Louis, 1992, Mosby.)

forming the channels.¹⁷ The junctions so identified are not evenly distributed throughout the lens, with few near the poles, more toward the equator, and seemingly fewer junctions in deeper layers.^{10,17,18} Micropinocytic vesicles at apical and basal aspects of fiber membranes and significant areas of membrane fusion also allow movement of material from fiber to fiber, contributing to communication between fibers in addition to the gap-type junctions described.^{10,16,18,23}

EPITHELIUM-FIBER INTERFACE

The border between the apical membrane of the anterior epithelium and the apical membrane of the elongating fiber is known as the epithelium-fiber interface (EFI). Nutrients and ions are exchanged across the EFI. It was once assumed that such movement was facilitated by gap junctions, but disagreement now exists on whether gap junctions are present.^{15,18,22,23} Gap junctions are usually found on the lateral cell membrane, and the EFI involves apical surfaces. Few true gap junctions have been visualized in tissue preparations. Minimal coupling occurs between the epithelium and fibers in the central zone (i.e., near the poles and sutures), but such junctions increase toward the germinative zone.¹⁷

Pinocytosis does occur at this interface, facilitating exchange.¹⁴

DIVISIONS OF LENS

The primary lens fibers from the elongating posterior epithelium form the very center, the **embryonic nucleus**, and all subsequent lens fibers are laid down outer to this core. Cell mitosis then begins in the preequatorial region of the epithelium, and the new cell elongates, forming a lens fiber. All such fibers formed are secondary lens fibers. The fibers laid down around the embryonic nucleus before birth are known as the **fetal nucleus**. The fibers formed between birth and sexual maturation form the **adult nucleus**. The **lens cortex** contains the fibers formed after sexual maturation (Figure 5-8, C). The cortex can be divided into superficial, internal, and deep zones,¹⁰ but these are arbitrary divisions and generally are not clinically significant. Some consider the fibers formed before sexual maturation the "juvenile nucleus," those added before middle age the "adult nucleus," and the remaining fibers the "cortex."²⁰ The lens cortex has the lowest and the embryonic nucleus has the highest index of refraction.

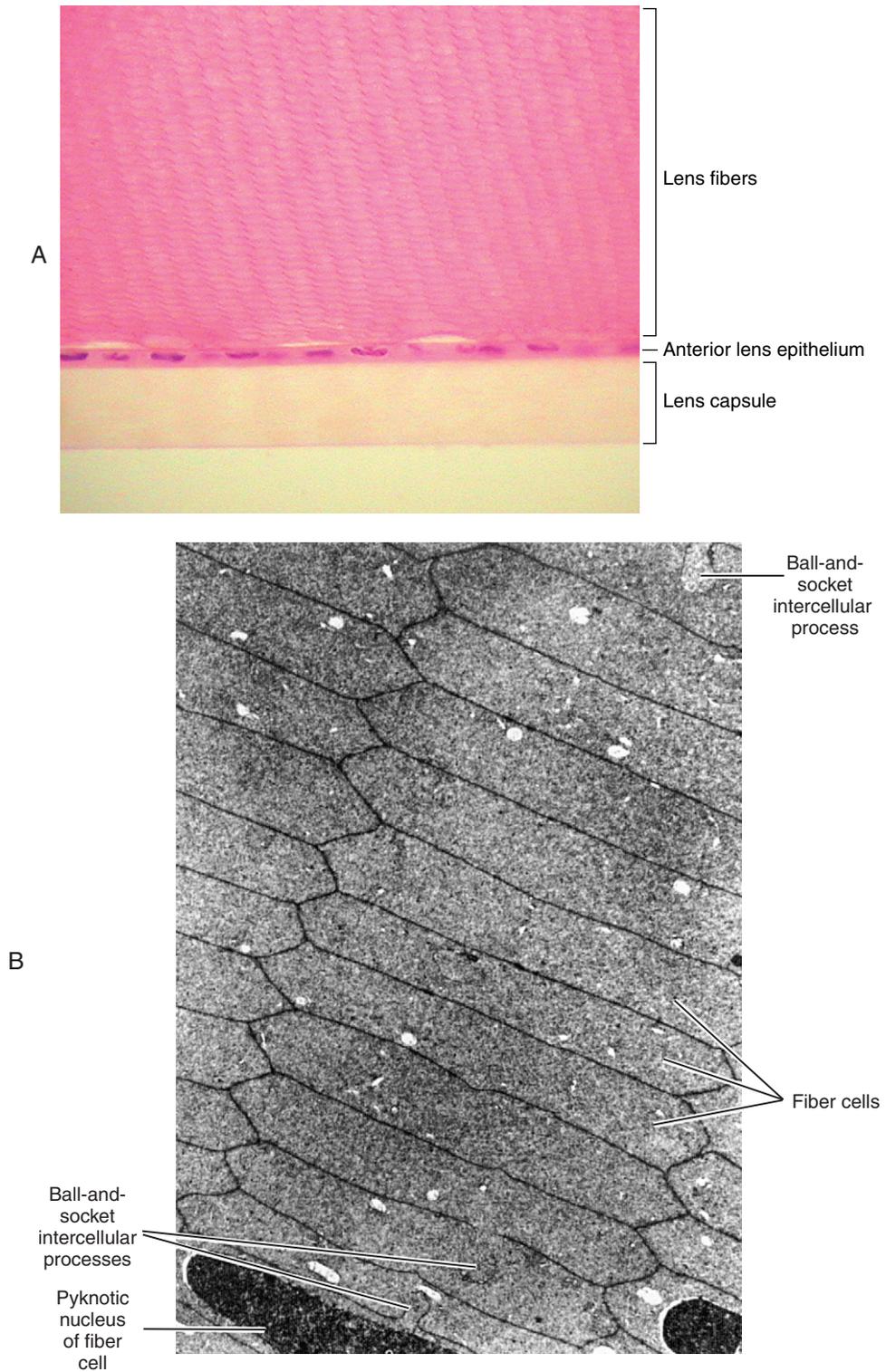


FIGURE 5-7

A, Light micrograph showing lens capsule, anterior lens epithelium, and lens fibers of cortex. **B**, Fiber cells of lens cortex. (Transmission electron microscope; $\times 6000$.) (**B** from Krause WJ, Cutts JH: *Concise text of histology*, Baltimore, 1981, Williams & Wilkins.)

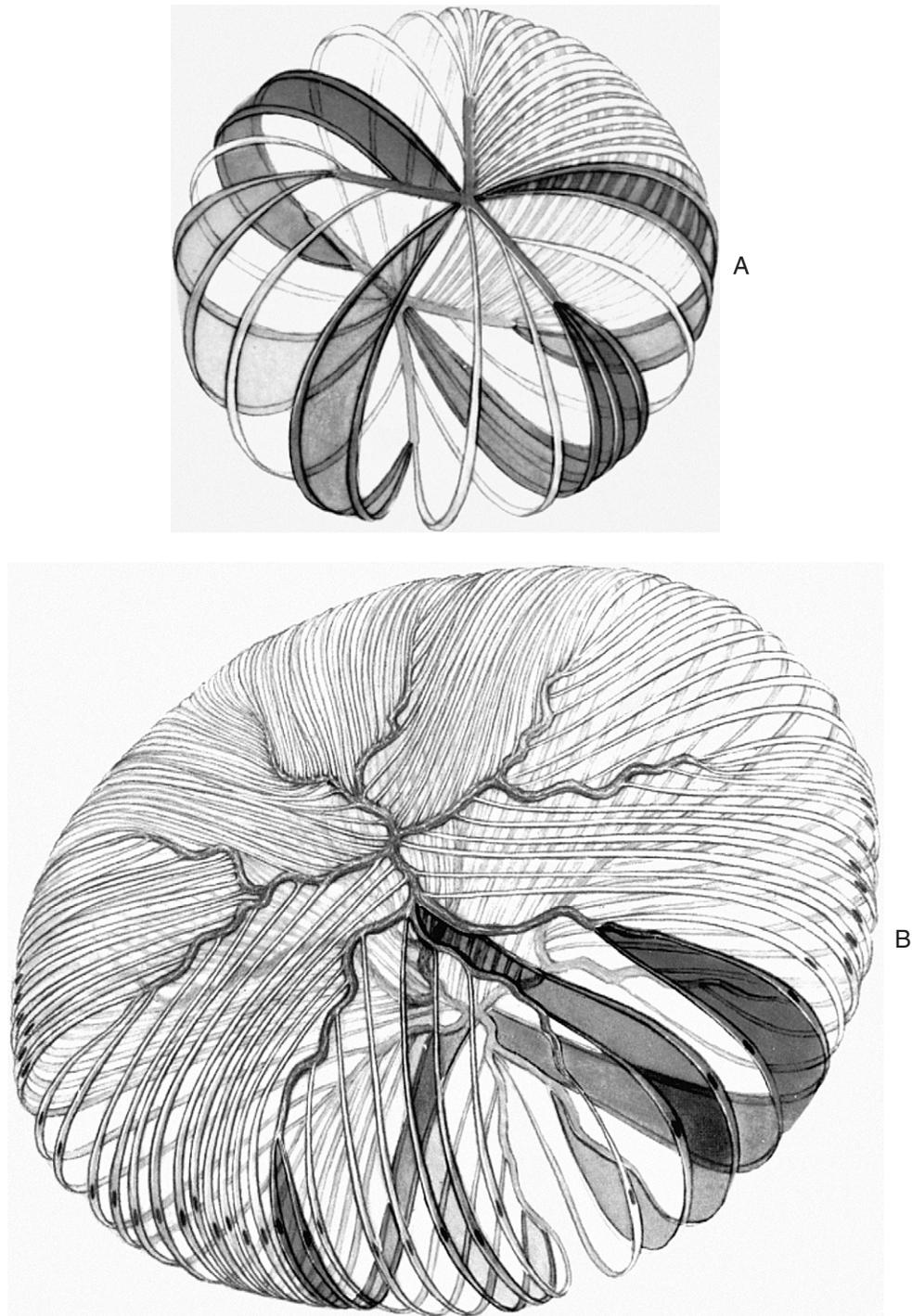


FIGURE 5-8

Fetal and adult lenses, showing sutures and arrangement of lens cells. **A**, Fetal nucleus. Anterior Y suture is at *a*, and posterior suture is at *b*. Lens cells are depicted as wide bands. Cells that attach to tips of Y sutures at one pole of lens attach to fork of Y at opposite pole. **B**, Adult lens cortex. Anterior and posterior organization of sutures is more complex. Lens cells that arise from tip of a suture branch insert farther anteriorly or posteriorly into a fork at opposite pole. This arrangement conserves shape of lens. In this drawing, for educational purposes, the suture appears to lie in a single plane, but the reader should remember that the suture extends throughout the thickness of the cortex and nucleus to the level of the Y sutures in the fetal nucleus.

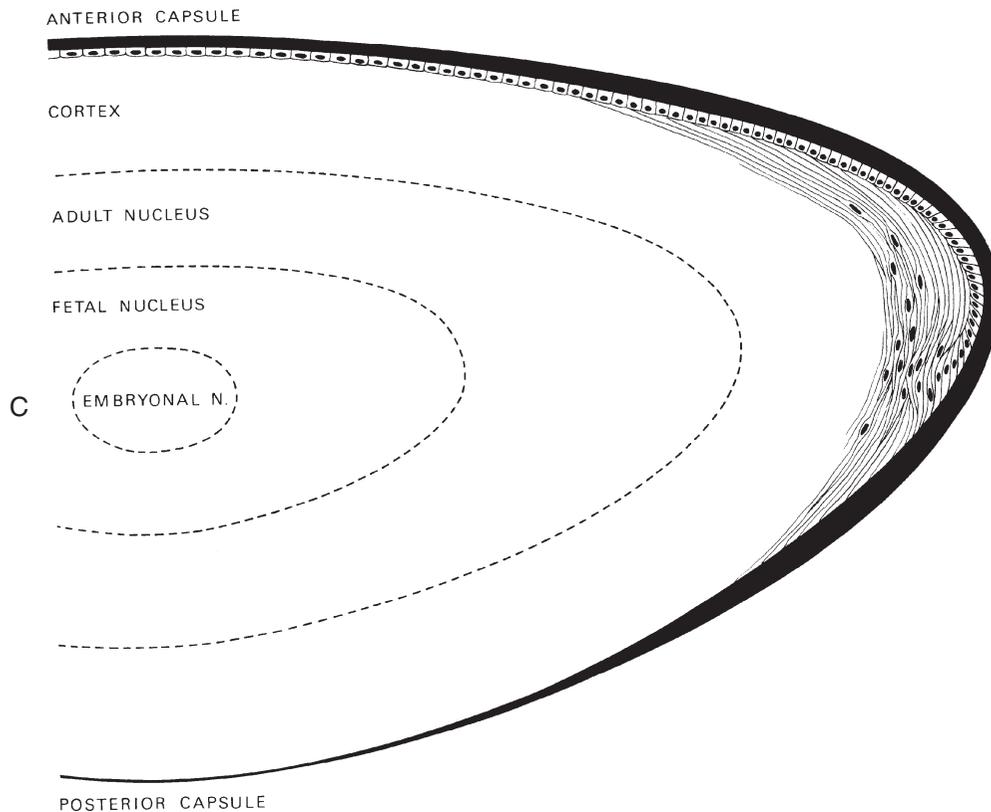


FIGURE 5-8 cont'd

C, Adult lens, showing nuclear zones, epithelium, and capsule. Thickness of lens capsule in various zones is shown. (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

LENS SUTURES

As the lens fibers reach the poles they meet with the other fibers in their layer, forming a junction known as a suture. The **anterior suture** is formed by overlapping *apical* aspects of the fibers, and the **posterior suture** is formed by the overlapping *basal* aspects.^{3,10} The fibers formed during embryologic development meet in three branches, forming **Y sutures**. The anterior suture is an *upright-Y shape* and the posterior suture an *inverted-Y shape* (see Figure 5-8, A).¹⁴ As growth continues and the lens becomes larger, the sutures become asymmetric and dissimilar. The limbs of the anterior and posterior sutures are offset, and the complexity of the sutures contributes to lens transparency.²⁴ The sutures formed after birth are more stellate shaped; sutures formed through early adulthood have 6 to 9 branches; and 9 to 15 complex branched stars are formed in middle to old age²⁴ (see Figure 5-8, B).

CLINICAL COMMENT: SLIT-LAMP APPEARANCE OF LENS

An optic section through the lens demonstrates the biconvexity of the structure (Figure 5-9). The first bright line is convex forward and is the anterior lens capsule; posterior to this is a dark line, the anterior epithelium; the next bright line is the cortex; then various gray zones (zones of discontinuity) are seen. The anterior Y suture of the fetal nucleus may be evident. The vertical center, the embryonic nucleus, has no anterior or posterior curvature. The posterior inverted-Y suture may be seen in the posterior aspect of the fetal nucleus. Posterior to this, the zones of discontinuity are concave forward, with the final zone being the posterior capsule.²⁵ A diffuse view of the anterior lens surface illustrates **lens shagreen**, with the lens surface resembling the surface of an orange, likely caused by the conformation of the capsule to the epithelial cell undulations.²⁶ The zones of discontinuity are apparent because of changes in light-scattering properties (Table 5-1).

Rights were not granted to include this figure in electronic media.
Please refer to the printed publication.

CLINICAL COMMENT: THE LENS PARADOX

Because the lens continues to grow, it would seem that its refractive power should change, yet it remains constant. With age the radii of curvature decrease; the anterior radius of curvature decreases to approximately 8.25 mm and the posterior radius to about 7 mm by 80 years of age.²⁷ As the lens surface becomes more steeply curved, refractive power should increase. However, the lens thickness increases (primarily in the width of the lens cortex) and the refractive index of the lens changes with age. The gradient nature of the index precludes accurate measurement of these changes, but these changes apparently compensate for the increased surface curvatures, and the power of the lens remains stable.²⁸⁻³⁰

FIGURE 5-9

Optical section of normal adult lens. 1, Anterior capsule; 2, anterior line of disjunction (anterior epithelium); 3, anterior surface of adult nucleus; 4, anterior surface of fetal nucleus; 5, inner layer of anterior half of fetal nucleus, containing anterior Y suture; 6, inner layer of posterior half of fetal nucleus, containing posterior Y suture; 7, posterior surface of fetal nucleus; 8, posterior surface of adult nucleus; 9, posterior line of disjunction; 10, posterior capsule. (From Phelps CD: In Duane TD, editor: *Clinical ophthalmology*, vol 1, Hagerstown, Md, 1978, Harper & Row.)

ZONULES (OF ZINN)

The lens is attached to the ciliary body by a group of threadlike fibers, the **zonules (of Zinn)**, or the **suspensory ligament of the lens** (Figure 5-10). These fibers are aggregates of vitreous filaments and, although highly elastic, have no true elastic fibers.^{11,31} The fibers arise from the basement membrane of the nonpigmented ciliary epithelium in the pars plana and from the valleys between the ciliary processes in the pars plicata.³ Most fibers attach to the lens capsule at the preequatorial and postequatorial regions; few attach directly at the equator.³² The zonules are interwoven into the components of the capsule. Those that attach to

Table 5-1 Zones of Discontinuity in Crystalline Lens

Zone	Correlative Lens Morphology
Anterior capsular zone	Anterior lens capsule
Anterior subcapsular zone	Anterior lens epithelium, elongating fibers, outermost cortical fibers
Anterior zone of disjunction	Anterior segments of cortical fibers formed after sexual maturation; complex sutures
Anterior zone of adult nucleus	Anterior half of adult nucleus consisting of secondary fibers formed after birth and up to sexual maturation
Anterior zone of fetal nucleus	Anterior half of fetal nucleus consisting of secondary fibers formed before birth Location of upright-Y suture
Zone of embryonic nucleus	Embryonic nucleus consisting of primary lens fibers formed during first 2 months of embryonic development
Posterior zone of fetal nucleus	Posterior half of fetal nucleus consisting of secondary fibers formed before birth Location of inverted-Y suture
Posterior zone of adult nucleus	Posterior half of adult nucleus consisting of secondary fibers formed after birth and up to sexual maturation
Posterior subcapsular zone	Posterior segments of elongating fibers and outermost cortical fibers; complex sutures
Posterior capsular zone	Posterior lens capsule

Modified from Kuszak JR, Deutsch TA, Brown HG: In Albert DM, Jakobiec FA, editors: *Principles and practice of ophthalmology*, Philadelphia, 1994, Saunders, p 564.



Rights were not granted to include this figure in electronic media.
Please refer to the printed publication.

FIGURE 5-10

Scanning electron micrograph of anterior zonular insertion after removal of cornea and iris. Note angle between anterior and posterior zonules and attachment to lens capsule. (From Streeton BW: In Jakobiec JA, editor: *Ocular anatomy, embryology, and teratology*, Hagerstown, Md, 1982, Harper & Row.)

the lens are known as *primary zonules*. *Secondary zonules* join the primary zonules with each other or connect processes to one another or to the pars plana, and “tension” fibers anchor the primary zonules to the ciliary valleys to form a fulcrum.³²

ACCOMMODATION

When the emmetropic eye is viewing a distant object, the ciliary muscle is relaxed and the image lies on the retina. When a near object is to be focused on the retina, an increase in the refractive power of the eye must occur. This increase in power is called **accommodation** and is accomplished by a change in lens shape brought about by contraction of the ciliary muscle. Von Helmholtz³³ is credited with determining that the following occur during accommodation:

1. Lens thickness increases anterior to posterior.
2. The lens thins along the equator.
3. The anterior lens surface moves forward, and thus the anterior chamber becomes shallower.
4. There is no change in the position of the posterior pole.

These factors result in a thickened lens with more sharply curved surfaces and thus increased lens power. The stimulus that initiates the accommodative mechanism is *retinal blur*.³⁴

When the ciliary muscle contracts, the diameter of the ciliary ring surrounding the lens decreases, reducing the tension that the zonules exert on the lens and allowing the lens capsule to assume its preferred spheric shape. The lens capsule transmits the reduction in the zonular pull to the lens, molding the lens into its accommodated form.

The lens becomes more sharply curved, and because of the thickness variation of the capsule, a bulge is most apparent at the center of the anterior surface.^{35,36} The posterior surface increases in curvature only slightly; however, the steepness of the anterior surface does not become greater than that of the posterior surface.⁹ As the lens thickens axially, the equatorial diameter decreases, and the anterior lens pole moves toward the cornea. It was previously thought that there was no posterior lens movement, but a small amount of movement of the posterior pole in a posterior direction has been identified.^{5,37,38} The curvature of the internal surfaces, seen at the zones of discontinuity and the boundaries of the nuclei, mimics the changes in the surface curvatures and contributes to the increase in the total dioptric power.⁵ This thickening of the lens from anterior to posterior occurs in the nuclear region, but the thickness of the lens cortex remains unchanged.³⁹ The vitreous has a passive role in accommodation, probably serving only as support for the lens.⁴⁰

During ciliary muscle contraction, the choroid is pulled forward slightly, perhaps aiding in the correct orientation of the photoreceptors in relation to the entrance pupil. Contraction of the ciliary body in accommodation, by decreasing the circumference of the sclera, may lead to an elongation of the eye axial length.³⁸ The ciliary muscle and trabecular meshwork are both attached to the scleral spur, so accommodation causes a widening of the intertrabecular spaces; this facilitates aqueous outflow and can result in decreased intraocular pressure (IOP).⁴¹

When the ciliary muscle relaxes, the muscle is moved outward, and the ciliary body is stretched posteriorly by the elastic tissue of Bruch’s membrane. The ciliary ring expands, and the tension in the zonules stretches the capsule, restoring the lens to its unaccommodated state.

CLINICAL COMMENT: PRESBYOPIA

*The ability to focus at near decreases with age, and this loss in accommodative ability is called **presbyopia**. The easiest response to patients when explaining presbyopia is that a “weakness of the muscle” causes this decrease in focusing ability. However, changes in the ciliary body, zonules, lens capsule, and lens itself all play some role; still the precise nature of that role may be unclear. Although ciliary muscle tissue is lost and replaced by connective tissue, this occurs in very old age, not when presbyopia begins.⁴² No loss of parasympathetic innervation occurs that would account for decreased muscle contraction. The diameter of the unaccommodated ciliary ring decreases in older eyes, but maximal contractile ability of the muscle decreases only slightly with age.⁴ The insertion of the anterior zonular fibers shifts onto the anterior lens surface,⁴⁴ but there is no apparent change in zonular length or tension, and the elasticity of the zonular complex does not change with age.⁵ The lens capsule becomes thicker, less elastic, and more brittle with age, older lens fibers become sclerotic and more resistant to deformity, and thus the ability of the lens to change shape in response to the forces exerted by the capsule diminishes with age.^{7,45-48} As the lens continues to grow throughout life, the mass and volume increase, with a forward movement of the center of the lens. The increase in the bulk of the lens and the anterior displacement alter the vector relationship between the lens and the zonules and may be an additional factor in the progress of presbyopia.⁵ As the lens becomes more curved and little change occurs in lens power, greater force will be required to increase the power necessary for near focus.^{7,27}*

LENS PHYSIOLOGY

The primary function of the lens is the refraction of light, and it is imperative that the transparent lens have minimal light scatter. Transparency is a function of (1) the absence of blood vessels, (2) few cellular organelles in the light path, (3) an orderly arrangement of fibers, and (4) the short distance between components of

differing indices relative to the wavelength of light.⁴⁹ Since extensive metabolic activity occurs in the anterior epithelium to maintain cell and fiber function, and the preequatorial region has a high level of mitotic activity a significant amount of energy is used by these cells. Because the lens is avascular, most nutrients are obtained from the surrounding aqueous, with a small contribution from the vitreous. Thus, the epithelium is rich in transport mechanisms (e.g., Na⁺/K⁺ ATPase pumps) that maintain electrolyte balance. Anaerobic glycolysis is the source of the energy required for cellular metabolism and cellular replication within the lens.

Free radicals are a normal by-product of metabolic processes, and ultraviolet (UV) light absorption can also produce oxidative changes within tissue causing the formation of free radicals. Free radicals disrupt cellular processes and cause cellular damage. Within the lens free radicals cause the formation of high-molecular-weight aggregates. **Glutathione** is a reducing agent that detoxifies free radicals, thus preventing such damage. This important molecule also plays a role in maintaining membrane transport mechanisms.⁵⁰ Glutathione is found in significant concentrations in lens tissue and in the aqueous humor. It is synthesized and regenerated in the lens cortex and moves easily throughout the young lens, but with age its movement into the lens nucleus is impeded. The deficiency in internal transport may contribute to a decrease in glutathione in the center of the lens and this transport impediment may be a factor in the oxidative modification of protein that occurs in nuclear cataract.⁵¹

Ascorbic acid is another molecule that may provide some protection to lens epithelium against UV-induced damage to deoxyribonucleic acid (DNA). Ascorbic acid is present in relatively high levels in the aqueous humor.⁵²

ULTRAVIOLET RADIATION

The cornea absorbs wavelengths below 300 nm, the lens absorbs wavelengths between 300 and 400 nm, and wavelengths greater than 400 nm are transmitted to the retina. The lens absorbs almost all UV light to which it is exposed, and any resulting unstable free radicals cause molecular changes.⁵³ The first active tissue of the lens that encounters UV radiation is the lens epithelium, which is susceptible to damage from free radicals. Morphologic changes apparent in the epithelial layer may lead to irreversible changes throughout the lens, although the mechanism by which this progresses is not defined.⁵⁴

UV radiation absorbed by lens fibers causes oxidative damage leading to degradation and modification of lens proteins, and an association between ocular exposure and increased risk of lens opacity has been documented.^{55,56} UV absorption also increases chromophore

concentration, fluorescence increases, and yellow pigments accumulate in the center of the lens.⁵³ The yellowing may progress to a dark-brown hue that is called **lens brunescence**.²⁰

CLINICAL COMMENT: CATARACT

*Although any lens opacity is accurately called a **cataract**, the clinician should be aware of the impact that the word “cataract” may have on a patient. Cataracts are the greatest cause of blindness worldwide. The etiology of cataract formation is complex, and cataract development is often the result of multiple factors that influence lens metabolism. Risk factors include aging, disease, genetics, nutritional or metabolic deficiencies, trauma, congenital factors, and environmental stress (e.g., radiation), with age being the major contributor.⁵⁷ As mentioned, free radicals can affect cell function, damage lens DNA, and cause high-molecular-weight crystallin aggregations, any of which can cause opacities that increase light scatter.²⁰ Glutathione provides some protection from free radical damage, and a decrease in glutathione concentration is associated with cataract development.^{51,58}*

*Cataracts are named according to location or cause and can be graded based on severity (Figure 5-11). An opacity located in the embryonic or fetal nucleus is called a **nuclear cataract** (Figure 5-12). The most common nuclear cataract is **senile nuclear sclerosis**, associated with oxidative damage to lens fiber components and modifications to crystallins. Brunescence accompanies nuclear cataract caused by increased chromophore concentration. The increase in yellow coloration results in the absorption of wavelengths in the blue end of the spectrum, which may actually provide some protection for the macula. Studies have found that individuals with nuclear cataract have a normal level of glutathione in the cortex but a reduced level in the nucleus.^{50,58}*

*A **cortical cataract**, located in the cortex, has a spokelike shape; thicker in the periphery and tapering toward the lens center, it follows the shape of the fiber (Figure 5-13). Cortical cataracts generally progress slowly; with time the spoke width expands as the opacity spreads to adjacent fibers.^{59,60} If water vacuoles are present, membrane rupture in the equatorial area can occur.⁶⁰ Cortical cataracts affect vision only when they spread into the center of the lens and cause light scatter in the pupillary region.*

*A **posterior subcapsular cataract** is a disturbance located just beneath the posterior capsule (Figure 5-14). It can result from an accumulation of epithelial-like cells in this area caused by abnormal cell migration or aberrant differentiation of lens fibers.⁶¹ A significant risk factor for posterior subcapsular cataract is long-term high-dose steroid use. The causative mechanism is not known.*

*A **diabetic cataract** can develop rapidly and results from elevated glucose levels. With increased blood glucose, excess glucose present in the aqueous enters the lens, and this excess glucose goes through the sorbitol pathway. As sorbitol concentration increases within the lens fiber, water is drawn into the fiber because sorbitol does not readily pass through the fiber membrane. The fibers swell, the lens loses transparency, and the fibers may eventually rupture.*

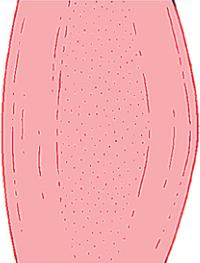
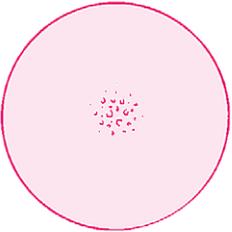
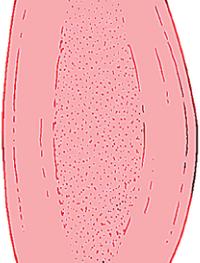
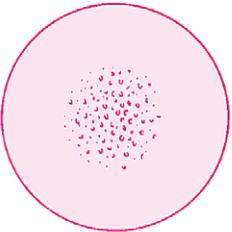
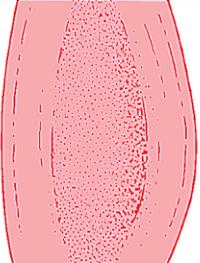
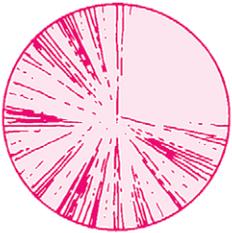
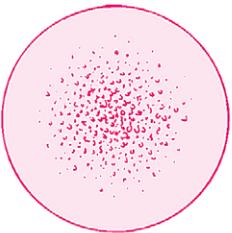
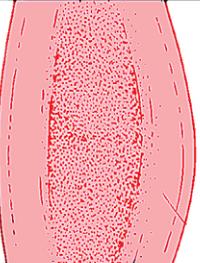
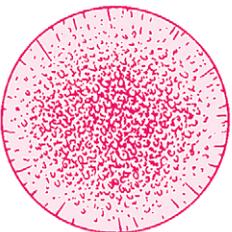
	NUCLEAR SCLEROSIS	CORTICAL SPOKING	POSTERIOR SUBCAPSULAR
GRADE 1			
GRADE 2			
GRADE 3			
GRADE 4			

FIGURE 5-11

Grading system for age-related cataracts. Nuclear sclerotic changes are shown in cross section, with anterior surface to the left. Cortical and posterior subcapsular changes are seen in retroillumination. (From Fingeret M, Casser L, Woodcome HT: *Atlas of primary eyecare procedures*, Norwalk, Conn, 1992, Appleton & Lange.)

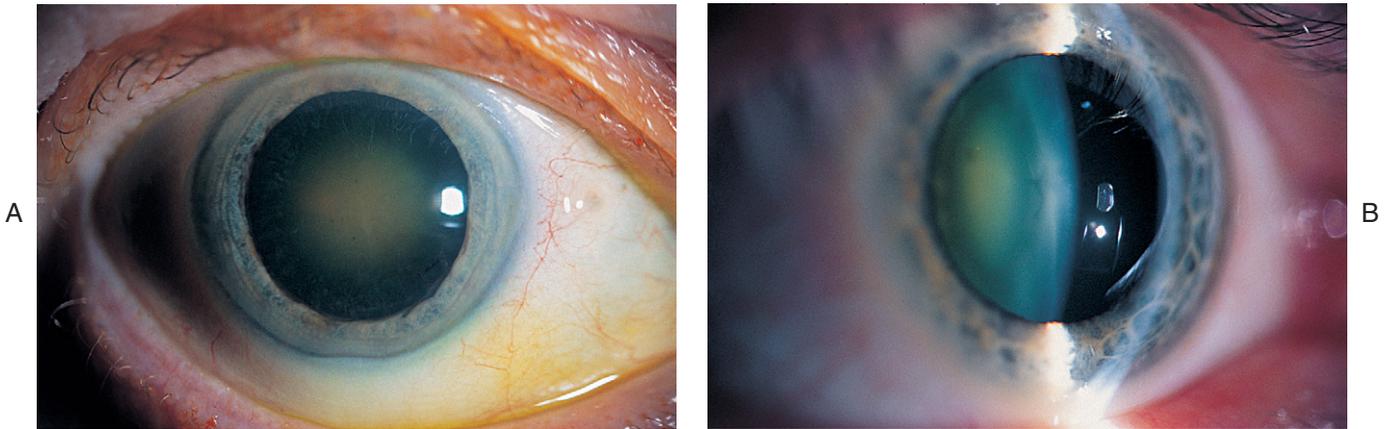


FIGURE 5-12
Nuclear cataract seen with **A**, diffuse illumination, and **B**, optic section. (From Kanski JJ, Nischal KK: *Ophthalmology: clinical signs and differential diagnosis*, St Louis, 2000, Mosby.)

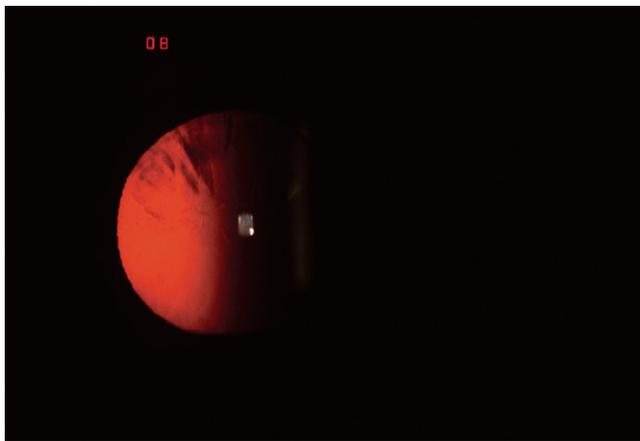


FIGURE 5-13
Spokes of a cortical cataract visible against the red reflex. (Courtesy Pacific University Family Vision Center, Forest Grove, Ore.)



FIGURE 5-14
Posterior subcapsular cataract. (From Kanski JJ, Nischal KK: *Ophthalmology: clinical signs and differential diagnosis*, St Louis, 2000, Mosby.)

CLINICAL COMMENT: CATARACT SURGERY

The decision for cataract removal is determined by the cataract's effect on the patient's everyday life. When a person is not able to perform the usual daily activities because of reduced acuity caused by the opacity, the lens should be removed. Cataract extraction is a relatively safe surgical procedure usually done under local anesthesia. A small incision is made to allow entrance of surgical instruments into the anterior chamber. The anterior lens capsule is opened and the lens epithelium and all fibers are removed, with the lens capsule remaining intact. An intraocular lens (IOL) can then be inserted into the lens capsule to replace the power of the missing lens. Multifocal IOLs that correct for presbyopia may be an option.

AGING CHANGES IN CRYSTALLINE LENS

The lens grows throughout life, with an increase in the surface curvatures, a forward movement of the center of the lens, and a decrease in anterior chamber depth.^{2,30,47} Changes occur in lens physiology as mature lens fibers lose all cellular organelles. A coincident decrease in transport of ions, nutrients, and antioxidants may lead to the damage contributing to cataract formation.⁶²

The major changes associated with aging are presbyopia and cataract formation, as discussed earlier. Both these processes affect vision and are a significant concern to the patient and to the clinician, particularly

because few preventive measures are available. The primary recommendation should be the use of UV-absorbing lenses when outdoors; the incidence of cataract is higher in those exposed to greater levels of sunlight.⁵³

REFERENCES

- Patterson CA, Delamere NA: The lens. In Hart WM, editor: *Adler's physiology of the eye*, ed 9, St Louis, 1992, Mosby, p 348.
- Dubbelman M, van der Heijde GL, Weeber HA: The thickness of the aging human lens obtained from corrected Scheimpflug images, *Optom Vis Sci* 78(6):411, 2001.
- Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders, p 638.
- Strenk SA, Semmlow JL, Strenk LM et al: Age-related changes in ciliary muscle and lens: a magnetic resonance imaging study, *Invest Ophthalmol Vis Sci* 40:1162, 1999.
- Glasser A, Kaufman PL: Accommodation and presbyopia. In Kaufman PL, Alm A, editors: *Adler's physiology of the eye*, ed 10, St Louis, 2003, Mosby, p 197.
- Smith G, Pierscionek BK: The optical structure of the lens and its contribution to the refractive status of the eye, *Ophthalmic Physiol Opt* 18(1):21, 1998.
- Pierscionek BK: Refractive index contours in the human lens, *Exp Eye Res* 64:887, 1997.
- Borish IM: *Clinical refraction*, ed 3, Chicago, 1975, Professional Press, p 169.
- Koretz JE, Handelmann GH, Brown NP: Analysis of human crystalline lens curvature as a function of accommodative state and age, *Vis Res* 24:1141, 1984.
- Kuszak JR, Brown HG: Embryology and anatomy of the lens. In Albert DM, Jakobiec FA, editors: *Principles and practice of ophthalmology*, Philadelphia, 1994, Saunders, p 82.
- Alexander RA, Garner A: Elastic and precursor fibres in the normal human eye, *Exp Eye Res* 36:305, 1983.
- Krag S, Olsen T, Andreassen TT: Biomechanical characteristics of the human anterior lens capsule in relation to age, *Invest Ophthalmol Vis Sci* 38(2):357, 1997.
- Kuwabara T: The maturation of the lens cell: a morphologic study, *Exp Eye Res* 20:427, 1975.
- Kuszak JR, Peterson KL, Brown HG: Electron microscopic observations of the crystalline lens, *Microsc Res Tech* 33:441, 1996.
- Bassnett S, Kuszak JR, Reinisch L et al: Intercellular communication between epithelial and fiber cells of the eye lens, *J Cell Sci* 107:799, 1994.
- Rae J: Physiology of the lens. In Albert DM, Jakobiec FA, editors: *Principles and practice of ophthalmology*, Philadelphia, 1994, Saunders, p 123.
- Kuszak JR, Novak LA, Brown HG: An ultrastructural analysis of the epithelial-fiber interface (EFI) in primate lenses, *Exp Eye Res* 61:579, 1995.
- Lo WK, Harding CV: Structure and distribution of gap junctions in lens epithelium and fiber cells, *Cell Tissue Res* 244(2):253, 1986.
- Lo WK, Harding CV: Tight junctions in the lens epithelia of human and frog: freeze-fracture and protein tracer studies, *Invest Ophthalmol Vis Sci* 24(4):396, 1983.
- Vavvas D, Azar NF, Azar DT: Mechanisms of disease: cataracts, *Ophthalmol Clin North Am* 15:49, 2002.
- Clark JI: Development and maintenance of lens transparency. In Albert DM, Jakobiec FA, editors: *Principles and practice of ophthalmology*, Philadelphia, 1994, Saunders, p 114.
- Mathias RT, Rae JL: Transport properties of the lens, *Am J Physiol* 249(3):181, 1985.
- Dahm R, van Marle J, Prescott AR et al: Gap junctions containing alpha8 connexin (MP70) in the adult mammalian lens epithelium suggests a re-evaluation of its role in the lens, *Exp Eye Res* 69:45, 1999.
- Kuszak JR, Peterson KL, Sivak JG et al: The interrelationship of lens anatomy and optical quality. II. Primate lenses, *Exp Eye Res* 59(5):521, 1994.
- Brandreth RH: *Clinical slit lamp biomicroscopy*, Berkely, Calif, 1978, Brandreth.
- Sasaki K, Kojirna M, Hara T: In vivo observation of the crystalline lens capsule, *Ophthalmic Res* 20(3):154, 1988.
- Brown N: The change in lens curvature with age, *Exp Eye Res* 19:175, 1974.
- Pierscionek BK: Age-related response of human lenses to stretching forces, *Exp Eye Res* 60:325, 1995.
- Moffat BA, Atchison DA, Pope JM: Age-related changes in refractive index distribution and power of the human lens as measured by magnetic resonance micro-imaging in vitro, *Vis Res* 42:1683, 2002.
- Dubbelman M, van der Heijde GL: The shape of the aging human lens: curvature, equivalent refractive index and the lens paradox, *Vis Res* 41:1867, 2001.
- Streeten BW, Licari PA: The zonules and the elastic microfibrillar system in the ciliary body, *Invest Ophthalmol Vis Sci* 24(6):667, 1983.
- Rohen JW: Scanning electron microscopic studies of the zonular apparatus in human and monkey eyes, *Invest Vis Sci* 18:133, 1979.
- Von Helmholtz HH: *Treatise on physiologic optics*, Mineola, NY, 1962, Dover (Translated by JPC Southhall), p 143.
- Von Noorden G: *Burien and von Noorden's binocular vision and ocular motility*, ed 5, St Louis, 1996, Mosby, p 85.
- Garner LF, Smith G: Changes in equivalent and gradient refractive index of the crystalline lens with accommodation, *Opt Vis Sci* 74(2):114, 1997.
- Garner LF, Yap MK: Changes in ocular dimensions and refraction with accommodation, *Ophthalmic Physiol Opt* 17(1):12, 1996.
- Drexler W, Baumgartner A, Findl O et al: Biometric investigation of changes in the anterior eye segment during accommodation, *Vis Res* 39:1267, 1999.
- Drexler W, Findl O, Schmetterer L et al: Eye elongation during accommodation in humans: differences between emmetropes and myopes, *Invest Ophthalmol Vis Sci* 39(11):2140, 1998.
- Koretz JE, Bertasso AM, Neider MW et al: Slit-lamp studies of the rhesus monkey eye. II. Changes in crystalline lens shape, thickness, and position during accommodation and aging, *Exp Eye Res* 43:317, 1987.
- Fisher RF: The vitreous and lens in accommodation, *Trans Ophthalmol Soc UK* 102:318, 1982.
- Mauger RR, Likens CP, Applebaum M: Effects of accommodation and repeated applanation tonometry on intraocular pressure, *Am J Optom Physiol Opt* 6(1):28, 1984.
- Pardue MT, Sivak JG: Age-related changes in human ciliary muscle, *Optom Vis Sci* 77:204, 2000.
- Croft MA, Glasser A, Kaufman PL: Accommodation and presbyopia, *Int Ophthalmol Clin* 41(2):33, 2001.
- Sakabe I, Oshika T, Lim SJ et al: Anterior shift of zonular insertion onto the anterior surface of human crystalline lens with age, *Ophthalmology* 105(2):295, 1998.
- Krag S, Andreassen TT: Mechanical properties of the human posterior lens capsule, *Invest Ophthalmol Vis Sci* 44:691, 2003.
- Seland JH: Ultrastructural changes in the normal human lens capsule from birth to old age, *Acta Ophthalmol* 52:688, 1974.
- Glasser A, Campbell MC: Biometric, optical and physical changes in the isolated human crystalline lens with age in relation to presbyopia, *Vis Res* 39:1991, 1999.

48. Beers AP, van der Heijde GL: Age-related changes in the accommodation mechanism, *Opt Vis Sci* 73(4):235, 1996.
49. Trokel S: The physical basis for transparency of the crystalline lens, *Invest Ophthalmol* 1:493, 1962.
50. Reddy VN: Glutathione and its function in the lens: an overview, *Exp Eye Res* 50:771, 1990.
51. Sweeney MH, Truscott RJ: An impediment to glutathione diffusion in older normal human lenses: a possible precondition for nuclear cataract, *Exp Eye Res* 67:587, 1998.
52. Reddy VN, Giblin FJ, Lin LR et al: The effect of aqueous humor ascorbate on ultraviolet-B-induced DNA damage in lens epithelium, *Invest Ophthalmol Vis Sci* 39(2):344, 1998 (abstract).
53. Young RW: The family of sunlight-related eye diseases, *Opt Vis Sci* 71(2):125, 1994.
54. Hightower KR, Reddan JR, McCreedy JP et al: Lens epithelium: a primary target of UVB irradiation, *Exp Eye Res* 59:557, 1994.
55. Hightower KR: The role of the lens epithelium in development of UV cataract, *Curr Eye Res* 14:71, 1995.
56. West SK, Duncan DD, Muñoz B et al: Sunlight exposure and risk of lens opacities in a population-based study, *Arch Ophthalmol* 116:1666, 1998 (abstract).
57. Cruickshanks KJ, Klein BE, Klein R: Ultraviolet light exposure and lens opacities: the Beaver Dam Eye Study, *Am J Public Health* 82(12):1658, 1992.
58. Truscott RJ: Age-related nuclear cataract: a lens transport problem, *Ophthalmol Res* 32:185, 2000.
59. Brown NP, Harris ML, Shun-Shin GA et al: Is cortical spoke cataract due to lens fibre breaks? The relationship between fibre breaks, waterclefs and spoke cataract, *Eye* 7:672, 1993.
60. Vrensen G, Willekens B: Biomicroscopy and scanning electron microscopy of early opacities in the aging human lens, *Invest Ophthalmol Vis Sci* 31(8):1582, 1990.
61. Beebe DC: The lens. In Kaufman PL, Alm A, editors: *Adler's physiology of the eye*, ed 10, St Louis, 2003, Mosby, p 117.
62. Moffat BA, Landman KA, Truscott RJ et al: Age-related changes in the kinetics of water transport in normal human lenses, *Exp Eye Res* 69(6):663, 1999.

The eye contains three chambers: anterior, posterior, and vitreous. The anterior and posterior chambers contain aqueous humor, and the vitreous chamber contains the vitreous gel. This chapter discusses these chambers' boundaries, contents, and anatomic relationships with surrounding structures.

ANTERIOR CHAMBER

The **anterior chamber** is bounded anteriorly by the corneal endothelium; peripherally by the trabecular meshwork, a portion of the ciliary body, and the iris root; and posteriorly by the anterior iris surface and the pupillary area of the anterior lens (Figure 6-1). The center of the anterior chamber is deeper than the periphery. The **anterior chamber angle** is formed at the periphery of the chamber, where the corneoscleral and uveal coats meet. The aqueous humor exits the anterior chamber through the structures located in this angle.

ANTERIOR CHAMBER ANGLE STRUCTURES

The structures through which aqueous exits, collectively called the **filtration apparatus**, consist of the trabecular meshwork and Schlemm's canal. These structures and the scleral spur occupy the excavated area located at the internal corneoscleral junction known as the **internal scleral sulcus**.

Scleral Spur

The **scleral spur** lies at the posterior edge of the internal scleral sulcus (see Chapter 2). The posterior portion of the scleral spur is the attachment site for the tendon of the longitudinal ciliary muscle fibers, whereas many of the trabecular meshwork sheets attach to the spur's anterior aspect, such that the collagen of the spur is continuous with that of the trabeculae¹ (Figure 6-2).

Trabecular Meshwork

The **trabecular meshwork** encircles the circumference of the anterior chamber. In cross section it has a triangular shape, with its apex at the termination of Descemet's

membrane (Schwalbe's line) and its base at the scleral spur (Figure 6-3). The inner face borders the anterior chamber, and the outer side lies against corneal stroma, sclera, and Schlemm's canal. The meshwork is composed of flattened perforated sheets, with three to five sheets at the apex. These sheets branch into 15 to 20 sheets as they extend posteriorly from Schwalbe's line to the scleral spur.² The trabecular meshwork is an open lattice-work, the branches of which interlace. The intertrabecular spaces between the sheets are connected through pores, or openings within the sheets (historically called the "spaces of Fontana").³ The openings are of varying sizes and become smaller near Schlemm's canal. No apertures directly join the meshwork with the canal.²

The meshwork can be separated into two anatomic divisions. The **corneoscleral meshwork** is the outer region; its sheets attach to the scleral spur. The inner sheets, which lie inner to the spur and attach to the ciliary stroma and longitudinal muscle fibers, make up the **uveal meshwork**; some of these sheets may attach to the iris root.^{3,4} The two portions differ slightly in structure; the corneoscleral meshwork is sheetlike, and the uveal meshwork is cordlike² (Figure 6-4). Occasional projections from the surface layer of the iris, known as iris processes, connect to the trabeculae, usually projecting no farther forward than the midpoint of the meshwork.²

The meshwork trabeculae consist of an inner core of collagen and elastic fibers⁵ embedded in ground substance and covered by endothelium and basement membrane⁶ (Figure 6-5). The endothelial cells are a continuation of the corneal endothelium.^{4,7} The endothelial cells contain the cellular organelles for protein synthesis and apparently are capable of replacing the connective tissue components. These cells also contain lysosomes, which give them the capacity for phagocytosis.⁴ Gap junctions and short areas of tight junctions join the endothelial cells; no zonula occludens are found.⁸ Cytoplasmic projections connect cells of neighboring sheets.^{4,8,9}

At the scleral spur the trabecular sheets lose their endothelial covering, but the collagenous and elastic fibers continue into the connective tissue of the spur and ciliary body.^{2,4} Some of the connective tissue fibers of the ciliary muscle pass forward and merge with the inner sheets of the meshwork.

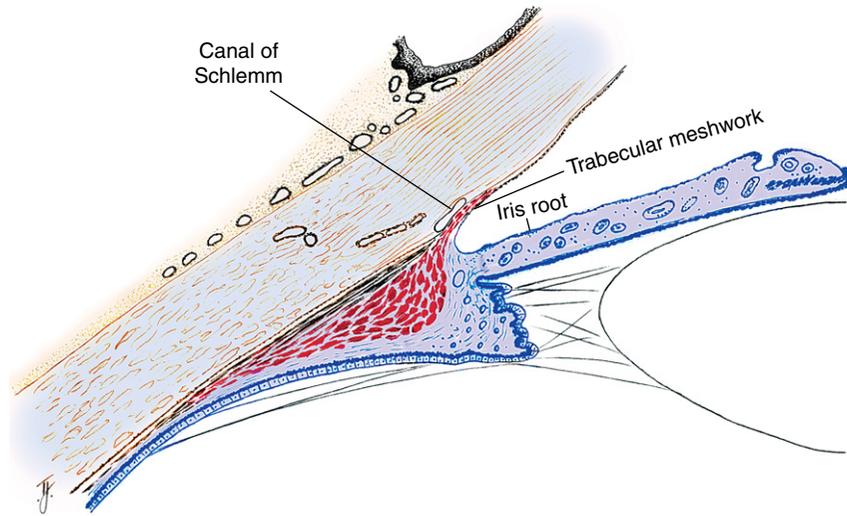


FIGURE 6-1
Periphery of the anterior segment. Structures of the anterior chamber angle are labeled.

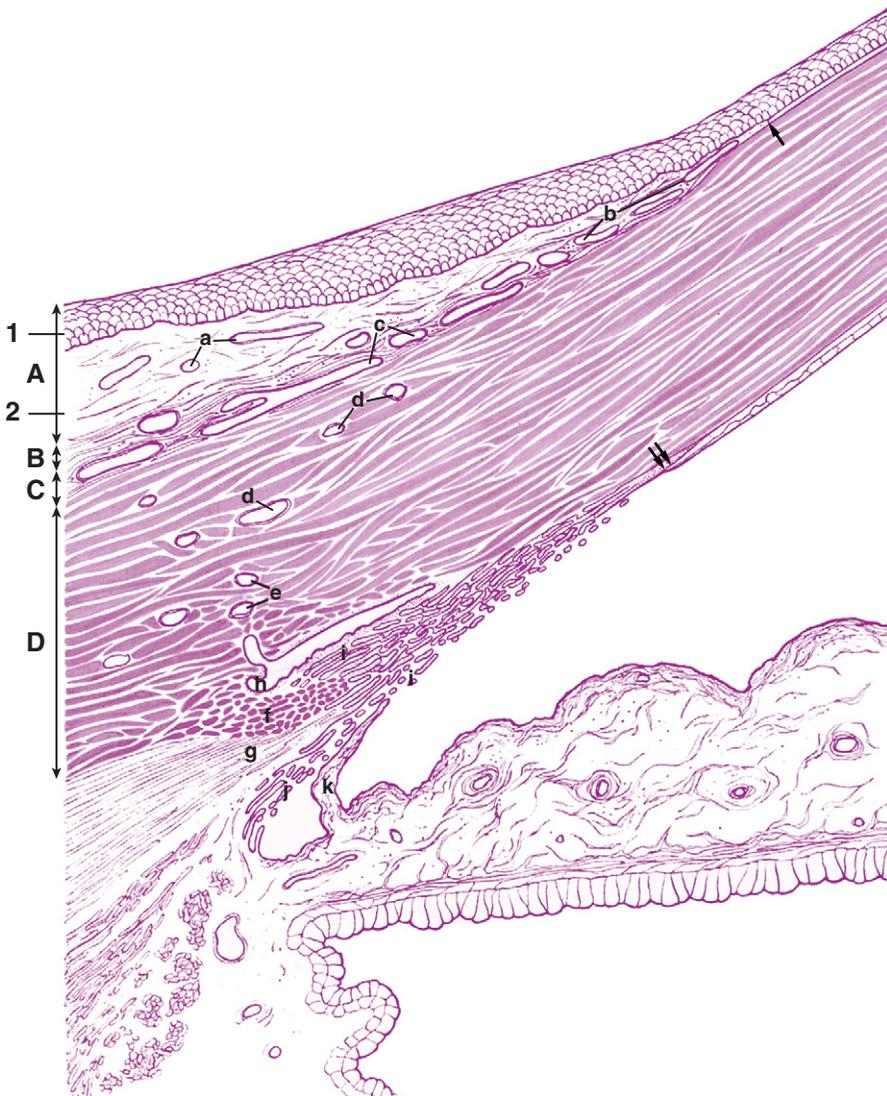


FIGURE 6-2
Drawing of the limbus. Limbal conjunctiva (A) is formed by an epithelium (1) and a loose connective tissue stroma (2). Tenon's capsule (B) forms a thin, poorly defined connective tissue layer over episclera (C). Limbal stroma occupies the area (D) and is composed of scleral and corneal tissues, which merge in this region. Conjunctival stromal vessels are seen at a; they form peripheral corneal arcades (b), which extend anteriorly to termination of Bowman's layer (arrow). Episcleral vessels (c) are cut in different planes. Vessels forming intrascleral plexus (d) and deep scleral plexus (e) are shown within limbal stroma. Scleral spur, with its coarse, dense collagen fibers, is shown at f. Anterior part of longitudinal portion of ciliary muscle (g) merges with scleral spur and trabecular meshwork. Lumen of Schlemm's canal (h) and loose tissues of its wall are clearly seen. Sheets of trabecular meshwork (i) are outer to cords of uveal meshwork (j). An iris process (k) arises from iris surface and joins trabecular meshwork at level of anterior portion of scleral spur. Descemet's membrane terminates (double arrows) within anterior portion of the triangle, outlining aqueous outflow system. (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

Canal of Schlemm

The **canal of Schlemm** is a circular vessel and is considered to be a venous channel, although it normally contains aqueous humor rather than blood. It is outer to the trabecular meshwork and anterior to the scleral spur. The external wall of the canal lies against the limbal sclera, and the internal wall lies against the trabeculae and the scleral spur (see Figure 6-2). Thin tissue septa may bridge the lumen, dividing it into two or three channels.^{2,3}

The lumen is lined with endothelial cells, many of which are joined by zonula occludens.^{2,8,10} The endothelial cells have an incomplete basement membrane.^{2,3,6} Pores and pinocytotic vesicles in the cell membrane may be an avenue for passage of aqueous humor.^{2,3,11-13}

The region separating the endothelial cell lining of the canal from the trabecular meshwork is called the **cribriform layer**,^{4,12,14} or **juxtacanalicular tissue**.^{5,11} It consists of endothelial-like cells, collagen and elastic-like fibers, and ground substance.^{12,15-17} Schlemm's canal endothelium is anchored to the cribriform layer by a network of fibers that is also connected to the tendon of the ciliary muscle.¹⁶

CLINICAL COMMENT: GONIOSCOPY

The condition of the anterior chamber angle structures is clinically important because this angle is the location of exit for aqueous humor, which must be able to flow freely from the anterior chamber. If this exit is blocked, pressure within the eye will increase, and ocular tissue damage will ensue. The width of the angle can be estimated and graded using biomicroscopy to determine whether the angle appears wide enough to provide easy access to the trabecular meshwork.

*If the angle does not appear to be wide enough or if there is concern that aqueous exit is inadequate, a view of the chamber angle structures might be necessary. A direct view of the angle cannot be achieved because the limbus is opaque and light directed obliquely through the cornea into the angle does not exit because of total internal reflection. Therefore a clinical procedure, **gonioscopy**, is performed that uses a special lens, a **goniolens** (Figure 6-6). A goniolens contains mirrors in which the examiner views the angle. The examiner sees an image as if facing the angle and sighting along the anterior surface of the iris. If all structures can be seen, they appear in the following order, beginning at the inferior aspect: iris root, ciliary body, scleral spur, trabecular meshwork, and Schwalbe's line (Figure 6-7). Schlemm's canal lies behind the trabecular meshwork in this view and appears as a thin red line within the meshwork if blood is backed up in the canal. Such pooling of blood occurs if the examiner exerts pressure on the goniolens, thereby compressing the episcleral veins and causing the episcleral venous pressure to exceed intraocular pressure.¹⁸*

In a wide-open anterior chamber angle, the entire trabecular meshwork can be seen. As peripheral iris tissue approaches the meshwork, the angle becomes narrower, and access to the trabecular openings may be diminished. In certain conditions, cellular debris or pigment accumulates within the meshwork, interfering with aqueous drainage; such an occurrence would be evident with gonioscopy.

FUNCTION OF THE FILTRATION APPARATUS

The primary function of Schlemm's canal and the trabecular meshwork is to provide an exit for the aqueous humor. In addition, with the movement of aqueous through these structures, nutrients can diffuse into

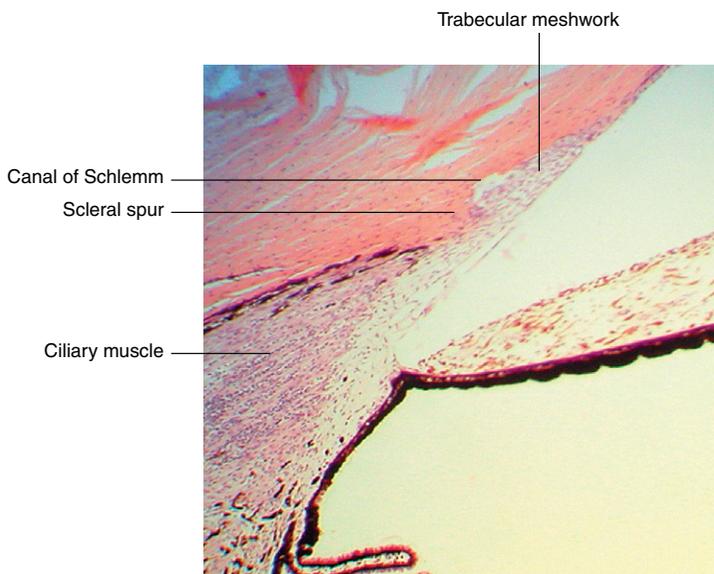


FIGURE 6-3

Light micrograph of transverse section through anterior chamber angle showing trabecular meshwork, scleral spur, and Schlemm's canal.

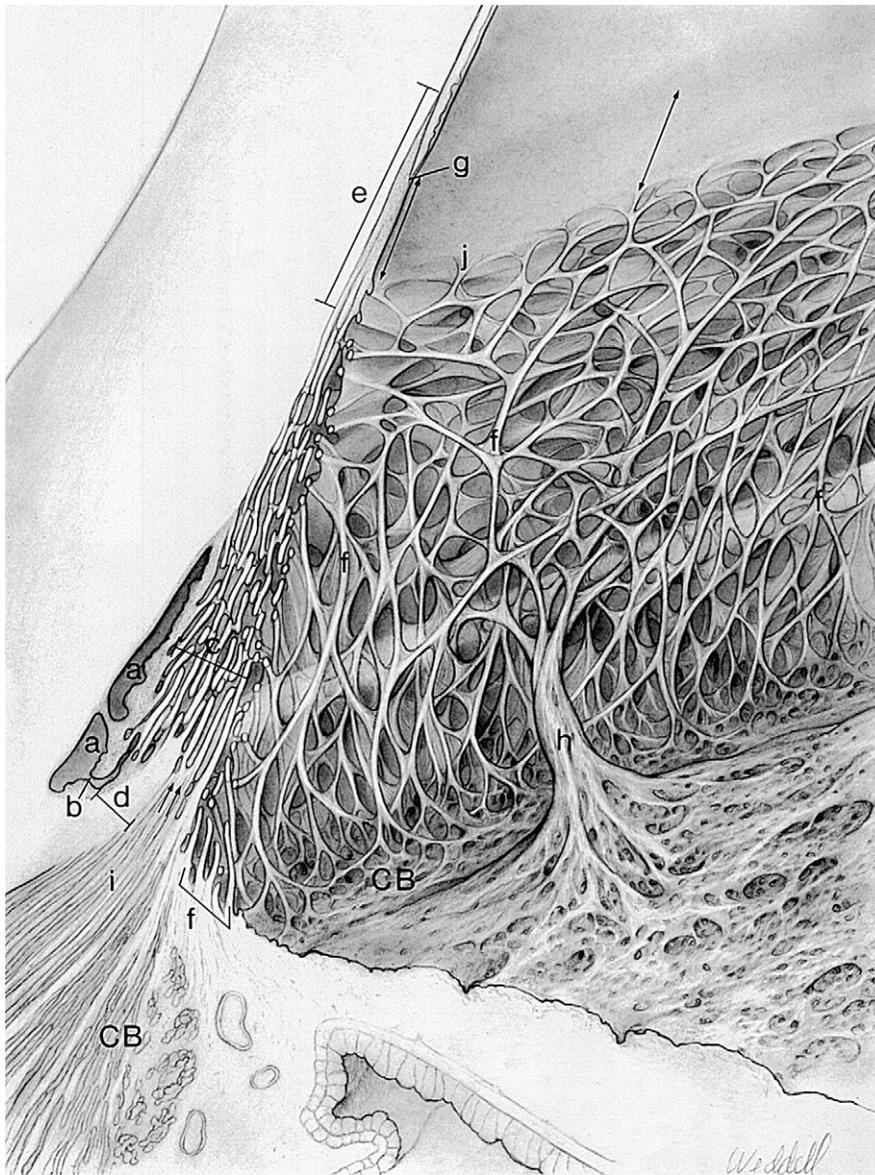


FIGURE 6-4

Drawing of aqueous outflow apparatus and adjacent tissues. Schlemm's canal (a) is divided into two portions. An internal collector channel (of Sondermann) (b) opens into posterior part of canal. Sheets of corneoscleral meshwork (c) extend from corneolimbus (e) anteriorly to scleral spur (d). Ropelike components of uveal meshwork (f) occupy inner portion of trabecular meshwork; they arise in ciliary body (CB) near the angle recess and end just posterior to termination of Descemet's membrane (g). An iris process (h) extends from iris root to merge with uveal meshwork at approximately the level of anterior part of scleral spur. Longitudinal ciliary muscle (i) is attached to scleral spur, but a portion of muscle joins corneoscleral meshwork (arrows). Descemet's membrane terminates within deep corneolimbus. Corneal endothelium becomes continuous with trabecular endothelium at j. A broad transition zone (double-headed arrows) begins near termination of Descemet's membrane and ends where uveal meshwork joins deep corneolimbus. (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

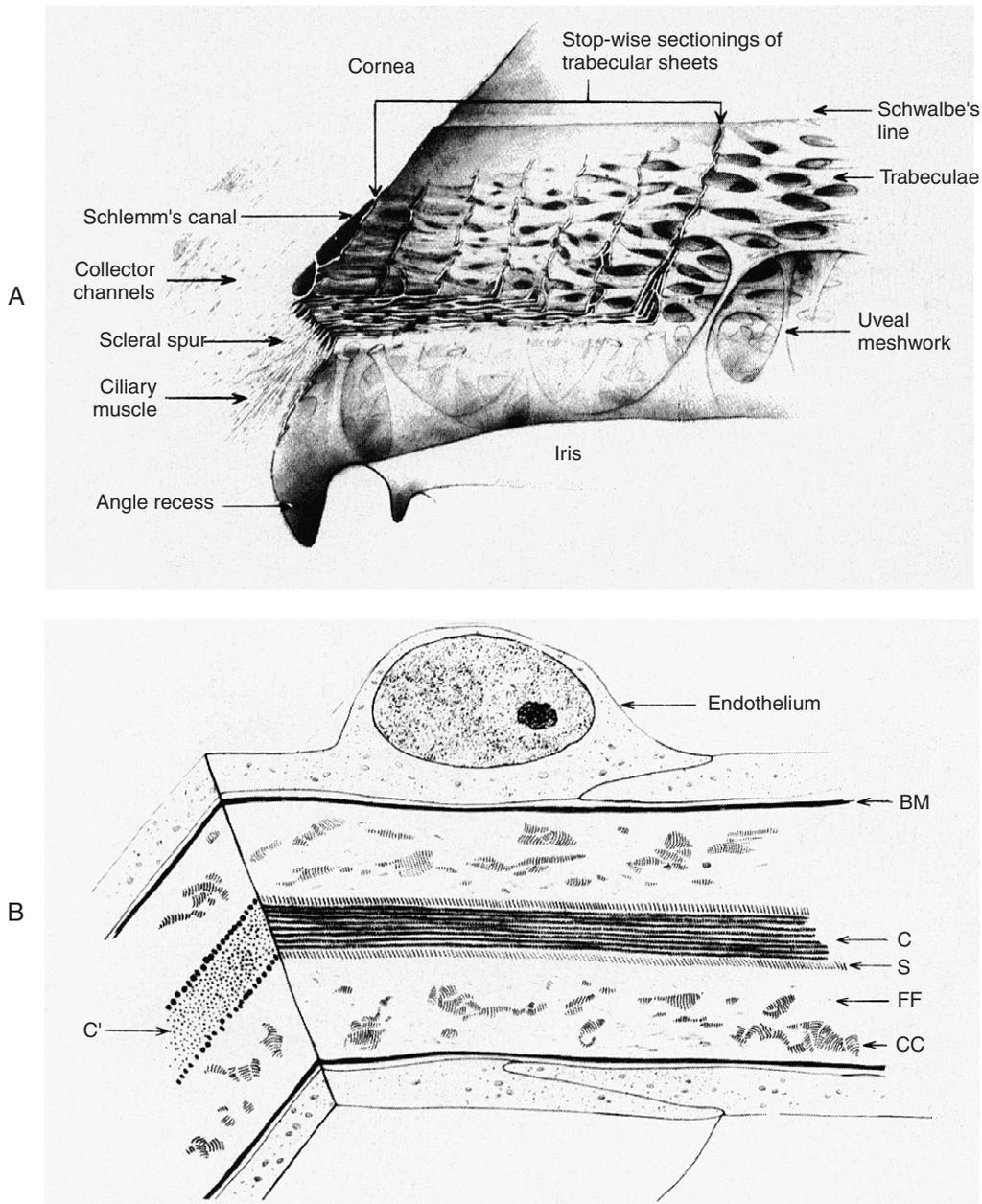
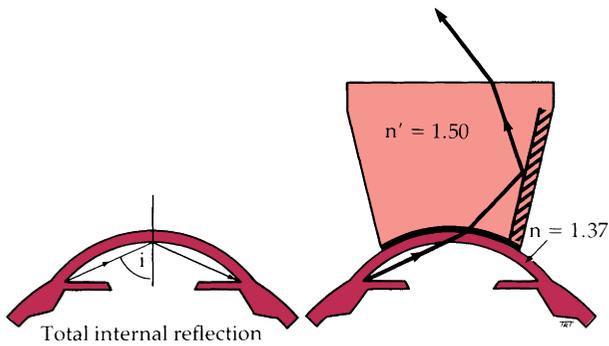


FIGURE 6-5

A, Trabecular area. Trabecular meshwork is cut away at progressively deeper levels to show size of openings and disposition of layer. Note large openings in uveal meshwork and progressive diminution of the size of these openings as Schlemm's canal is approached.

B, Tilted frontal and meridional representation of corneoscleral trabecular sheet. *C*, Central collagenous tissue; *S*, sheath of thick fibers; *FF* and *CC*, zone of ground substance containing irregular clumps of material and very fine fibrils; *BM*, basement membrane; *C'*, collagen fibers cut in cross section when trabeculae are sectioned in meridional plane. (From Garron LK, Feeney ML: *Arch Ophthalmol* 62:966, 1959.)

**FIGURE 6-6**

Optical principles of gonioscopy: n and n' , refractive index. (From Kanski JJ: *Clinical ophthalmology: a systematic approach*, ed 5, Oxford, England, 2003, Butterworth-Heinemann.)

surrounding tissue, thereby supplying nutrients to the nearby deep limbal and scleral tissue.⁷

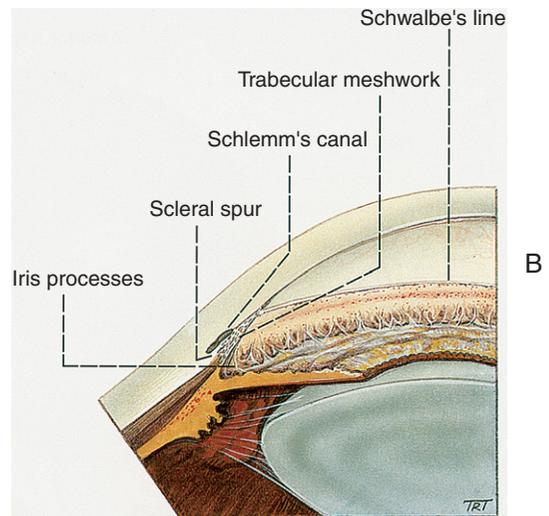
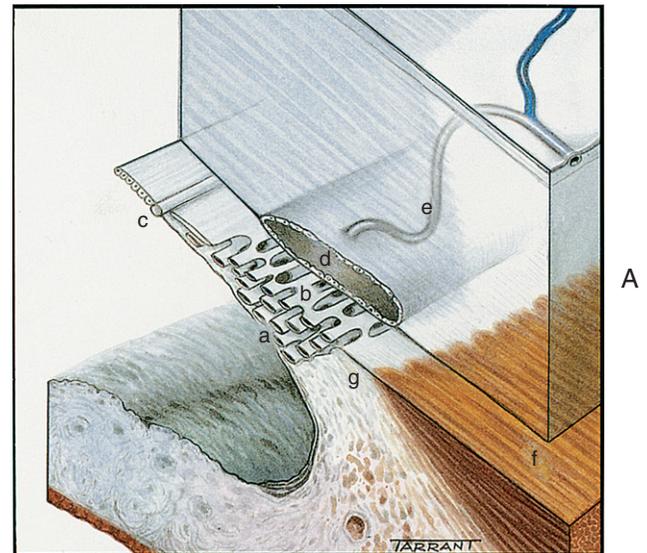
POSTERIOR CHAMBER

The **posterior chamber** is an annular area located behind the iris and bounded by the posterior iris surface, the equatorial zone of the lens, the anterior face of the vitreous, and the ciliary body. The ciliary processes that secrete the aqueous humor project into the posterior chamber. The zonule fibers arise from the internal limiting membrane of the nonpigmented epithelium of the ciliary body, pass through the posterior chamber, and insert into the lens capsule.¹ The posterior chamber contains two regions: The area occupied by the zonules is the **canal of Hannover**, and the retrozonular space, the area from the most posterior zonules to the vitreal face, is the **canal of Petit**² (Figure 6-8).

AQUEOUS DYNAMICS

The aqueous humor provides necessary metabolites, primarily oxygen and glucose, to the avascular cornea and lens. It is produced by the epithelium of the pars plicata of the ciliary body and is secreted into the posterior chamber from the ciliary processes. It passes between the iris and lens, entering the anterior chamber through the pupil (Figure 6-9). In the anterior chamber the aqueous circulates in convection currents, moving down along the cooler cornea and up along the warmer iris and exiting through the periphery of the chamber.

The aqueous passes through the spaces within the uveal meshwork. A relatively small amount (variously reported in the literature as 5% to 35% of the total outflow^{19,20}) then passes into the connective tissue spaces surrounding the ciliary muscle bundles.²¹ This

**FIGURE 6-7**

A, Anatomy of outflow channels: *a*, uveal meshwork; *b*, corneoscleral meshwork; *c*, Schwalbe's line; *d*, Schlemm's canal; *e*, collector channels; *f*, longitudinal muscle of ciliary body; *g*, scleral spur. **B**, Anatomy of anterior chamber angle structures. (From Kanski JJ: *Clinical ophthalmology: a systematic approach*, ed 3, Oxford, England, 1995, Butterworth-Heinemann.)

fluid moves into the suprachoroidal space and is absorbed into anterior ciliary veins and vortex veins.²² Additional veins have been identified that may represent suprachoroidal collector channels to accommodate this uveoscleral flow.¹⁹ The rest of the aqueous moves into the narrower pores of the corneoscleral meshwork and through the juxtacanalicular tissue and the endothelial lining into Schlemm's canal.¹⁵ In histologic sections many of the endothelial cells lining the inner wall of the canal have been found to contain giant vacuoles,^{6,10,13,23-25} some of which exhibit openings into the lumen.^{9,26,27}

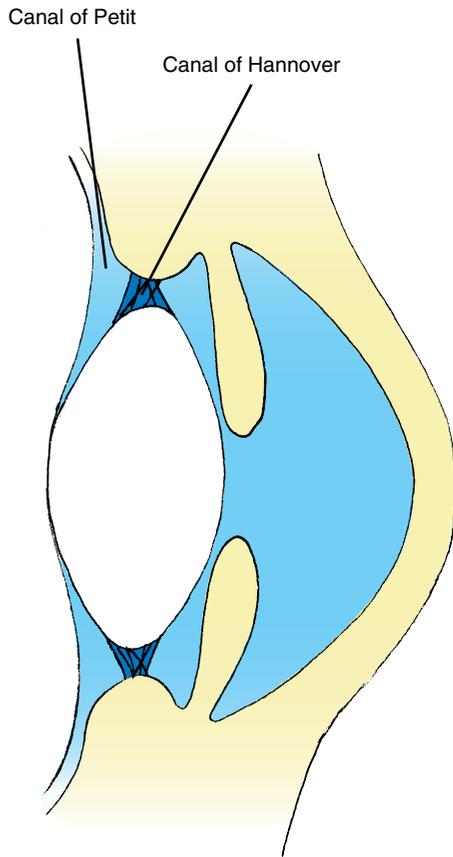


FIGURE 6-8
Regions of the posterior chamber.

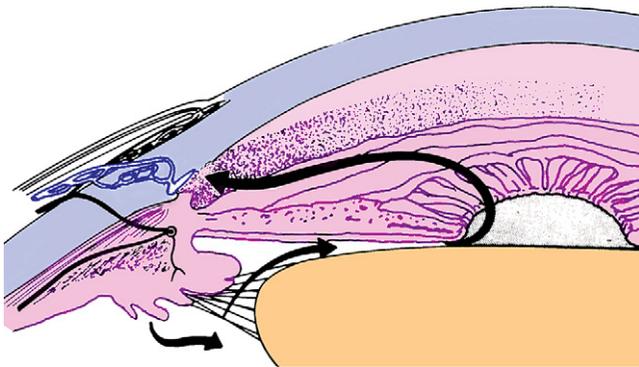


FIGURE 6-9
Normal flow of aqueous humor. Aqueous is formed in ciliary processes, moves out around crystalline lens and through pupil, and flows out of anterior chamber through trabecular meshwork into Schlemm's canal and then to episcleral veins. (From Bartlett JD, Jaanus SD: *Clinical ocular pharmacology*, ed 2, Boston, 1989, Butterworth-Heinemann.)

The vacuoles apparently open and close intermittently, creating transient, transcellular, unidirectional channels that provide a means for transporting large molecules, such as proteins, across the endothelium. Flow occurs only *into* the canal.^{11,12,28} An indentation forms in the basal surface of the endothelial cell, gradually enlarges, and eventually opens onto the apical surface (Figure 6-10). Then the cytoplasm in the basal aspect of the cell moves to occlude the opening.²⁸ The number of pores throughout the endothelium is uncertain because some may be artifacts caused by tissue preparation.²⁹ Smaller pinocytic vesicles also provide an active transport system for substances. However, the greatest volume of aqueous humor diffuses passively into Schlemm's canal. Recent speculation suggests that the tight intercellular junctions may respond to changing physiologic conditions (i.e., effects of pharmacologic agents) by modifying their permeability and increasing the ease by which aqueous flows into the canal.^{8,10}

The internal wall of Schlemm's canal contains a number of evaginations, or blind pouches, that extend into the juxtacanalicular tissue toward the trabecular meshwork. These **internal collector channels (of Sondermann)**³⁰ can be fairly long and branching and serve to increase the surface area of the canal² (Figure 6-11). Their endothelium is always separated from the trabecular space by a sheet of tissue.

The endothelial cells lining the external wall of Schlemm's canal are joined by zonula occludens and contain no vacuoles. Approximately 25 to 35 **external collector channels** branch from the outer wall of Schlemm's canal and empty into either the **deep scleral plexus** or the **intrascleral plexus** of veins,^{4,31,32} which in turn drains into the episcleral and conjunctival veins.² **Aqueous veins (of Ascher)**, which pass directly to the episcleral veins, provide another route from the canal.³³

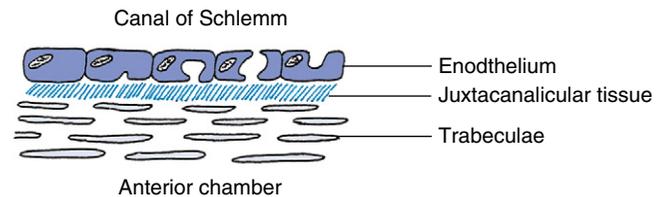


FIGURE 6-10
Formation of giant vacuoles in endothelial cells lining Schlemm's canal. (Modified from Bartlett JD, Jaanus SD: *Clinical ocular pharmacology*, ed 2, Boston, 1989, Butterworth-Heinemann.)

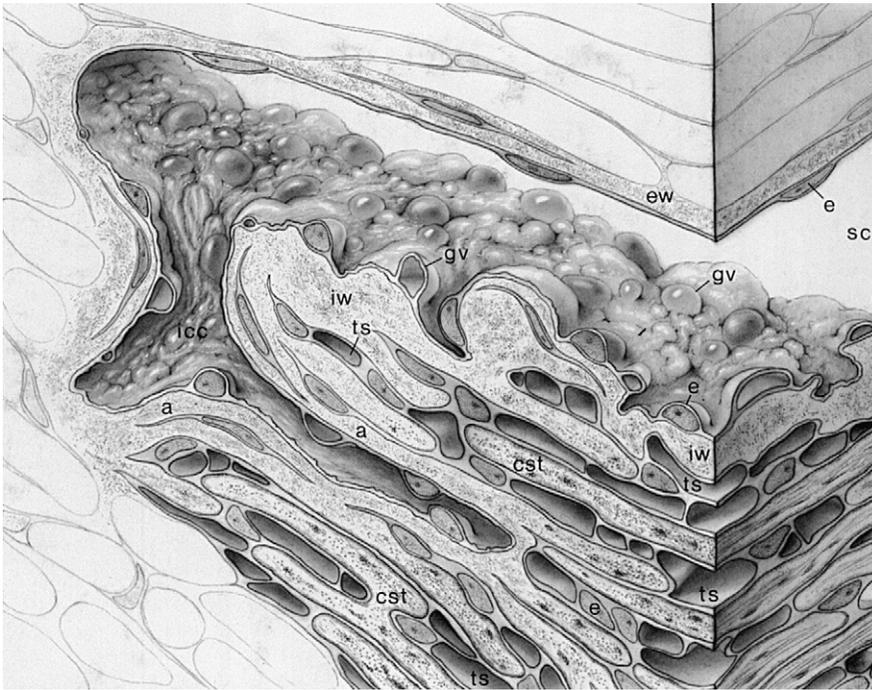


FIGURE 6-11

Drawing of Schlemm's canal, an internal collector channel, and adjacent tissues. Lumen of canal (sc) is lined by endothelium (e). Endothelium of inner wall is very irregular, with many folds and outpouchings. Giant vacuoles (gv) are seen in endothelial cells along inner wall. External wall of canal (ew) is shown. Internal wall (iw) lies between endothelium and nearest trabecular space (ts). Internal collector channel (icc) arises near posterior canal wall and extends into trabecular meshwork, where it is lost. As with Schlemm's canal, it is surrounded by a wall (a) that separates its lumen from adjacent trabecular spaces. Corneoscleral trabecular sheets (cst) branch frequently, and their endothelial cells often form bridges between adjacent sheets. (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

CLINICAL COMMENT: INTRAOCULAR PRESSURE

Intraocular pressure (IOP) can be estimated clinically using a tonometer. IOP is maintained within a fairly small range by the complex equilibrium between production and outflow of the aqueous humor. Homeostatic mechanisms normally preserve this balance, but small variations in either the production or the outflow of aqueous can cause significant changes in IOP. Production has been demonstrated to remain fairly constant, so most cases of increased IOP are caused by decreased aqueous outflow. Several theories have been developed to explain this decrease. Flow can be impeded at various sites along the aqueous exit pathway. Deposits of pigment or debris on the trabecular sheets and cords can restrict aqueous flow through the trabecular spaces. Proliferation of the juxtacanalicular tissue increases with age and has been found to cause a decrease in outflow.⁴ Conversely, the outflow may be increased by ciliary muscle contraction that causes the trabecular sheets to spread, thus decreasing the resistance through the meshwork. Current investigations are examining the meshwork's potential ability to self-regulate the aqueous outflow.³⁴

contributes to damage of the retinal nerve fiber layer, either directly by mechanical pressure or indirectly through impeded blood flow. Treatment might consist of attempts to reduce the pressure with drugs that decrease aqueous production or facilitate aqueous outflow. One treatment plan includes the use of drugs that cause the iris sphincter and ciliary muscle to contract. Ciliary muscle contraction changes the configuration of the trabecular sheets, which is believed to facilitate outflow.^{37,38} Other drugs, such as prostaglandins, may act on the connective tissue of the ciliary muscle, allowing more aqueous to exit through the uveoscleral outflow.^{20,39,40}

CLINICAL COMMENT: GLAUCOMA

Glaucoma is a complex and poorly understood disease process. Histologic preparations of ocular tissue from glaucomatous eyes indicate fewer pores in the endothelial lining and a smaller cross-sectional diameter in Schlemm's canal than in the normal eye.^{35,36} Many patients with glaucoma have higher-than-normal IOP. Increased IOP

AGING CHANGES IN THE ANTERIOR CHAMBER

With age the anterior chamber angle width narrows and the anterior chamber volume decreases, probably secondary to lens growth. This narrowing is more significant in women and may be related to the higher incidence of angle-closure glaucoma in elderly women.⁴¹

Other aging changes may be in response to an age-related decrease in aqueous production, including uveoscleral outflow reduction, a decrease in the density and size of giant vacuoles, and an increase in the outflow resistance of the inner wall of Schlemm's canal.^{42,43} Since no age-related increase in IOP is seen in healthy individuals with pressures below 22 mm Hg, these factors apparently offset each other.⁴²

VITREOUS CHAMBER

The **vitreous chamber** is filled with the gel-like vitreous body and occupies the largest portion of the globe. It is bounded on the front by the posterior surface of the lens and the retrozonular portion of the posterior chamber. Peripherally and posteriorly, it is bounded by the pars plana of the ciliary body, the retina, and the optic disc. All surfaces that interface with the vitreous are basement membranes. The center of the anterior surface contains the **patellar fossa**, an indentation in which the lens sits.

VITREAL ATTACHMENTS

The vitreous forms several attachments to surrounding structures. The strongest of these is the vitreous base, located at the ora serrata. The other attachments (in order of decreasing strength) are to the posterior lens, to the optic disc, at the macula, and to retinal vessels.

The **vitreous base**, the most extensive adhesion, extends 1.5 to 2 mm anterior to the ora serrata, 1 to 3 mm posterior to it, and several millimeters into the

vitreous^{2,44} (Figure 6-12). The vitreal fibers that form the base are embedded firmly in the basement membrane of the nonpigmented epithelium of the ciliary body and the internal limiting membrane of the peripheral retina.^{31,45}

The **hyaloideocapsular ligament (of Weiger)**, or **retrolental ligament**, forms an annular attachment 1 to 2 mm wide and 8 to 9 mm in diameter between the posterior surface of the lens and the anterior face of the vitreous.⁴⁴ This is a firm attachment site in young persons, but the strength of the bond diminishes with age. Within the ring formed by this ligament is a potential space, the **retrolental space (of Berger)**, which is present because the lens and vitreous are juxtaposed but not joined.²

The peripapillary adhesion around the edge of the optic disc also diminishes with age. The annular ring of attachment at the macula is 3 to 4 mm in diameter.²

The attachment of the vitreous to retinal blood vessels consists of fine strands that extend through the internal limiting membrane to branch and surround the larger retinal vessels.^{45,46} These strands may account for

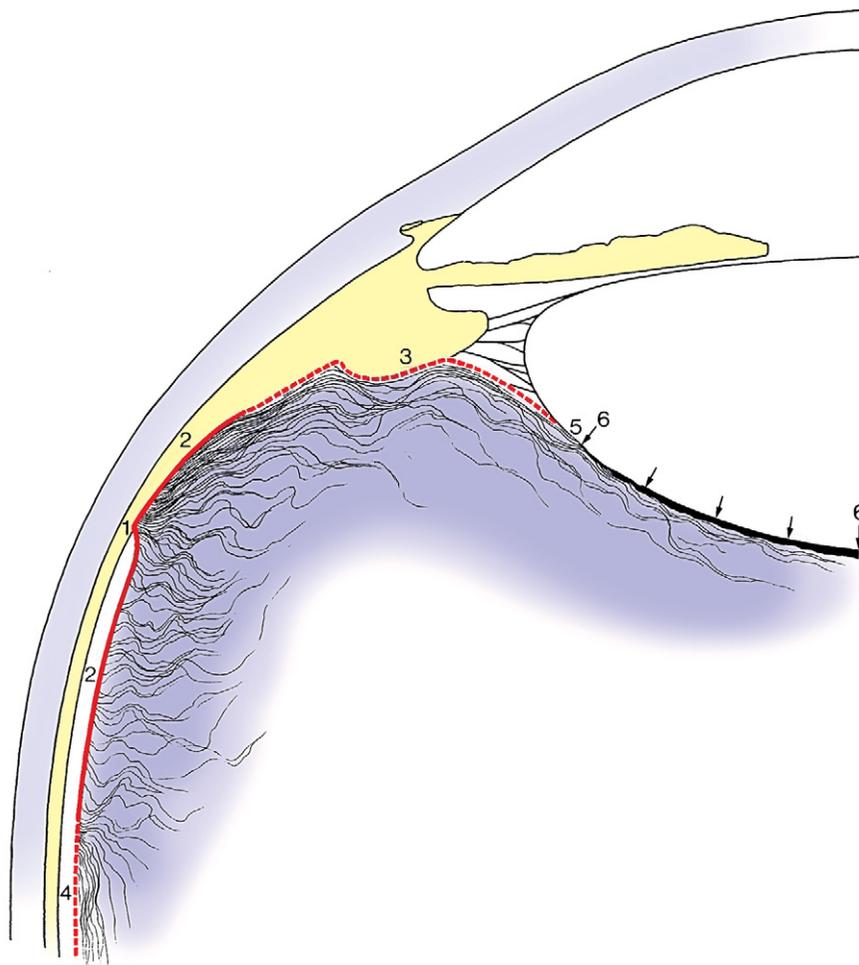


FIGURE 6-12

Vitreous relationships in the anterior eye. Ora serrata (1) is termination of retina. Vitreous base (2) extends forward approximately 2 mm over ciliary body and posteriorly approximately 4 mm over peripheral retina. Collagen in this region is oriented at a right angle to surface of retina and ciliary body, but anteriorly over pars plana, it is more parallel to inner surface of ciliary body. Posterior hyaloid (4) is continuous with retina and anterior hyaloid (3) with zonules and lens. Also depicted are hyaloideocapsular ligament (5) and space of Berger (6). (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

hemorrhages that occur when there is vitreal traction on the retina. The nature of the attachment between the vitreous and the retinal internal limiting membrane remains uncertain. It is unlikely that fibrils from the posterior vitreous insert into the internal limiting membrane.⁴⁷⁻⁴⁹ The actual interface probably is below the resolution of the electron microscope at a chemical bond level.^{2,50}

VITREOUS ZONES

The vitreous can be divided into zones that differ in relative density. The outermost zone is the vitreous cortex, the intermediate zone is inner to the cortex, and the center zone is occupied by Cloquet's canal.

Vitreous Cortex

The **vitreous cortex**, also called the **hyaloid surface**, is the outer zone.⁵¹ It is 100 μm wide,² and it is composed of tightly packed collagen fibrils, some of which run parallel and some perpendicular to the retinal surface.^{52,53} The anterior cortex lies anterior to the base and is adjacent to the ciliary body, posterior chamber, and lens. The posterior cortex extends posterior to the base and is in contact with the retina. It contains transvitreal channels that appear as holes—the prepapillary hole, the premacular hole, and prevascular fissures. The *prepapillary hole* can sometimes be seen clinically when the posterior vitreous detaches from the retina.⁴⁴ The *premacular hole*, a weak area, may be a region of decreased density rather than an actual hole.^{44,53} The *prevascular fissures* provide the avenue by which fine fibers enter the retina and encircle retinal vessels.⁴⁵

Intermediate Zone

The **intermediate zone** contains fine fibers that are continuous and unbranched and that run antero-posteriorly.^{44,52,54} These fibers arise at the region of the vitreous base and insert into the posterior cortex.⁵⁵ The peripheral fibers parallel the cortex, whereas the more central fibers parallel Cloquet's canal. Membrane-like condensations, called vitreous tracts, may be differentiated as areas that have differing fiber densities (Figure 6-13).⁵³

Cloquet's Canal

Cloquet's canal, also called the **hyaloid channel** or the **retrolental tract**, is located in the center of the vitreous body.² It has an S shape, rotated 90 degrees with the center dip downward, and is the former site of the hyaloid artery system, which was formed during

embryologic development (see Chapter 7). Cloquet's canal arises at the retrolental space. Its anterior face is approximately 4 to 5 mm in diameter.² It terminates at the **area of Martegiani**, a funnel-shaped space at the optic nerve head that extends forward into the vitreous to become continuous with the canal.^{2,44}

COMPOSITION OF VITREOUS

The highly transparent vitreous is a dilute solution of salts, soluble proteins, and hyaluronic acid contained within a meshwork of the insoluble protein collagen. Vitreous is 98.5% to 99.7% water and has been

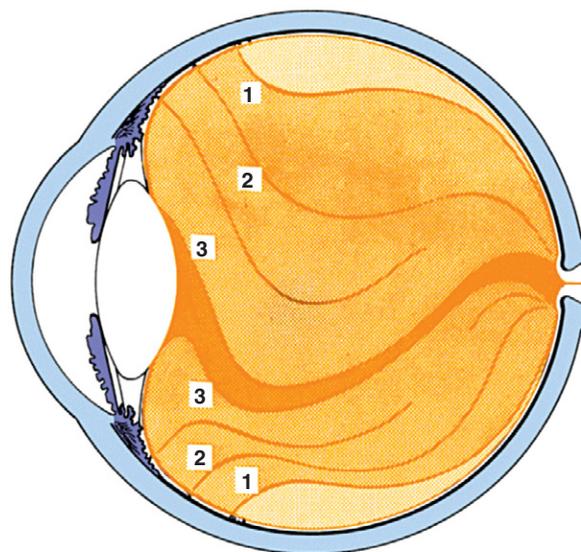


FIGURE 6-13

Eisner's interpretation⁵³ of vitreous structures (according to slit-lamp examinations of eyes obtained at autopsy). Vitreous body is divided into three zones: Externally, as far as retina extends, there is a relatively thick vitreous cortex (*light orange*). It has holes at characteristic locations: in front of papilla, in region of fovea centralis, in front of vessels, and in front of anomalies of ora serrata region (enclosed ora bays, meridional folds, zonular traction tufts). Intermediate zone (*medium orange*) contains vitreal tracts, membranelles that form funnels packed into one another and that diverge from region of papilla anteriorly. Central channel (*dark orange*) is space delimited by hyaloid tract. It is closed off anteriorly by a retrolental section of anterior vitreous membrane. It contains no typical tracts but only irregularly arranged vitreous fibers, part of which are residua of Cloquet's canal. Outermost vitreous tract, the preretinal tract (1), separates intermediary substance from vitreous cortex. Innermost tract, the hyaloid tract (3), inserts at the edge of the lens. Between these tracts extends the median tract (2) to median ligament of pars plana and the coronary tract to coronary ligament. (From Sebag J: The vitreous. In Hart WM Jr, editor: *Adler's physiology of the eye*, ed 9, St Louis, 1992, Mosby.)

described as having connective tissue status and being an extracellular matrix.^{53,56} Because of its high water content, study of the vitreous is difficult: Attempts at tissue fixation often have dehydrating effects that introduce artifacts. Recent investigations suggest that the epithelium of the pars plana has a significant role in the production and secretion of several connective tissue macromolecules of the vitreous body.⁵⁶

Collagen

The **collagen** content of the vitreous is highest in the vitreous base, next highest in the posterior cortex, next in the anterior cortex, and lowest in the center.⁴⁴ A fine meshwork of uniform collagen fibrils, each 8 to 16 nm in diameter, is evident on electron microscopy and fills the vitreous body.^{51,57-60} The individual fibrils cannot be seen with the slit lamp, but the pattern of variations in their density and regularity can be seen. The density of this collagen fibril network differs throughout the vitreous.³⁴

Hyaluronic Acid

The second major vitreal component, **hyaluronic acid (HA)**, is a long unbranched chain of molecules coiled into a twisted network.⁵⁴ This macromolecule is located in specific sites within the collagen fibril network and is believed to maintain the wide spacing between fibrils.⁴⁴ The concentration of HA is highest in the posterior cortex and decreases centrally and anteriorly.⁶⁰ The interaction between HA and collagen fibrils contributes to the viscoelastic properties of the vitreous^{61,62} and influences the physical properties (gel and liquid) of the vitreous state.⁴⁴

Hyalocytes

Vitreous cells, or **hyalocytes**, are located in a single, widely spaced layer in the cortex near the vitreal surface and parallel to it.^{44,54} Various functions have been attributed to these cells. Some investigators have determined that these cells synthesize HA.⁶³⁻⁶⁵ Others have found evidence that hyalocytes synthesize glycoproteins for the collagen fibrils.^{44,66} Still others indicate that hyalocytes have phagocytic properties.^{54,65,67} Apparently, hyalocytes can have different appearances depending on their activity at a given time.⁴⁴ Cells located in the vitreous base are fibroblast-like when anterior to the ora serrata and macrophage-like when posterior to it.⁴⁷

Fibroblasts present in the vitreous are located in the vitreous base near the ciliary body and near the optic disc. Although composing less than 10% of the cell population, fibroblasts may have been mistaken for hyalocytes in the past. It is believed that fibroblasts

synthesize the collagen fibrils that run anteroposteriorly and are active in pathologic conditions.⁴⁴

Other cells that have been identified as macrophages likely originate in the nearby retinal blood vessels.^{2,53}

VITREAL FUNCTION

The vitreous body is a storage area for metabolites for the retina and lens and provides an avenue for the movement of these substances within the eye.³³ The vitreous, because of its viscoelastic properties, acts as a “shock absorber,” protecting the fragile retinal tissue during rapid eye movements and strenuous physical activity.^{2,53} The vitreous transmits and refracts light, aiding in focusing the rays on the retina. Minimal light scattering occurs in the vitreous because of its extremely low concentration of particles and the wide interfibrillar spacing ensured by the HA-collagen complex. A disruption in the HA-collagen complex causes the collagen fibrils to aggregate into bundles, which may become large enough to be visible clinically, a phenomenon often referred to as *floaters*.

AGE-RELATED VITREAL CHANGES

In the infant the vitreous is a very homogeneous, gel-like body. With maturation, changes occur in which the gel volume decreases and the liquid volume increases.⁴⁴ By age 40 years the vitreous is 80% gel and 20% liquid, and by 70 or 80 years it is 50% liquid,⁵² with most of the liquefaction occurring in the central vitreous.⁵³ Both HA and collagen may be detrimentally affected by free radicals.⁶⁸ Conformational changes in the HA molecule and the subsequent displacement of collagen from the HA-collagen network influence the change from gel to liquid.⁶⁹ As the dissolution of the HA-collagen complex occurs, the macromolecule moves out of the collagen network, causing the fibrils to coalesce into fibers and then bands; the HA pools in areas adjacent to these bundles, forming areas of liquid vitreous.⁷⁰ The pockets of liquid formed by these changes are called *lacunae*.^{70,71}

CLINICAL COMMENT: PERIPHERAL RETINAL TRACTION

With aging, the vitreous base adhesion extends further posteriorly, and the border approaches the equator.^{72,73} These changes can increase traction on peripheral retina and might contribute to the development of retinal tears and detachment.

CLINICAL COMMENT: POSTERIOR VITREAL DETACHMENT

As the HA is displaced from the collagen network and as the fibrils coalesce into bundles, the bundles can contract and apply traction to the vitreous and thus to the posterior retina. One of the most common abnormalities that occur at the posterior retinal–vitreous interface is a **posterior vitreal detachment** caused by this traction. The vitreous usually detaches from the retinal internal limiting membrane at the peripapillary ring, forming a retrocortical space. If glial tissue is torn away with the vitreous, a circular condensation, Weiss' ring (senile annular ring), may be visible within the vitreous.⁷⁴ If liquid vitreous seeps into the retrocortical space through the prepapillary and premacular areas, a syneresis, or collapse, of the vitreous can be caused by the volume displacement.^{70,75}

REFERENCES

1. Fine BS, Yanoff M. The vitreous body. In Fine BS, Yanoff M, editors: *Ocular histology*, ed 2, Hagerstown, Md, 1979, Harper & Row, p 131.
2. Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.
3. Warwick R: *Eugene Wolff's anatomy of the eye and orbit*, ed 7, Philadelphia, 1976, Saunders.
4. Lütjen-Drecoll E, Rohen JW: Functional morphology of the trabecular meshwork. In Tasman W, Jaeger EA, editors: *Duane's foundations of clinical ophthalmology*, vol 1, Philadelphia, 1994, Lippincott, p 1.
5. Alexander RA, Garner A: Elastic and precursor fibres in the normal human eye, *Exp Eye Res* 36:305, 1983.
6. Gong H, Ruberti J, Overby D et al: A new view of the human trabecular meshwork using quick-freeze, deep-etch electron microscopy, *Exp Eye Res* 75:347, 2003.
7. Fine BS: Structure of the trabecular meshwork and Schlemm's canal, *Trans Am Acad Ophthalmol Otolaryngol* 70:791, 1966.
8. Bhatt K, Gong F, Freddo TF: Freeze-fracture studies of interendothelial junctions in the angle of the human eye, *Invest Ophthalmol Vis Sci* 36(7):1379, 1995.
9. Raviola G, Raviola E: Paracellular route of aqueous in the trabecular meshwork and canal of Schlemm, *Invest Ophthalmol Vis Sci* 21:52, 1981.
10. Ye W, Gong H, Sit A et al: Interendothelial junctions in normal human Schlemm's canal respond to changes in pressure, *Invest Ophthalmol Vis Sci* 38(12):2460, 1997.
11. Bill A: Scanning electron microscopic studies of the canal of Schlemm, *Exp Eye Res* 10:214, 1970.
12. Epstein DL, Rohen JW: Morphology of the trabecular meshwork and inner wall after cationized ferritin perfusion in the monkey eye, *Invest Ophthalmol Vis Sci* 32:160, 1991.
13. Ethier CR, Coloma FM, Sit AJ et al: Two pore types in the inner-wall endothelium of Schlemm's canal, *Invest Ophthalmol Vis Sci* 39(11):2041, 1998.
14. Lütjen-Drecoll E, Futa R, Rohen JW: Ultrahistochemical studies on tangential sections of the trabecular meshwork in normal and glaucomatous eyes, *Invest Ophthalmol Vis Sci* 21:563, 1981.
15. Inomata H, Bill A, Smelser GK: Aqueous humor pathways through the trabecular meshwork and into Schlemm's canal in the cynomolgus monkey (*Macaca irus*), *Am J Ophthalmol* 73:760, 1972.
16. Rohen JW, Futa R, Lütjen-Drecoll E: The fine structure of the cribriform network in normal and glaucomatous eyes seen in tangential sections, *Invest Ophthalmol Vis Sci* 21:574, 1981.
17. Umihira J, Nagata S, Nohara M et al: Localization of elastin in the normal and glaucomatous human trabecular meshwork, *Invest Ophthalmol Vis Sci* 35(2):486, 1994.
18. Kanski JJ: *Clinical ophthalmology*, ed 3, Oxford, England, 1994, Butterworth-Heinemann.
19. Krohn J, Bertelsen T: Corrosion casts of the suprachoroidal space and uveoscleral drainage routes in the human eye, *Acta Ophthalmol Scand* 75:32, 1997.
20. Nilsson SF: The uveoscleral outflow routes, *Eye* 11:149, 1997.
21. Bill A: Some aspects of aqueous humour drainage, *Eye* 7:14, 1993.
22. Krohn J, Bertelsen T: Light microscopy of uveoscleral drainage routes after gelatine injections into the suprachoroidal space, *Acta Ophthalmol Scand* 76(5):521, 1998 (abstract).
23. Holmberg AS: The fine structure of the inner wall of Schlemm's canal, *Arch Ophthalmol* 62:956, 1959.
24. Speakman JS: Drainage channels in the trabecular wall of Schlemm's canal, *Br J Ophthalmol* 44:513, 1960.
25. Parc CE, Johnson DH, Brilakis HS: Giant vacuoles are found preferentially near collector channels, *Invest Ophthalmol Vis Sci* 41:2984, 2000.
26. Feeney ML, Wissig S: Outflow studies using an electron dense tracer, *Trans Am Acad Ophthalmol Otolaryngol* 70:791, 1966.
27. Anderson DR: Scanning electron microscopy of primate trabecular meshwork, *Am J Ophthalmol* 71:90, 1971.
28. Tripathi EC: Mechanism of the aqueous outflow across the trabecular wall of Schlemm's canal, *Exp Eye Res* 11:116, 1971.
29. Sit AJ, Coloma FM, Ethier CR et al: Factors affecting the pores of the inner wall endothelium of Schlemm's canal, *Invest Ophthalmol Vis Sci* 38(8):1517, 1997.
30. Sondermann R: The formation, morphology and function of Schlemm's canal, *Acta Ophthalmol* 11:280, 1933.
31. Theobald GD: Schlemm's canal: its anastomosis and anatomic relations, *Trans Am Ophthalmol Soc* 32:574, 1934.
32. Ashton N: Anatomical study of Schlemm's canal and aqueous veins by means of neoprene casts. I. Aqueous veins, *Br J Ophthalmol* 35:291, 1951.
33. Ascher KW: Aqueous veins: preliminary notes, *Am J Ophthalmol* 25:31, 1942.
34. Selbach JM, Gottanka J, Wittmann M et al: Efferent and afferent innervation of primate trabecular meshwork and scleral spur, *Invest Ophthalmol Vis Sci* 41(8):2184, 2000.
35. Johnson S, Chan D, Read AT et al: The pore density in the inner wall endothelium of Schlemm's canal of glaucomatous eyes, *Invest Ophthalmol Vis Sci* 43(9):2950, 2002.
36. Allingham RR, de Kater AW, Ethier CR: Schlemm's canal and primary open angle glaucoma: correlation between Schlemm's canal dimensions and outflow facility, *Exp Eye Res* 62(1):101, 1996 (abstract).
37. Rohen JW, Unger HH: Studies on the morphology and pathology of the trabecular meshwork in the human eye, *Am J Ophthalmol* 46:802, 1958.
38. Grierson I, Lee WR, Abraham S: Effects of pilocarpine on the morphology of human outflow apparatus, *Br J Ophthalmol* 62:302, 1978.
39. Alm A: Uveoscleral outflow, *Eye* 14:488, 2000.
40. Lütjen-Drecoll E, Gabelt AT, Tian B et al: Outflow of aqueous humor, *J Glaucoma* 19(suppl):42, 2001.
41. Chen HB, Kashiwagi K, Yamabayashi S et al: Anterior chamber angle biometry: quadrant variation, age change and sex difference, *Curr Eye Res* 17(2):129, 1998 (abstract).
42. Toris CB, Yablonski ME, Yun-Liang W et al: Aqueous humor dynamics in the aging human eye, *Am J Ophthalmol* 127:407, 1999.

43. Boldea RC, Roy S, Mermoud A: Ageing of Schlemm's canal in nonglaucomatous subjects, *Int Ophthalmol* 24:67, 2002.
44. Sebag J: The vitreous. In Hart WM Jr, editor: *Adler's physiology of the eye*, ed 9, St Louis, 1992, Mosby, p 268.
45. Mutlu F, Leopold IH: Structure of the human retinal vascular system, *Arch Ophthalmol* 71:93, 1964.
46. Wolter JR: Pores in the internal limiting membrane of the human retina, *Arch Ophthalmol* 42:971, 1964.
47. Gartner J: Vitreous electron microscopic studies on the fine structure of the normal and pathologically changed vitreoretinal limiting membrane, *Surv Ophthalmol* 9:219, 1964.
48. Matsumoto B, Blanks JC, Ryan SJ: Topographic variations in rabbit and primate internal limiting membrane, *Invest Ophthalmol Vis Sci* 25:71, 1984.
49. Malecaze F, Caratero C, Caratero A et al: Some ultrastructural aspects of the vitreoretinal junction, *Ophthalmologica* 191:22, 1985.
50. Russell SR, Shepherd JD, Hageman GS: Distribution of glycoconjugates in the human retinal internal limiting membrane, *Invest Ophthalmol Vis Sci* 32(7):1986, 1991.
51. Schwarz W: Electron microscopic observations on the human vitreous body. In Smelser GK, editor: *Structure of the eye*, New York, 1961, Academic Press, p 283.
52. Balazs EA: Functional anatomy of the vitreous. In Tasman W, Jaeger EA, editors: *Duane's foundations of clinical ophthalmology*, vol 1, Philadelphia, 1994, Lippincott.
53. Eisner G: Clinical anatomy of the vitreous. In Tasman W, Jaeger EA, editors: *Duane's foundations of clinical ophthalmology*, vol 1, Philadelphia, 1994, Lippincott.
54. Balazs EA, Toth LZ, Eckl EA et al: Studies on the structure of the vitreous body. XII. Cytological and histochemical studies on the cortical tissue, *Exp Eye Res* 3:57, 1964.
55. Sebag J, Balazs EA: Morphology and ultrastructure of human vitreous fibers, *Invest Ophthalmol Vis Sci* 30:1867, 1989.
56. Bishop PN, Takanosu M, le Goff M et al: The role of the posterior ciliary body in the biosynthesis of vitreous humour, *Eye* 16:454, 2002.
57. Pirie A, Schmidt G, Waters JW: Ox vitreous humor. I. The residual protein, *Br J Ophthalmol* 32:321, 1948.
58. Matoltsy AG: A study on the structural protein of the vitreous body (vitrosin), *J Gen Physiol* 36:29, 1952.
59. Gross J, Matoltsy AG, Cohen C: Vitrosin: a member of the collagen class, *J Biophys Biochem Cytol* 1:215, 1955.
60. Bembridge BA, Crawford CN, Pirie A: Phase-contrast microscopy of the animal vitreous body, *Br J Ophthalmol* 36:131, 1952.
61. Weber H, Landwehr G: A new method for the determination of the mechanical properties of the vitreous, *Ophthalmic Res* 14:326, 1982.
62. Weber H, Landwehr G, Kilp H et al: The mechanical properties of the vitreous of pig and human donor eyes, *Ophthalmic Res* 14:335, 1982.
63. Osterlin SE: The synthesis of hyaluronic acid in the vitreous. IV. Regeneration in the owl monkey, *Exp Eye Res* 7:524, 1968.
64. Hultsch E, Balazs EA: In vitro synthesis of glycosaminoglycans and glycoproteins by cells of the vitreous, *Invest Ophthalmol Vis Sci* 14(suppl):43, 1973.
65. Freeman MI, Jacobson B, Balazs EA: The chemical composition of vitreous hyalocyte granules, *Exp Eye Res* 29:479, 1979.
66. Ayad S, Weiss JB: A new look at vitreous humor collagen, *Biochem J* 218:835, 1984.
67. Szirmai JA, Balazs EA: Studies on the structure of the vitreous body: cells in the cortical layer, *Arch Ophthalmol* 59:34, 1958.
68. Lund-Andersen H, Sander B: The vitreous. In Kaufman PL, Alm A, editors: *Adler's physiology of the eye*, ed 10, St Louis, 2003, Mosby, p 293.
69. Armand G, Chakrabarti B: Conformational differences between hyaluronates of gel and liquid human vitreous: fractionation and circular dichroism studies, *Curr Eye Res* 6:445, 1987.
70. Sebag J: Age-related differences in the human vitreoretinal interface, *Arch Ophthalmol* 109(7):966, 1991.
71. Kishi S, Shimizu K: Posterior precortical vitreous pocket, *Arch Ophthalmol* 108:979, 1990.
72. Teng CC, Che HH: Vitreous changes and the mechanism of retinal detachment, *Am J Ophthalmol* 44:335, 1957.
73. Wang J, McLeod D, Henson DB et al: Age-dependent changes in the basal retinovitreal adhesion, *Invest Ophthalmol Vis Sci* 44(5):1793, 2003.
74. Spalton DJ, Hitchings RA, Hunter PA: *Atlas of clinical ophthalmology*, Philadelphia, 1984, Lippincott, p 124.
75. Lindner B: Acute posterior vitreous detachment and its retinal complications, *Acta Ophthalmol Suppl* 87:1, 1966.



This chapter follows the chapters describing the globe and orbit because the study of embryology can be difficult if the adult structure, organization, and function of the eye are not known. Although studying the development of a structure *after* studying the structure itself might seem backward, in my experience this has proved to be a useful sequence for the student. *In this chapter, the development of each structure is described separately, but the reader must keep in mind that these events are occurring simultaneously.*

With the explosion of information from improved technology and human genome study, new information is reported daily about the processes that control cellular development, structure, and function. A number of growth factors have been identified that bind to receptor sites on target cells that control normal development by modulating proliferation, migration, and differentiation.¹ These processes are at the basis of structure development. Cells from germ layers migrate to a specific location and then proliferate, forming the population of cells that will differentiate into the specific cell type necessary.

One particular gene that appears to be important in the development of ocular structures is the Pax-6 gene. Animal studies indicate that the gene influences the development of lens, cornea, and conjunctiva. An increase in Pax-6 in mice is associated with multiple lens defects, including abnormal fiber shape and fiber-to-fiber and fiber-to-cell interactions.² In chick embryos the Pax-6 gene is expressed in the corneal and conjunctival epithelium and may regulate and maintain cell structure. The Pax-6 gene is speculated to also have a role in the proliferation of corneal and conjunctival stem cells.³

DEVELOPMENT OF OCULAR STRUCTURES

During the third week of embryonic development, the three primary germ layers—ectoderm, mesoderm, and endoderm—have formed the embryonic plate.⁴ (Of these three, only ectoderm and mesoderm will take part in the developing ocular structures.) A thickening in the ectoderm, visible on the dorsal surface of the embryo, forms the **neural plate**, which will give rise to the central nervous system, including ocular structures. A groove forms down the center of this plate at approximately

day 18 of gestation, and the ridges bordering the groove grow into **neural folds**. As the groove expands, these folds grow toward one another and fuse to form the **neural tube** along the dorsal aspect of the embryo. The neural tube is formed on or near day 22.⁴

The ectoderm now lining the tube is **neural ectoderm** and that surrounding the tube is **surface ectoderm**, which differ both in anatomic location and in differentiation potentials (Box 7-1). An area of cells on the crest of each of the neural folds separates from the ectoderm. These **neural crest cells** come to lie between the neural tube and the surface ectoderm. Cells from the middle

BOX 7-1

Embryologic Derivation of Ocular Structures

Surface ectoderm gives rise to:

- Lens
- Corneal epithelium
- Conjunctival epithelium and lacrimal glands
- Epithelium of eyelids and cilia, meibomian glands, and glands of Zeis and Moll
- Epithelium lining nasolacrimal system

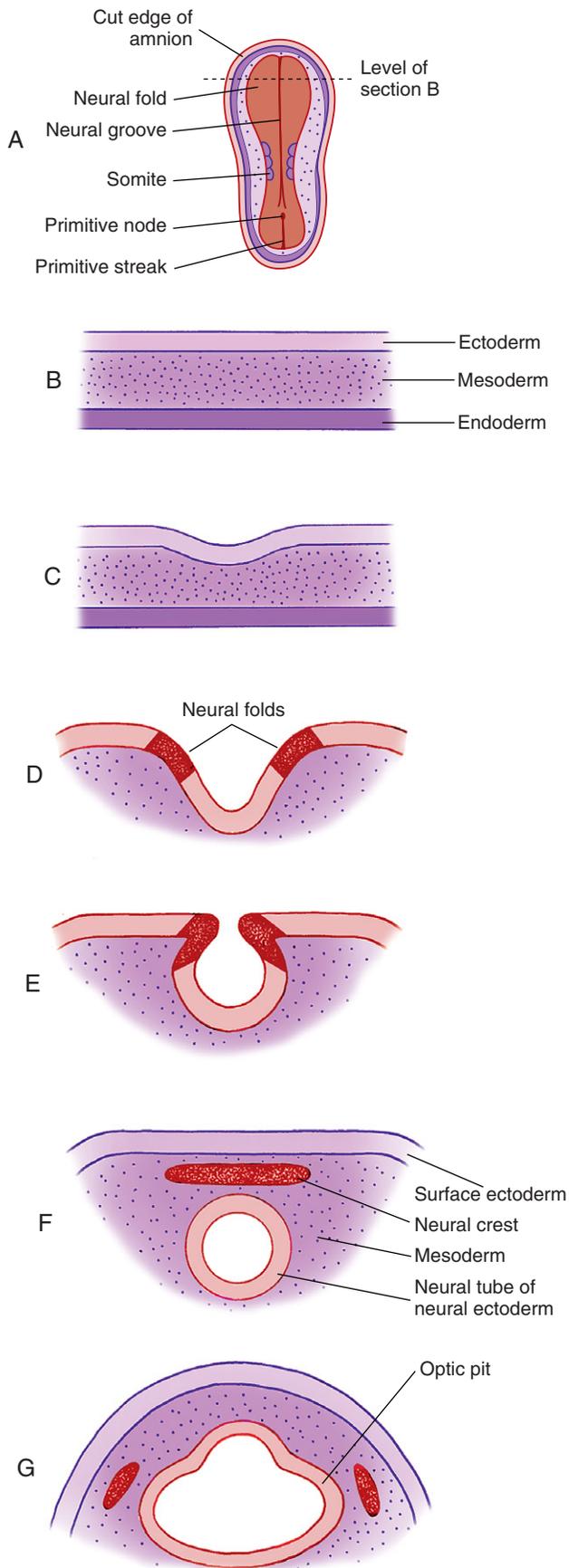
Neural ectoderm gives rise to:

- Retinal pigment epithelium
- Neural retina
- Optic nerve fibers
- Neuroglia
- Epithelium of ciliary body
- Epithelium of iris, including iris sphincter and dilator muscles

Neural crest gives rise to:

- Corneal stroma (which gives rise to Bowman's layer)
- Corneal endothelium (which gives rise to Descemet's membrane)
- Most (or all) of sclera
- Trabecular structures
- Uveal pigment cells
- Uveal connective tissue
- Vascular pericytes

Modified from Beauchamp GR, Knepper PA: *J Pediatr Ophthalmol Strabismus* 21(6):209, 1984; and Tasman W, Jaeger EA, editors: *Duane's foundations of clinical ophthalmology*, vol 1, Philadelphia, 1994, Lippincott.



embryonic layer, the **mesoderm**, also are located between the neural tube and the surface ectoderm. Figure 7-1 illustrates these events.

OPTIC PITS

The **optic pits** form as indentations on both sides of the neural tube in the forebrain region even before the tube is completely closed. On approximately day 25, after the neural tube has closed, the optic pits form lateral sac-shaped extensions, the **optic vesicles**.⁵ The vesicles initially are in contact with surface ectoderm but gradually are separated from it by cells of neural crest origin and mesoderm.⁶

Neural crest cells and mesoderm collectively make up the **mesenchyme**, from which the connective tissue of the globe and orbit develop. Although most orbital connective tissue is derived from neural crest, determining whether a structure is of neural crest or mesodermal origin sometimes is difficult because mesodermal cells and neural crest cells appear similar cytologically.⁷ If the origin is uncertain, mesenchyme is cited as the germ layer.

As the optic vesicle evaginates, the tissue joining the vesicle to the neural tube constricts, forming the **optic stalk** (Figure 7-2). The cells lining the inner surface of this entire formation are ciliated, and the outer surface is covered by a thin basal lamina.⁵ The cavity of the optic stalk, as well as that of the optic vesicle, is continuous with the space that will become the third ventricle.

While the wall of the optic vesicle is in contact with surface ectoderm, it thickens and flattens to form the **retinal disc**.⁷ The lower wall of the optic vesicle and optic stalk begins to buckle and move inward toward the upper and posterior walls. This invagination forms a cleft, variously called the **optic fissure**, **embryonic fissure**, or **fetal fissure**. (It has also been called the "choroidal fissure," but this name is avoided because it may imply that the choroid is involved in the fissure, which it is not.) The inferior wall continues to move inward, pulling the anterior wall of the optic vesicle with it and placing the retinal disc in the approximate location of the future retina. The edges of the fissure grow toward one another and begin to fuse at 5 weeks;

FIGURE 7-1

Formation of neural tube. **A**, Dorsal surface of embryo as seen from above. **B**, Horizontal section through three-layered embryonic disc. **C**, Neural groove forms in neural plate area of ectoderm. **D**, Neural groove invaginates, and neural folds are formed. **E**, Neural folds continue to grow toward each other. **F**, Neural crest cells separate from ectoderm of neural folds as the folds fuse; neural tube is formed (of neural ectoderm); and surface ectoderm is again continuous. **G**, Evaginations in area of forebrain form the optic pits.

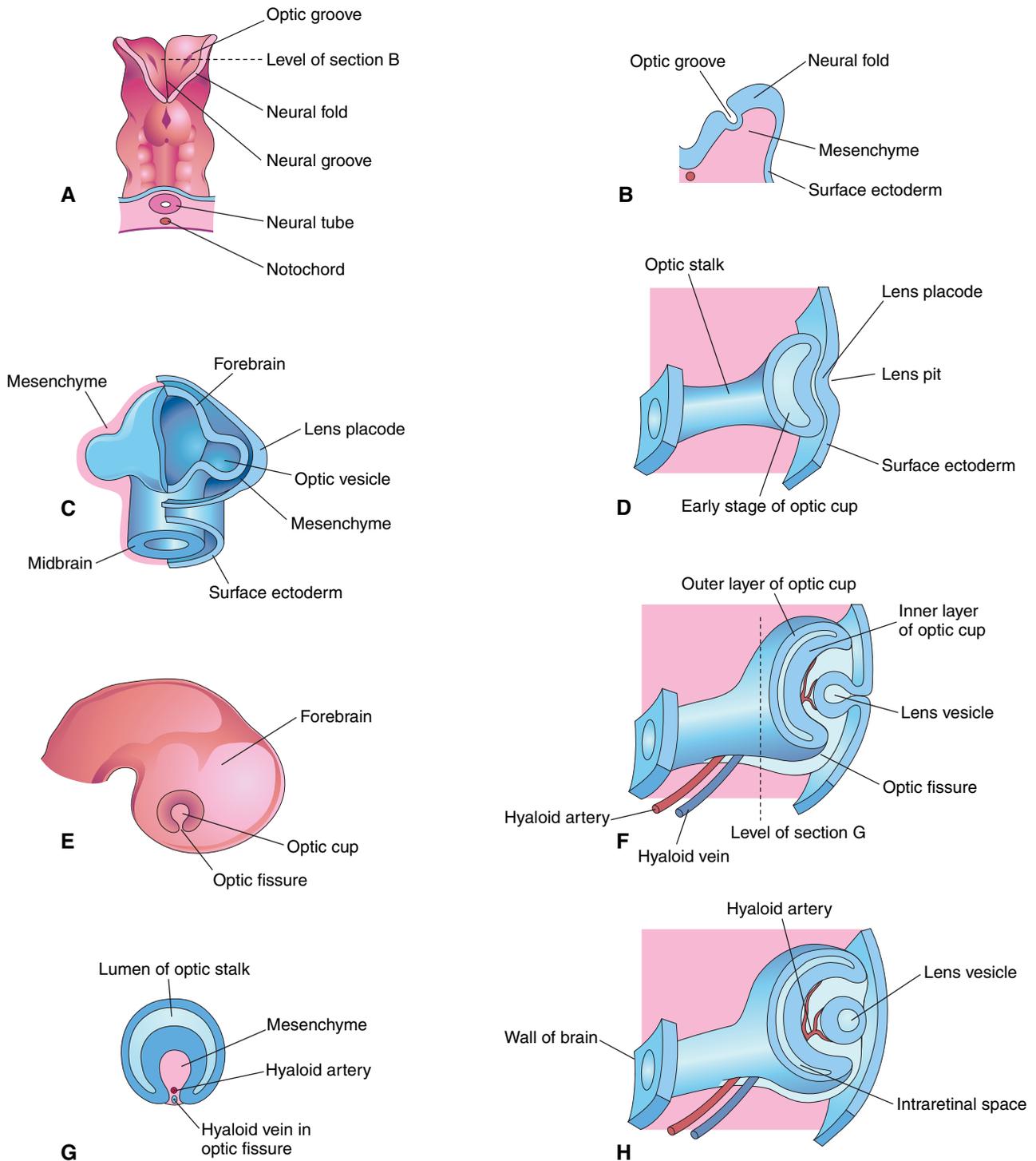


FIGURE 7-2

Early eye development. **A**, Dorsal view of cranial end of 22-day embryo showing first indication of eye development. **B**, Transverse section through neural fold showing an optic groove. **C**, Forebrain and its covering layers of mesenchyme and surface ectoderm from approximately 28-day-old embryo. **D**, **F**, and **H**, Sections of developing eye, illustrating successive stages in development of the optic cup and lens vesicle. **E**, Lateral view of brain of approximately 32-day-old embryo showing external appearance of optic cup. **G**, Transverse section through optic stalk showing optic fissure and its contents. (From Moore KL: *Before we are born: essentials of embryology and birth defects*, ed 5, Philadelphia, 1998, Saunders.)

fusion starts at the center and proceeds anteriorly toward the rim of the optic cup and posteriorly along the optic stalk. Closure is complete at 7 weeks, forming the two layers of the optic cup and optic stalk⁸ (Figure 7-3). Mesenchyme enters the fissure and moves into the cavity of the developing optic cup.

OPTIC CUP, LENS, AND RELATED STRUCTURES

Optic Cup

The **optic cup** at this stage of development is composed of two layers of cells (both neuroectodermal in origin) that are continuous with each other at the rim of the cup. The cells of the inner and outer layers of the optic cup are positioned apex to apex and are separated by the **intraretinal space** (see Figure 7-2, *H*), which, as the two layers approach each other, finally will become only a potential space. The outer layer of the optic cup will become the retinal pigment epithelium (RPE), the outer pigmented epithelium of the ciliary body, and the anterior iris epithelium. The inner layer will become the neural retina, the inner nonpigmented ciliary body epithelium, and the posterior iris epithelium.

Mesenchyme proliferates and migrates around the optic cup, and once the cells reach their destination, they proliferate and differentiate, contributing to the connective tissue of the orbit. Neural crest cells will form corneal stroma and endothelium, uveal stroma and melanocytes, ciliary muscle, much of the sclera, the connective tissue and meningeal sheaths of the optic nerve, and the connective tissue of the lids, conjunctiva, and orbit. Vascular endothelium and striated muscle are formed by mesoderm.¹

CLINICAL COMMENT: COLOBOMA

*Incomplete closure of the optic fissure may affect the developing optic cup or stalk and the adult derivations of these structures, resulting in an inferior nasal defect in the optic disc, retina, ciliary body, or iris. This defect is called a **coloboma** and can vary from a slight notch to a large wedgelike defect. A large iris coloboma produces a keyhole-shaped pupil, although the remainder of the iris develops normally (Figure 7-4, A). When the coloboma is unilateral the affected iris may have denser pigmentation than the opposite normal iris.¹⁰ Colobomas affecting the sensory retina and RPE also involve the choroid because its differentiation depends on an intact RPE layer.¹¹ Bare sclera is seen in the area affected, with retinal vessels passing over the defect (Figure 7-4, B).*

Induction

During embryologic development, formation and growth of structures depend on tissue differentiation

and interactions among these tissues. Some structures will not develop unless they are near another developing area at a specific time. There is some uncertainty regarding whether the two structures must actually come in contact or just be in proximity, but substances *must* be able to pass between them.¹² This influence that one developing structure has on another is termed **induction**. It is likely that the mechanism of induction is not a single event but a series of separate steps that presumably occur on a biochemical level.¹³

Lens

Induction occurs between the developing optic cup and the developing lens, apparently through a reciprocal relationship.¹⁴ As the surface ectoderm comes in contact with the optic vesicle, the invagination of the optic cup begins (approximately day 27), and the surface ectoderm adjacent to the vesicle begins to thicken, forming the **lens plate (lens placode)** (Figure 7-5 and 7-6, *A*). This thickening is caused by an elongation of the ectodermal cells and by a regional increase in cell division.⁷ If the area of contact between the optic vesicle and surface ectoderm is less than normal, a perfectly formed but microphthalmic eye will result.¹⁵ Some investigators believe that transformation of the lens plate into the lens vesicle might be independent of direct contact with the optic vesicle.¹⁶ In addition to signals from the developing optic vesicle, complete lens differentiation might also depend on factors that inhibit lens formation in the ectoderm adjacent to the lens plate.¹⁷

The center of the outer surface of the lens plate invaginates rapidly, forming a **lens pit**. As invagination continues, the lens vesicle is formed, which then separates from the surface ectoderm at approximately day 33.^{5,12} The **lens vesicle** is a hollow sphere composed of a single layer of cells surrounded by a thin basal lamina; with the addition of more material, the basal lamina will become the lens capsule (Figure 7-6, *B* and *C*).

Once the lens vesicle is formed, the posterior epithelial cells adjacent to the future vitreous cavity elongate to fill in the lumen within the lens vesicle (Figure 7-6, *D* and *E*). The proximity of the developing retina seems to be the inducing factor for this elongation. These posterior epithelial cells become the **primary lens fibers** and form the **embryonic nucleus** at the center of the lens. This nucleus has no sutures. The fact that the posterior epithelium was used to form the embryonic nucleus accounts for the lack of an epithelial layer beneath the posterior lens capsule in the fully formed lens. The anterior epithelial cells remain in place, and the cells near the equator begin to undergo mitosis. Each new cell elongates anteriorly and posteriorly, forming secondary lens fibers that are laid down around the embryonic nucleus. The first layer of **secondary fibers** is completed

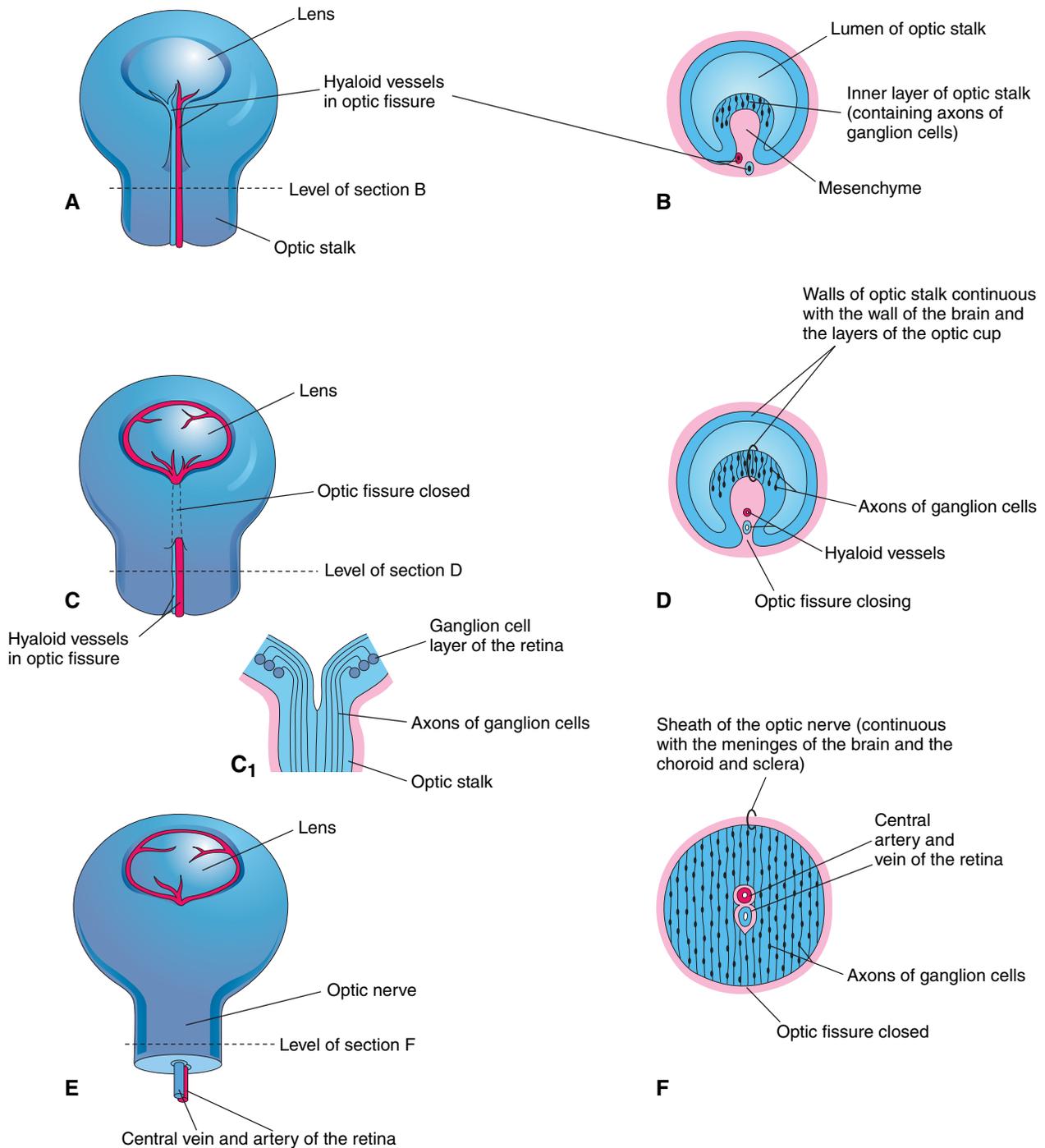
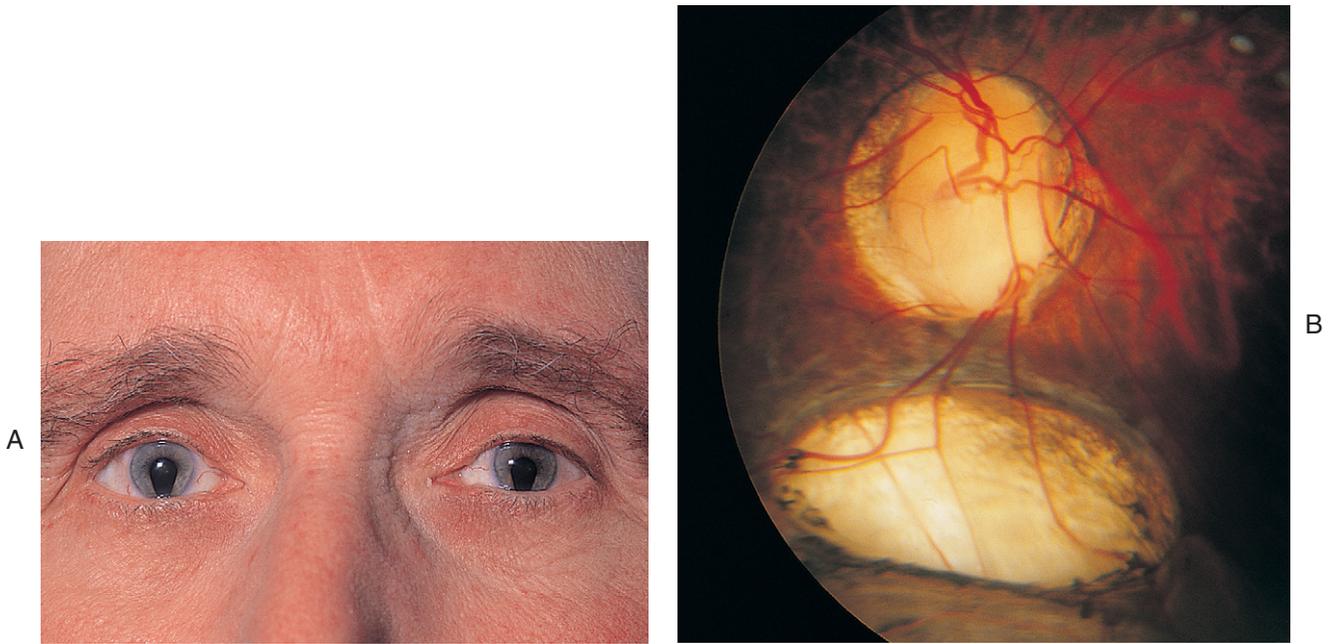
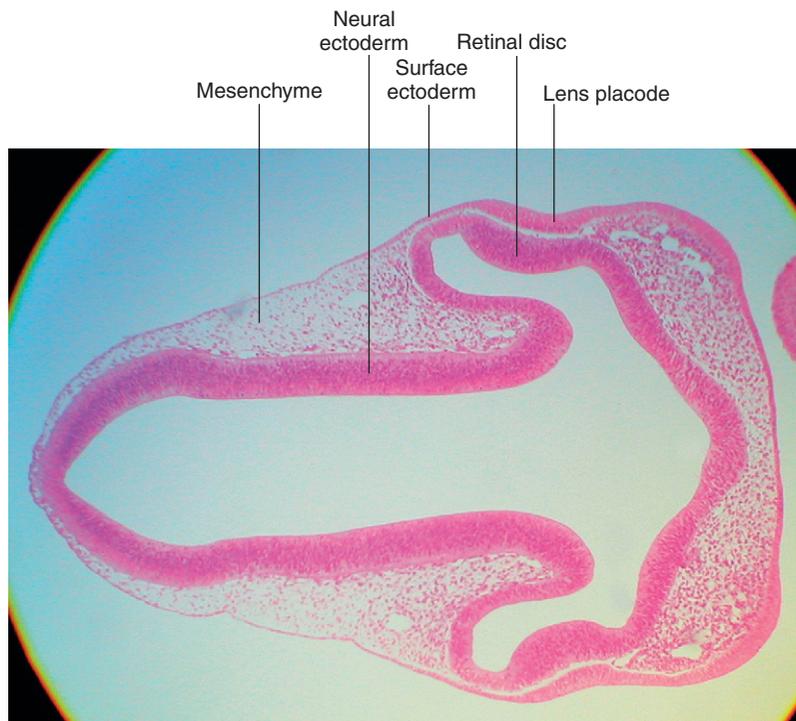


FIGURE 7-3

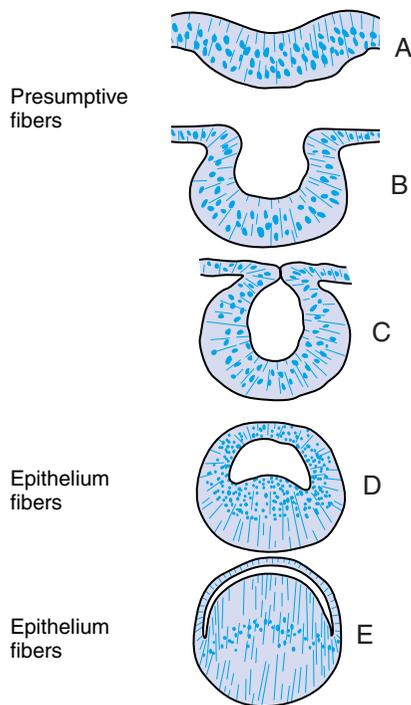
Closure of optic fissure and formation of optic nerve. **A, C, and E**, Views of inferior surface of optic cup and stalk showing progressive stages in closure of optic fissure. Longitudinal section of portion of optic cup and optic stalk (**C**) showing axons of ganglion cells of retina growing through optic stalk to brain. **B, D, and F**, Transverse sections through optic stalk showing successive stages in closure of optic fissure and formation of optic nerve. Optic fissure normally closes during sixth week. Defects of closure of optic fissure results in defect in iris known as coloboma of the iris. Note that lumen of optic stalk is obliterated gradually as axons of ganglion cells accumulate in the inner layer of the stalk. Formation of optic nerve occurs between sixth and eighth weeks. (From Moore KL: *Before we are born: essentials of embryology and birth defects*, ed 5, Philadelphia, 1998, Saunders.)

**FIGURE 7-4**

A, Iris coloboma (OU); pupil has keyhole appearance. **B**, Coloboma of retina. Retinal tissue and choroidal tissue are absent, retinal vessels course across the intact sclera. (**A** from Kanski JJ, Nischal KK: *Ophthalmology; clinical signs and differential diagnosis*, St Louis, 1999, Mosby; **B** courtesy Pacific University Family Vision Center, Forest Grove, Ore.)

**FIGURE 7-5**

Light micrograph of 6-mm pig embryo showing thickening of lens placode.

**FIGURE 7-6**

A, Formation of lens placode. **B**, Invagination forming lens vesicle. **C** to **E**, Development of embryonic nucleus. **C**, Hollow lens vesicle is lined with epithelium. **D**, Posterior cells elongate, becoming primary lens fibers. **E**, Primary lens fibers fill lumen, forming embryonic nucleus. Curved line formed by cell nuclei is called the lens bow. Anterior epithelium remains in place.

**FIGURE 7-7**

Light micrograph of 15-mm pig embryo showing lens vesicle filling with primary lens fibers; lens bow configuration is evident.

by week 7.¹² The ends of the secondary fibers meet in an **upright-Y** suture posterior to the *anterior* epithelium and in an **inverted-Y** suture anterior to the *posterior* capsule. These sutures are visible during the third month.¹⁸ The region containing the Y sutures continues to develop until birth, forming the **fetal nucleus**. If a line were drawn to connect the cellular nuclei within the lens fibers, an arcuate shape would be revealed. This configuration is called the **lens bow** (Figure 7-7).

Mitosis, cell elongation, and lens fiber formation continue throughout development and throughout life. The orientation of the lens is influenced by the developing vitreous.^{15,19} The lens is initially spheric in shape but becomes more ellipsoid with additional fibers.²⁰ The **lens capsule** is evident at 5 weeks, evolving from the basement membrane of the invaginating surface ectoderm and from secretions of the lens epithelium.¹⁸

CLINICAL COMMENT: CONGENITAL CATARACT

The spectrum of lens opacities that can result from problems during lens development range from pinpoint densities having no effect on vision to significant opacities causing extensive loss of vision.²¹ If the tissue near the developing lens fails to induce the lens fibers to elongate and pack together in an orderly way, the lens fibers will be misaligned, forming a cataract of the primary fibers. Interference with secondary lens fibers can lead to sutural cataracts.²²

Viral infection affecting the mother during the first trimester often causes congenital malformations, including a cataract. The developing lens is vulnerable to the rubella virus (German measles) between the fourth and seventh week of development, when the primary fibers are forming. After this period the virus cannot penetrate the lens capsule and thus will not affect the lens. The cataract usually is present at birth but may develop weeks to months later because the virus can persist within the lens for up to 3 years. The opacity may be dense and opaque or it may be diffuse; the cataract may affect the nucleus only or may involve most of the lens.²³

Hyaloid Arterial System

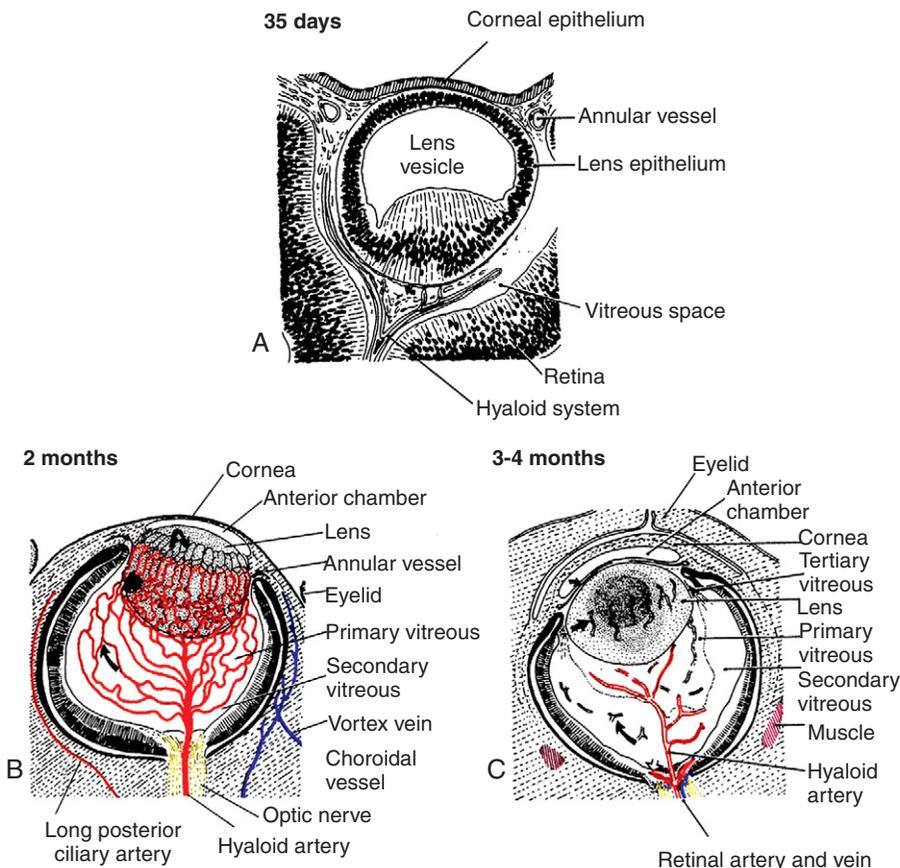
A branch of the internal carotid artery enters the optic cup through the fetal fissure to become the **hyaloid artery** during week 5.¹ This vessel produces a highly branching network that fills the vitreous cavity and forms the **posterior vascular tunic of the lens (posterior tunica vasculosa lentis)**, a vascular network covering the posterior lens (Figure 7-8). By the end of the second month the hyaloid vasculature is fully formed.¹ Branches near the lens equator anastomose with the **annular vessel** at the margin of the optic cup. The annular vessel sends loops forward onto the anterior surface of the

**FIGURE 7-8**

Light micrograph of 25-mm pig embryo showing the hyaloid arterial system filling future vitreal cavity. Vessels are evident extending through the optic stalk and the vascular network attached to posterior lens is evident.

lens to form the **anterior vascular tunic of the lens (anterior tunica vasculosa lentis)** during the seventh week^{1,24,25} (Figure 7-9). These vascular networks carry nutrients to the developing lens until production of the aqueous humor begins. These vessels drain into a network located in the region that will become the ciliary body.⁵ The vessels of the hyaloid system cannot be identified as arterial or venous on the basis of their histologic makeup.²⁴

Glial cells on the surface of the optic cup form a conelike mass of tissue around the base of the hyaloid artery. These cells proliferate, forming a glial mantle around the arterial system. The hyaloid vasculature reaches its peak development during the third month¹ and begins to atrophy during the fourth month, at the same time that the retinal vasculature is developing.^{1,26} By the seventh month, no blood flow is present in the hyaloid vasculature, which normally should be completely reabsorbed by birth.⁵ The extent of the degeneration of the glial tissue mass defines the extent of the adult physiologic optic cup.²⁷

**FIGURE 7-9**

Schema of main features in vitreous development and regression of hyaloid system, shown in drawings of sagittal sections. **A**, At 5 weeks, hyaloid vessels and branches occupy much of space between lens and neural ectoderm. **B**, By 2 months, vascular primary vitreous reaches its greatest extent. An avascular secondary vitreous of more finely fibrillar composition forms a narrow zone between peripheral branches of hyaloid system and retina. **C**, During fourth month, vessels of hyaloid system atrophy progressively. Zonular fibers (tertiary vitreous) begin to stretch from growing ciliary region toward lens capsule. Vessels through center of optic nerve connect with hyaloid vessels and send small loops into retina. (From Cook CS, Ozanics V, Jakobiec FA: Prenatal development of the eye and its adnexa. In Tasman W, Jaeger EA, editors: *Duane's foundations of clinical ophthalmology*, vol 1, Philadelphia, 1994, Lippincott.)

CLINICAL COMMENT: BERGMEISTER'S PAPPILLA AND MITTENDORF'S DOT

Remnants of the hyaloid system often are seen clinically during examination of a patient's ocular health. Glial tissue that persists on the nerve head is called **Bergmeister's papilla** (Figure 7-10), and a pinpoint remnant of the hyaloid artery on the posterior surface of the lens is called **Mittendorf's dot**. Rarely, a remnant of the entire hyaloid artery will be seen coursing through the vitreous from its attachment at the disc to the posterior lens.

Retinal Pigment Epithelium

Apposition of the two layers of the optic cup is essential for development of the **retinal pigment epithelium**,¹⁵ the first retinal layer to differentiate.²⁷ Cellular structures and melanosomes begin to appear in the outer layer of the optic cup, and pigmentation of the retinal epithelium occurs at approximately week 3 or 4; this is the earliest pigmentation evident in the embryo^{5,6,28} (see Figure 7-8). After week 6 the RPE is one cell thick, the cells are cuboidal to columnar in shape, and the base of each cell is external toward the developing choroid and the apex internal toward the inner layer of the optic cup.^{29,30}

Neural Retina

Between weeks 4 to 6 the cells of the inner layer of the optic cup (in the area that will become **neural retina**) proliferate, and two zones are evident.¹ The cells accumulate in the outer region, the **proliferative zone** or **germinating zone**. The inner **marginal zone (of His)** is anuclear. A thin lamina—the basement membrane of the inner layer of the optic cup and the precursor of the internal limiting membrane—separates the marginal zone from the vitreal cavity.¹⁸ At approximately week 7, cell migration occurs, forming the **inner and outer neuroblastic layers**, between which lies the **transient fiber layer of Chievitz**, a nucleus-free area.^{29,31} The formation of these two neuroblastic layers is complete during the third month. Differentiation of the neural retinal cells begins in central retina and proceeds to the periphery.¹

Ganglion cells and amacrine cells differentiate in the vitread portion of the inner neuroblastic layer.³² The ganglion cells migrate, forming a layer close to the basement membrane, and almost immediately send out their axonal processes, which become evident by week 8.¹⁸ Biomolecular agents guide the axonal growth toward termination in the lateral geniculate nucleus.^{33,34} Müller cells, located rather centrally in the inner neuroblastic layer, develop at the same time. The bodies of the Müller and amacrine cells remain in the inner neuroblastic layer but move slightly sclerad.³²

Bipolar cells migrate from the outer neuroblastic layer and settle near the Müller and amacrine cells; the



FIGURE 7-10

Raised glial tissue on optic disc; Bergmeister's papilla. (From Kanski JJ, Nischal KK: *Ophthalmology: clinical signs and differential diagnosis*, St Louis, 1999, Mosby.)

horizontal cells follow.¹ The fiber layer of Chievitz is gradually obliterated by this move of the prospective bipolar and horizontal cells.¹⁸ The photoreceptor cells remain in the outer neuroblastic layer. By week 12 the photoreceptors are aligned along the outer side of the inner layer of the optic cup. The photoreceptor cells are the last cells of neural retina to differentiate; this occurs during the fifth month.¹ The early inner segment produces a protuberance that becomes embedded in the RPE and continues to grow, forming the cilium and outer segment by week 24 or 25.^{18,35}

The horizontal, bipolar, amacrine, and Müller cells are developing in the inner nuclear layer, and the inner and outer plexiform layers are filling with neuronal processes.⁵ The fibers of the Müller cells appear and extend to the basal lamina, forming the primitive internal limiting membrane, and external processes extend between the rods and cones.^{5,29} The Müller cell provides a scaffolding for cell development and appears to be involved with guiding axonal fiber growth direction.³⁶ (The developing interplexiform neuron has not yet been identified.) Figures 7-11 and 7-12 show the development of neural retina.

Synaptic complexes begin to appear at about the same time as the plexiform layers, with the inner plexiform layer preceding the outer layer.^{29,37} Cone pedicles develop earlier than rod spherules, and photoreceptor synapses with bipolar cells are established before the outer segments are completed.²⁹

By month 5 the ganglion cell layer is well established.³⁸ Because retinal development is more advanced centrally than peripherally, the ganglion axons from the periphery

must take an arched route above and below the macular area to reach the nerve head.^{35,39} This line of deviation at the horizontal temporal meridian is termed the **horizontal raphe**.⁵

By 6 months of development the dense accumulation of nuclei in the macular area makes this region thicker than the rest of the retina;²⁷ up to nine rows of ganglion cells are evident.³⁸ Foveal development consists of three stages: (1) displacement of inner retinal components to form the depression; (2) migration of photoreceptors toward the center, which increases cone packing; and (3) maturation of the photoreceptors.⁴⁰ During the seventh month the ganglion cells and the cells of the inner nuclear layer begin to move to the periphery of the macula. By birth, however, there still is a single layer of ganglion cells and a thin inner nuclear layer across the now-depressed foveal area (Figure 7-13). By 4 months postpartum, both these layers are displaced to the sloping walls of the fovea, leaving the cones of the outer nuclear layer as the only neural cell bodies in the center of the depression.^{6,8} The foveal depression continues to deepen until about age 15 months as cells continue to move toward the macular periphery.⁴⁰

The **foveola**, the retinal area of sharpest visual acuity, is the last to reach maturity.⁴⁰ Before birth the rod-free area is large compared to that in the adult, but it becomes narrower with migration of the cones centrally, increasing cone density. When examining an area with a diameter of 100 μm at the center of the rod-free zone, the cone population is 18 in the 1-week-old infant. The cone population increases to 42 by age 4 to 5 years, which is the same count as seen in the adult.⁴⁰ The cone inner fibers elongate and adopt an oblique orientation (forming **Henle's fiber layer**) in order to synapse with the cells of the inner nuclear layer, which have been displaced to the sloping walls. During the first few years the outer segment continues to develop and the inner fiber lengthens.

CLINICAL COMMENT: OCULAR ALBINISM

Melanocytes that derive their pigment from neural crest (i.e., those located in choroid, skin, and hair) show a variance that is related to race. Melanocytes that are neuroectodermal in derivation (i.e., retinal pigment, iris, and ciliary body epithelia) are densely pigmented in all races.³⁸ Melanin production is gene regulated, and in an individual with albinism either or both types of melanocytes can be affected. Since normal development of sensory retina is influenced by a melanin-related agent produced in the RPE, when pigment is absent from this layer, as occurs in ocular albinism, a number of retinal abnormalities are present at birth in addition to absence of pigmentation. The macula is underdeveloped and the fovea may be absent. The number of rods may be decreased.⁴¹ Abnormal optic nerve projection to the lateral geniculate nucleus occurs, with more crossed fibers than normal, often resulting in binocular problems.⁴¹

Retinal Vessels

The fetal fissure along the optic stalk closes around the hyaloid artery, and the portions of the vessel within the stalk become the **central retinal artery**.⁵ A branch of the primitive maxillary vein located within the optic stalk is the likely precursor of the **central retinal vein**.²⁸ Early in the fourth month of development, primitive retinal vessels emerge from the hyaloid artery near the optic disc and enter the developing nerve fiber layer. Signals from biomolecular agents called *guidance molecules* guide the growth and pathway of neurons and likely also guide the growth of these retinal vessels.^{42,43} The vessels of the retina continue to develop but are not completed until approximately 3 months after birth, with the vessels to the nasal periphery completed before those to the temporal periphery.⁵

CLINICAL COMMENT: RETINOPATHY OF PREMATURITY

*Premature infants who are exposed to a high concentration of oxygen can develop **retinopathy of prematurity** (also called **retrolental fibroplasia**). The immature retinal blood vessels respond to a high concentration of oxygen with vasoconstriction and cease to develop. On removal of the oxygen, vasoproliferation occurs; however, the new vessel growth is composed of "leaky" vessels with poorly formed endothelial tight junctions. Potential complications include neovascular invasion of the vitreous and development of vitreoretinal adhesions, which may be followed by hemorrhage and retinal detachment.⁴⁴*

CORNEA

Through induction from the lens, the cornea begins to develop at about the time the lens vesicle separates from the surface ectoderm (day 33).^{15,19} One or two layers of epithelial cells from surface ectoderm become aligned, and during the sixth week, zonula occludens are evident.¹ The first component of the anchoring system is the basal lamina, which is evident by week 9, and hemidesmosomes are present by week 13.⁴⁵ By the fifth or sixth month, all the cellular layers of the **corneal epithelium** are present.⁴⁶ **Corneal endothelium**, formed from the first wave of mesenchyme that migrates into the space between the corneal epithelium and the lens, is one to two cells thick by week 6.⁵ At 4 months the endothelium is a single row of flattened cells with a basal lamina, the first evidence of **Descemet's membrane**.^{5,47} By the middle of the fourth month tight junctions are apparent in the endothelium, coinciding with the beginning of aqueous formation.⁴⁸ The material comprising Descemet's membrane before birth has a banded appearance, whereas the tissue secreted by

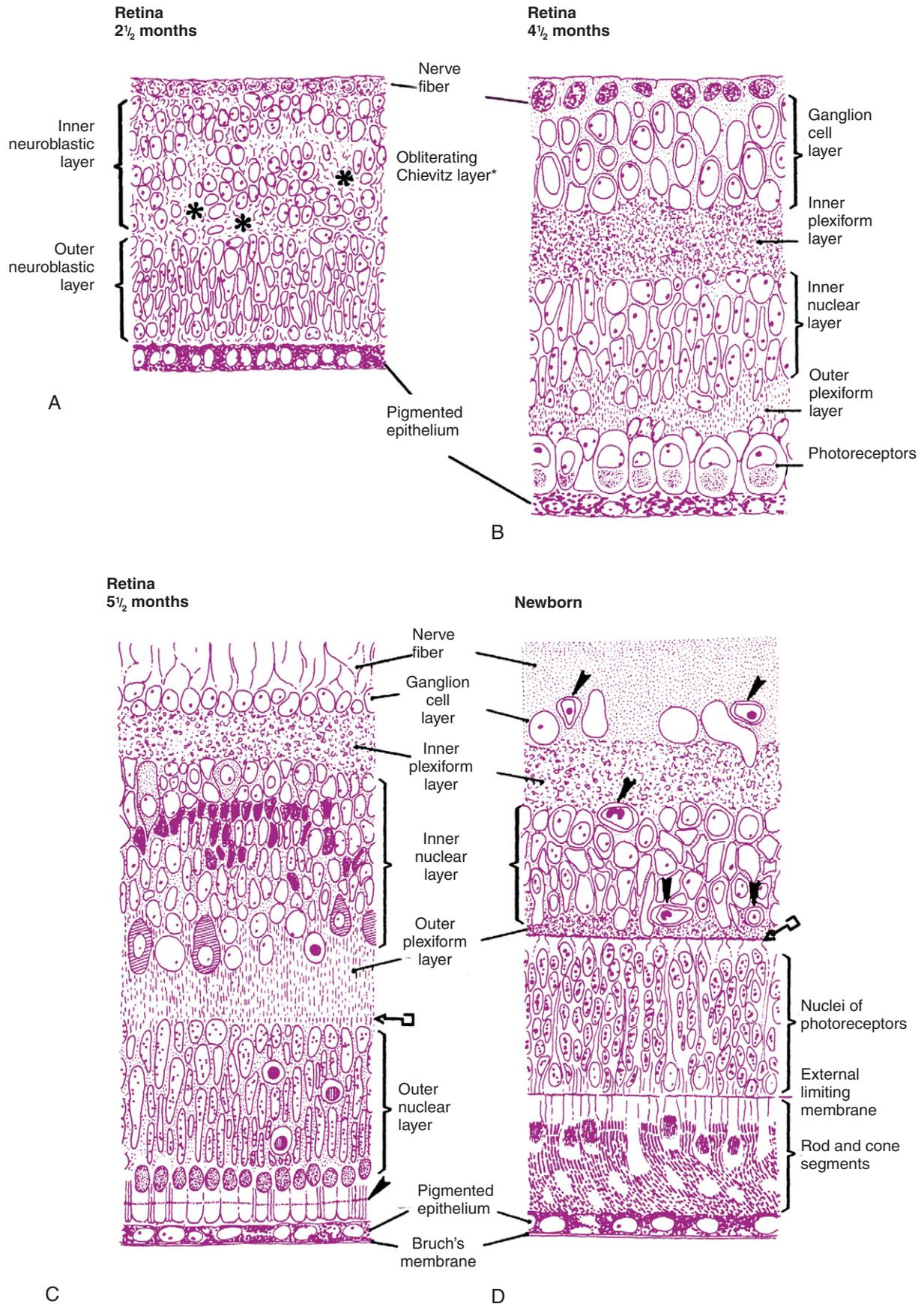


FIGURE 7-11

For legend see opposite page.

FIGURE 7-11

Developing retina. Region of posterior pole is represented in sagittal section in each diagram.

A. At 2.5 months, transient fiber layer of Chievitz, which separated inner from outer neuroblastic layers of primitive retina, is being obliterated slowly by shifting of nuclear elements and realignment of their processes. Uppermost cells, lying vitread, are differentiating into ganglion cells. Those below the uneven transient layer of Chievitz (*asterisks*) are immature but are destined to differentiate into amacrine and Müller cells. Future inner plexiform layer will be located between shifted nuclei of Müller and amacrine cells and those of ganglion cells. Outer neuroblastic layer contains photoreceptor, bipolar, and horizontal cell elements. **B.** At midterm (4.5 months), retinal lamination essentially is complete. Ganglion cells have multilayered arrangement. Inner plexiform layer, composed of fibers of bipolar, ganglion, and amacrine cells supported by müllerian fibers, has established sites of primitive conventional and ribbon synapses. In the inner nuclear layer the still-undifferentiated cellular components are recognizable by shape and position. In the outer nuclear layer, large cone nuclei are aligned adjacent to pigment epithelium, and smaller rod nuclei are positioned more vitread. Outer plexiform layer has primitive lamellar synapses between bipolar cell dendrites and cone pedicles (not indicated). Photoreceptor outer segments are not yet present. **C.** At 5.5 months, ganglion cells have thinned out to one to two layers (except in macular area). Cellular components of inner nuclear layer include amacrine cells with large, pale nuclei in innermost (vitread) zone of this layer and pleomorphic, dark-staining Müller cell nuclei. Both these types originally came from inner neuroblastic layer. Also included are smaller bipolar cells and large, pale-staining horizontal cells in an irregular arrangement sclerad. These two cell types, together with photoreceptors, are derived from outer neuroblastic layer. Outer plexiform layer has a linear arrangement of synapses between bipolar cells and rod spherules (*key symbol*). Outer nuclear layer consists of six to seven layers of nuclei; outermost layers are cones aligned to external limiting membrane. Growing photoreceptor outer segments project into space between pigment epithelium and external limiting membrane (*arrowhead*). Cell death is represented by round, dark-centered symbols. **D.** Newborn retina has adult configuration, with vascularization (*arrowheads*) reaching outer limits of inner nuclear layer. Outer plexiform layer is thinner than that in adult, but line of synapses is well established (*key symbol*). Rod and cone inner and outer segments are fully developed, and tips of outer segments contact pigment epithelium. (From Cook CS, Ozanics V, Jakobiec FA: Prenatal development of the eye and its adnexa. In Tasman W, Jaeger EA, editors: *Duane's foundations of clinical ophthalmology*, vol 1, Philadelphia, 1994, Lippincott.)

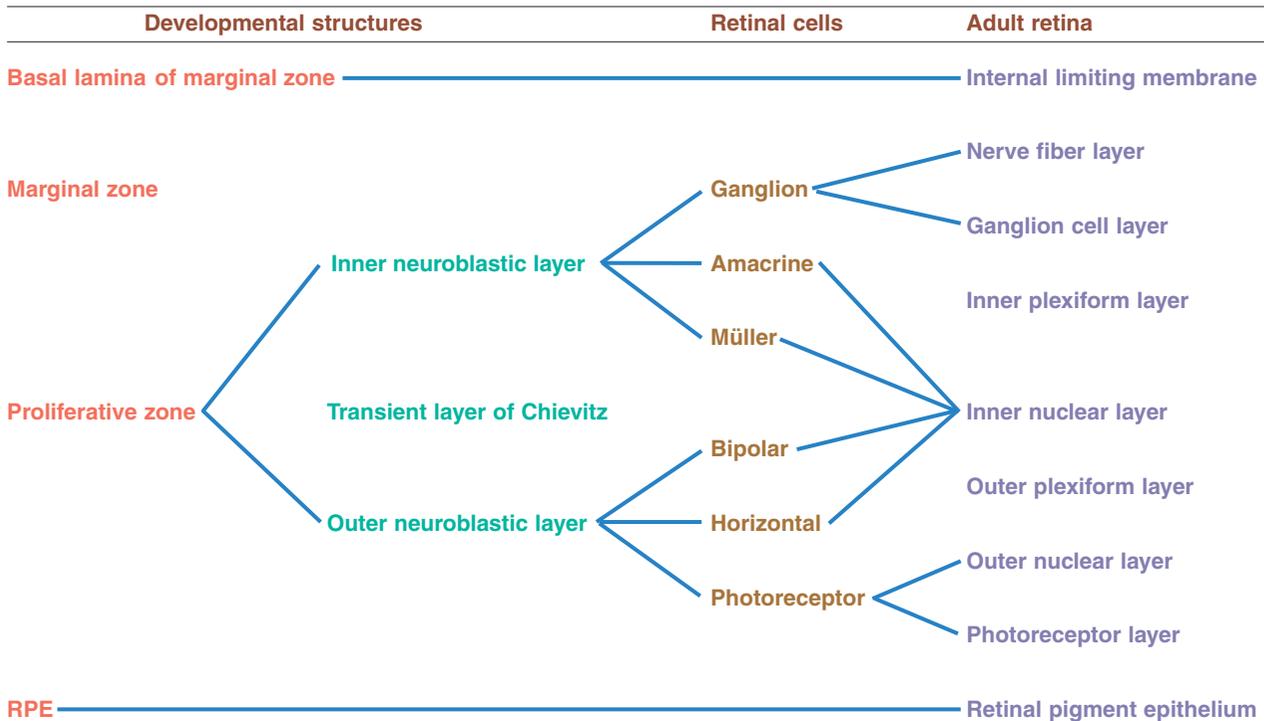


FIGURE 7-12

Flow chart of retinal development.

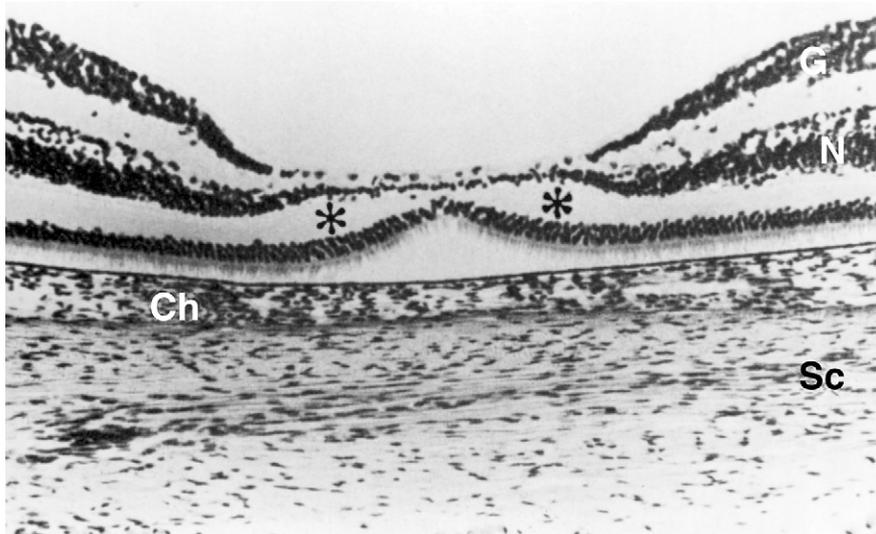


FIGURE 7-13

Fovea of *Macaca mulatta* just before birth (159 days; term at 162-165 days). One interrupted row of ganglion cells and one to two layers of bipolar cells still extend across foveal depression. Wide, well-developed horizontal outer plexiform layer of Henle (*asterisks*) and elongated cone inner and outer segments are present. Parafoveal area has large accumulation of cells in ganglion (*G*) and inner nuclear layer (*N*) characteristic of mature macula. *Ch*, Choroid; *Sc*, sclera. ($\times 95$.) (From Cook CS, Ozanics V, Jakobiec FA: Prenatal development of the eye and its adnexa. In Tasman W, Jaeger EA, editors: *Duane's foundations of clinical ophthalmology*, vol 1, Philadelphia, 1994, Lippincott.)

the endothelium after birth (which has a more posterior position) has a homogeneous, unbanded appearance.^{49,50}

By week 8 a second wave of mesenchyme proliferates and then splits. The posterior portion migrates into the area between the developing endothelium and lens, giving rise to the pupillary membrane. The anterior portion migrates between the developing epithelium and endothelium and gives rise to the fibroblasts, collagen, and ground substance of the **stroma**.^{5,51} This second wave of mesenchyme, as well as that giving rise to the sclera, is of neural crest origin (see Box 7-1).⁵ At 3 months all layers of the cornea are present (Figure 7-14) except **Bowman's layer**, which appears during the fourth month⁴⁵ and is presumably formed by fibroblasts of the anterior stroma and secretions of the epithelial cells^{2,52}; whatever the stage, Bowman's layer is always acellular.⁴⁹ Rapid growth of the corneal stroma causes an increase in curvature relative to the rest of the globe.⁷

SCLERA

The **sclera** first develops anteriorly from condensations in the mesenchyme near the limbus. Growth continues posteriorly until the sclera reaches the optic nerve, and by the end of the third month the sclera has surrounded

the developing choroid.²⁸ During the fourth month connective tissue fibers cross the scleral foramen, running through the optic nerve fibers and producing the first connective tissue strands of the **lamina cribrosa**.⁵ By the fifth month the sclera (including the scleral spur) is well differentiated.⁶

UVEA

Choroid

The mesenchyme that forms the **choriocapillaris** must be in contact with the developing pigment epithelium to differentiate.^{6,8} The vessels appear during the second month, and the diaphragm-covered fenestrations are evident by week 12.³⁰ During the fifth month the layers of the large and medium vessels are evident, as are the vessels that will become vortex veins.⁵³ The short posterior ciliary arteries also are evident and begin to anastomose to form the circle of Zinn.⁵

At midterm in fetal development the elastic sheet of **Bruch's membrane** is present, the basement membrane of the RPE is developing, and the collagenous layers are thickening. The basement membrane of the choriocapillaris is the last component to appear.⁵ By term the choroidal stroma is pigmented.³⁰

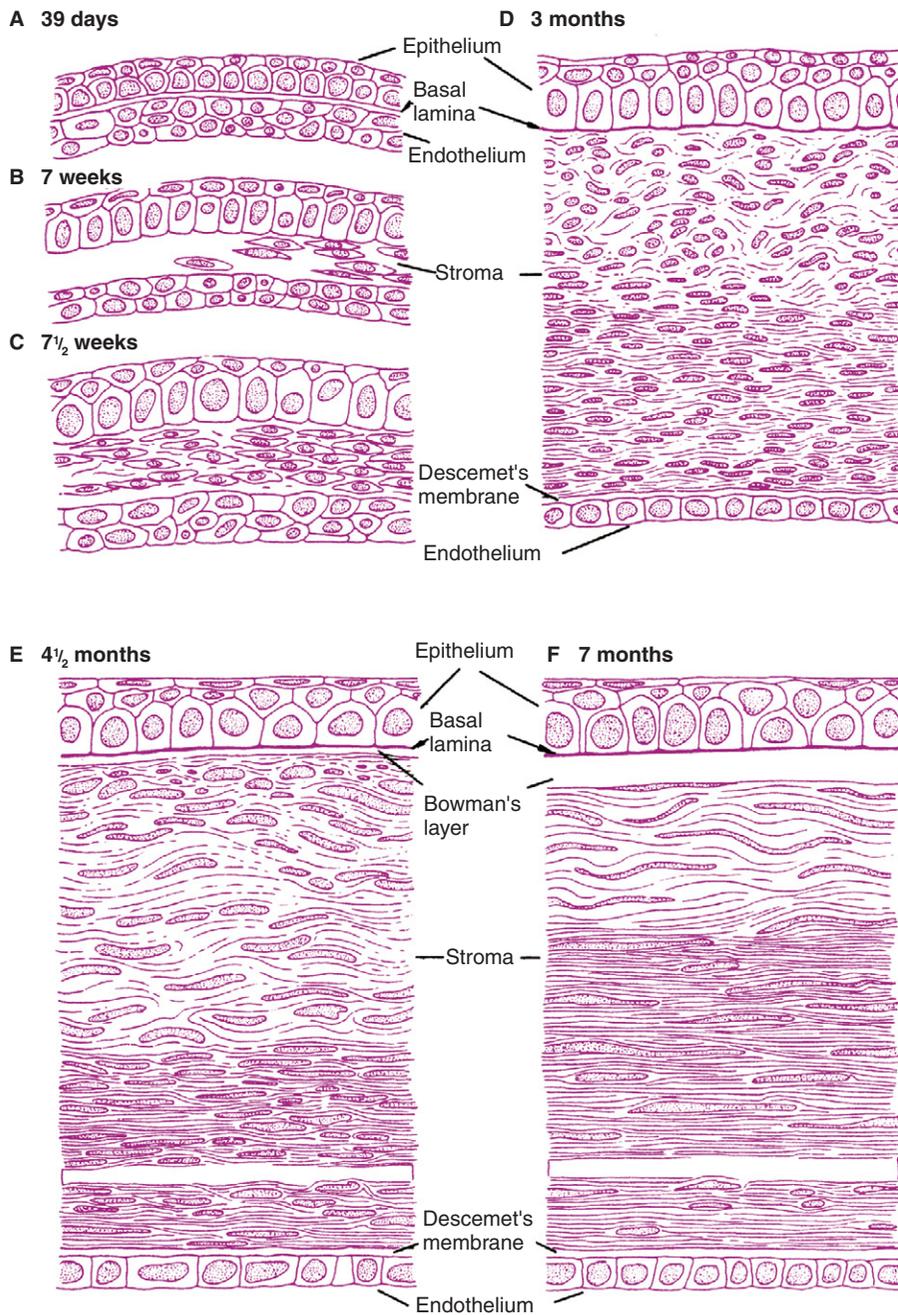


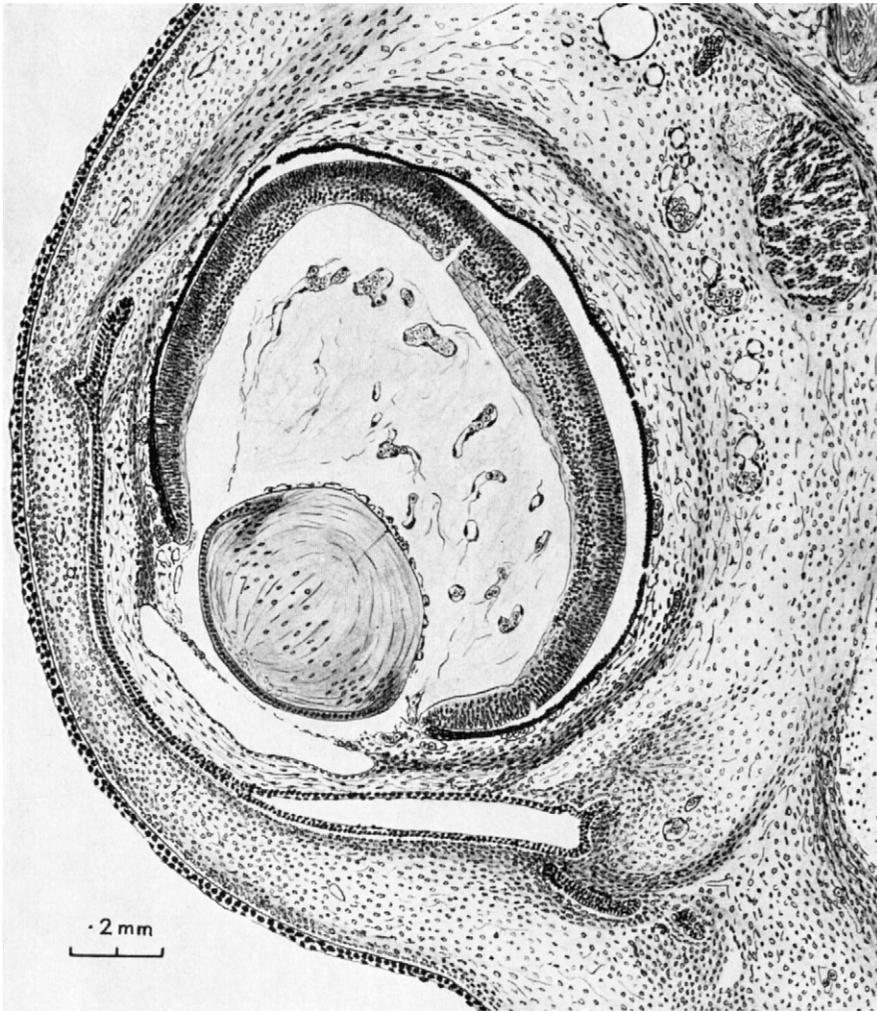
FIGURE 7-14

Developing cornea, central region. **A**, At 39 days, two-layered epithelium rests on a basal lamina. It is separated from two- to three-layered "endothelium" by narrow cellular space. **B**, At 7 weeks, mesenchyme from periphery migrates into space between epithelium and endothelium, the precursor of future corneal stroma. **C**, Mesenchyme (fibroblasts) is arranged in four or five incomplete layers by 7½ weeks, and a few collagen fibrils appear among them. **D**, By 3 months, epithelium has two or three layers of cells, and stroma has approximately 25 to 30 layers of fibroblasts (keratoblasts), which are more regularly arranged in its posterior half. Thin, uneven Descemet's membrane is between most posterior keratoblasts and monolayered endothelium. **E**, By midterm (4.5 months), some "wing cells" are forming above basal epithelial cells, and an indefinite, acellular Bowman's layer emerges beneath basal lamina. In almost one third of anterior portion of multilayered stroma, keratoblasts are strewn in a disorganized formation. Descemet's membrane is well developed. **F**, At 7 months, adult structure of cornea is established. A few mostly superficial keratoblasts still are randomly oriented with respect to corneal surface. Collagenous lamellae in rest of stroma are in parallel array, and only a few spaces in the matrix lack collagen fibrils. Breaks near bottom of **E** and **F** indicate that central portion of stroma is not represented. (From Cook CS, Ozanics V, Jakobiec FA: Prenatal development of the eye and its adnexa. In Tasman W, Jaeger EA, editors: *Duane's foundations of clinical ophthalmology*, vol 1, Philadelphia, 1994, Lippincott.)

Ciliary Body

The region of the outer layer of the optic cup, which will become the **outer pigmented epithelium** of the ciliary body, begins to form ridges late in the third month.⁵⁴ The **inner nonpigmented epithelium**, from the inner optic cup layer, grows and folds with it. These folds, almost 70 in number, become the **ciliary processes**. Zonula occludens are evident in the nonpigmented epithelium during the third month.¹ Neural crest dif-

ferentiates into stromal elements, and the fenestrations in the capillaries are visible in week 14.^{5,54} During the fourth month the major arterial circle of the iris is formed by the anastomosing long ciliary arteries and replaces the annular vessel.⁵⁵ The **ciliary muscle** begins to develop during the fifth month. However, the annular muscle (of Müller) remains incomplete at birth.^{5,6} Both epithelial layers begin to produce aqueous humor at 4 to 6 months of gestation.⁵⁴

**FIGURE 7-15**

Section through eye and surrounding structures in 35-mm human embryo (approximately 8 weeks). (From Mann I: *The development of the human eye*, New York, 1964, Grune & Stratton. Copyright 1964, British Medical Association.)

Iris

By the end of the third month the lip of the optic cup begins to elongate and grows between the lens and the developing cornea. The outer layer of the optic cup becomes the anterior iris epithelium and the inner layer forms the posterior iris epithelium. The proliferation of myofilaments in the basal aspect of the anterior epithelium adjoining the stroma transforms the layer into myoepithelium.⁵⁶ The group of cells that will become the **iris sphincter** breaks away from the pupillary zone of this epithelial layer during the fifth month and develops into smooth muscle within the iris stroma.^{8,56} During the sixth gestational month the fibers of the **dilator muscle** continue to develop within the epithelial layer, and both muscles are completed by birth. That the sphincter and dilator come from neural ectoderm is unusual, because most muscle tissue is derived from mesenchyme. Pigmentation in the anterior and posterior epithelium begins to appear at approximately week 10 and is complete during the seventh month.⁵

Mesenchymal cells line up, leaving large gaps between them, to form the **anterior border layer**. The stromal components are of neural crest origin and are said to migrate from a third wave of mesenchyme.^{1,57} A sparse distribution of collagen fibers begins to accumulate to form the **iris stroma**.⁵ Stromal melanocytes continue to produce more pigment, and the color of the iris can continue to darken for the first 6 postnatal months, with some stromal organization not complete until age 7 years.¹

PUPILLARY MEMBRANE

As the lens thickens, its anterior vascular tunic disconnects from the annular vessel, and its constituents are incorporated into the iris stroma; remnants contribute to the minor circle of the iris.⁵ During the third month the **pupillary membrane** forms between the lens epithelium and the corneal endothelium to replace the vascular tunic. This transitory membrane has components from the second wave of mesenchyme and branches from the major circle of the iris.^{1,58} (The pupillary

membrane can be seen in Figure 7-15 just anterior to the lens.) Three or four arcades of thin-walled blood vessels separated by a thin mesodermal membrane are completed by the end of the fifth month.⁵⁸ The vessels of the pupillary membrane cannot be identified as arterial or venous on the basis of their histologic makeup.²⁴

During gestational month 6 the central vessels atrophy and become bloodless. The more peripheral vessels contribute to the minor circle of the iris, and by 8½ months the central vessels have fragmented and disappeared.^{8,58} As reabsorption of the central pupillary membrane occurs, the loops of the midregion form the ridge of the collarette, with other components incorporated into the anterior border layer.⁵

CLINICAL COMMENT: PERSISTENT PUPILLARY MEMBRANE

Remnants of the central portion of the pupillary membrane that do not reabsorb may be seen with a biomicroscope and appear similar to strands of a spider web attached to the surface of the iris. A persistent pupillary membrane may have a variety of presentations, from a single strand of connective tissue (anchored at one or both ends) to several interconnecting strands; pigment cells also might be incorporated. A persistent pupillary membrane is present in 17% to 32% of the population.⁵⁸

ANTERIOR CHAMBER

A mass of cells of neural crest origin and from the first wave of mesenchyme accumulates adjacent to the ciliary body and the iris root in the anterior chamber angle area.^{50,59} The method whereby this mass is eliminated to expose the angle remains controversial. The mass may atrophy,⁶ the structure may split between the iris and the meshwork, with some tissue contributing to each,⁶⁰ or the intercellular spaces may enlarge and the cells reorganize into the surrounding tissue.⁶¹

The **trabecular meshwork** is visible as a triangular mass of mesenchymal cells during the fourth month; at least part of this tissue is of neural crest origin (see Box 7-1).⁶²⁻⁶⁴ The tissue progressively becomes more organized, and by 9 months the trabecular beams and pores are well developed. **Schlemm's canal** is derived from the deep scleral plexus.^{62,64} During the fourth month tight junctions are evident in the canal's endothelial lining.⁶¹

Once formed, the anterior chamber is lined by a continuous endothelium that covers the trabecular meshwork and the iridocorneal angle.⁶⁵ This membrane appears continuous at gestational month 7 but is discontinuous in the region of the meshwork by month 9.^{61,66} During the last few weeks before birth, splits occur between cells in the membrane, and the size and

number of these splits increase rapidly because of the increase in the size of the anterior ocular structures.⁶⁶ The loss of continuity in this membrane over the trabecular meshwork correlates significantly with an increase in the facility of aqueous outflow.⁶² Persistence of the uninterrupted endothelial membrane over the meshwork (Barkan's membrane) can be a causative factor in congenital glaucoma.^{5,11,66}

VITREOUS

The presence of the developing lens is essential for normal accumulation of vitreous.⁶⁷ The **primary vitreous** fills the vitreous space early in development (see Figure 7-8) and is made up of fibrils derived from the developing lens, the developing retina, and the degenerating hyaloid system.⁶¹

As the **secondary vitreous** develops, apparently produced by the neural retina and hyalocytes from the primary vitreous,¹ it encloses the primary vitreous in the region of the atrophying hyaloid vessels, thus forming the funnel-shaped **Cloquet's canal**. This zone, with its apex at the optic disc and its base at the posterior lens, is well formed by the fourth month. It persists in the adult. The secondary vitreous contains a fibril network and primitive hyalocytes.⁵ During the third month the secondary vitreous has formed attachments at the vitreous base and at the hyaloideocapsular ligament.¹

The zonule fibers develop from the **tertiary vitreous**, located between the lens equator and the ciliary body. Questions remain about whether the tertiary vitreous is mesenchymal or epithelial in origin.⁵ Early zonule fibers appear to be a continuation of a thickening of the internal limiting membrane of the ciliary body, formed by the ciliary epithelium; the fibers run from a zone near the ora serrata and from the valleys between the processes to the lens capsule.⁷

OPTIC NERVE

The optic stalk, the precursor of the **optic nerve**, joins the optic vesicle to the forebrain. As the optic fissure develops along the inferior stalk invagination, a two-layered optic stalk is created. The *outer layer* of the optic stalk becomes the neuroglial sheath that surrounds the optic nerve; it also gives rise to the glial components of the lamina cribrosa.⁵ Programmed cell death occurs in the cells of the *inner layer*, providing an avenue for passage of the axons from ganglion cells entering the optic stalk; other cells of the inner wall become the glial cells of the optic nerve. A band of glial tissue forms around the optic disc, separating it from the intraretinal space; this tissue will become the intermediary tissue of Kuhnt.¹ Ganglion cell axons fill the lumen of the optic

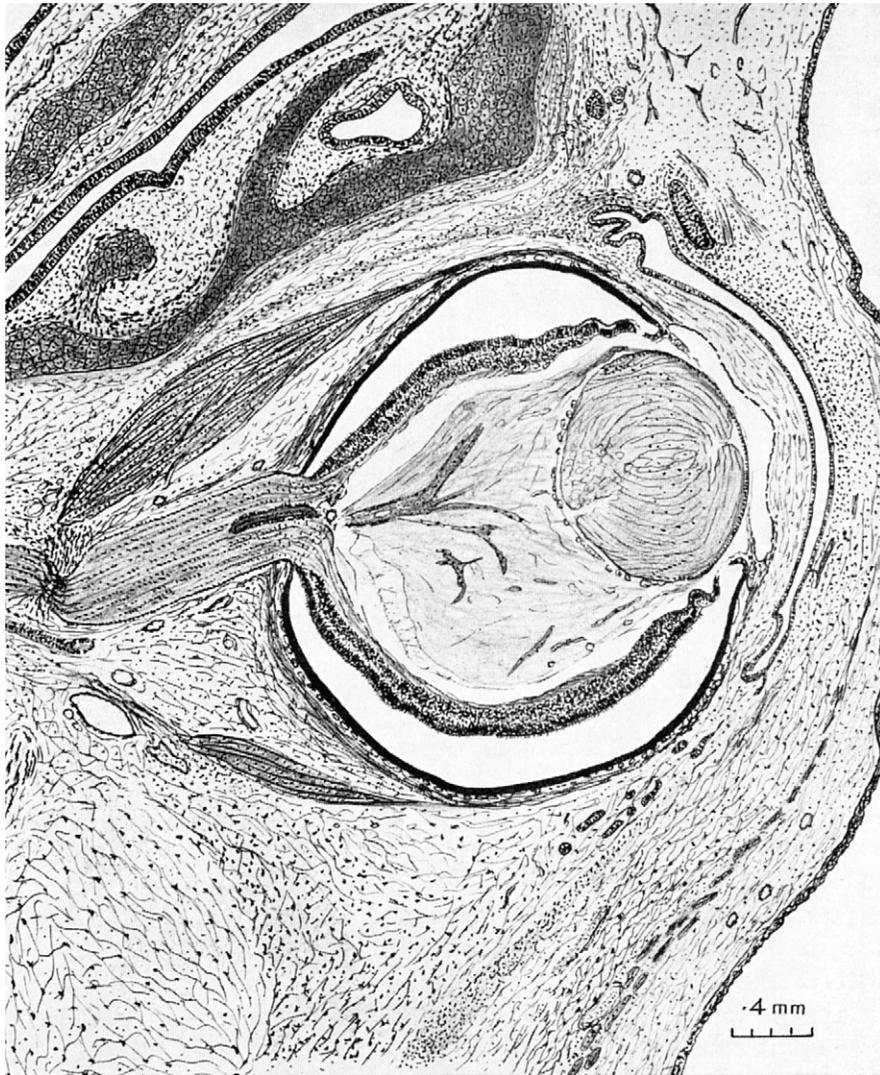


FIGURE 7-16

Section through eye and orbit of 48-mm human embryo (approximately 9.5 weeks). (From Mann I: *The development of the human eye*, New York, 1964, Grune & Stratton. Copyright 1964, British Medical Association.)

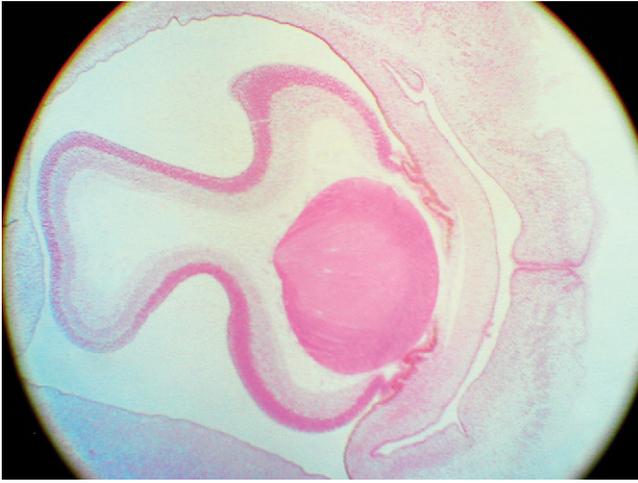
nerve (Figure 7-16) and grow toward their termination in the central nervous system. Myelination of the axons begins at the lateral geniculate nucleus during the fifth month of gestation, reaches the chiasm during the sixth month, and stops at the lamina cribrosa 1 to 3 months after birth.^{5,68}

CLINICAL COMMENT: EMMETROPIZATION

The globe continues to grow after birth, and the eye will become emmetropic as long as there is coordination between the length of the eye and the power of the refractive components. Although this growth is under genetic control, visual experience that provides feedback for normal growth may influence this process.¹

DEVELOPMENT OF OCULAR ADNEXA EYELIDS

Early in the second gestational month, folds of surface ectoderm filled with mesenchyme begin to grow toward one another anterior to the developing cornea; these folds will become the eyelids. Early formation of these folds can be seen in Figure 7-8. The upper fold is from the frontonasal process, and the lower fold is from the maxillary process.¹ The eyelid margins meet and fuse during the third month of development and remain fused until the lid structures have developed (Figure 7-17).²⁷ Two layers of epithelium cover the anterior surface, and

**FIGURE 7-17**

Light micrograph of eye of 2½-month human embryo; fused eyelids are seen. The mushroom-shape to the optic cup is an artifact.

one layer lines the inner surface.⁶⁹ The epithelial layers of the skin and conjunctiva, the hair follicles and cilia, and the meibomian glands, Zeis glands, and glands of Moll all develop from surface ectoderm; the tarsal plates, the orbicularis, the levator, and the tarsal muscle of Müller develop from mesenchyme.⁵ The fusion of the eyelids isolates the developing eye from the amniotic fluid⁷⁰ and “probably prevents the cornea and conjunctiva from keratinizing.”⁵ The desmosomes joining the margins break down during the fifth and sixth

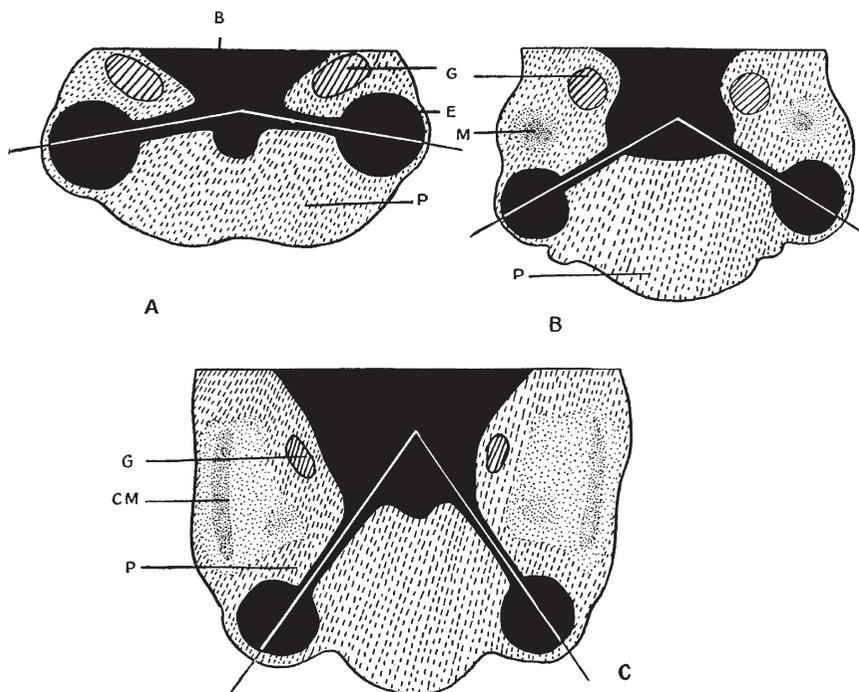
month, allowing the eyelids to separate; the lipid secretions of the meibomian glands may be responsible for this disjunction.^{5,7}

ORBIT

Orbital fat and connective tissue are derived from neural crest cells. The first evident orbital bone is the maxilla at 6 weeks; the frontal, zygomatic, and palatine bones are apparent at week 7. The lesser wing of the sphenoid bone and the optic canal are present at week 7, the greater wing is evident at week 10, and the wings join at week 16.⁷¹ Most of the orbital bones ossify and fuse between the sixth and seventh months.⁵ The angle between the orbits early in development is approximately 180 degrees, decreases to 105 degrees at 3 months, and is 71 degrees at birth and 68 degrees in adulthood (Figure 7-18). The globe reaches its adult size by age 3 years, but the orbit is not of adult size until age 16 years.⁵

EXTRAOCULAR MUSCLES

The extraocular muscles are of mesenchymal origin (Figure 7-19). The muscle cells are derived from mesoderm, whereas the connective tissue components originate in neural crest.¹ Extraocular muscles once were thought to develop in stages, first posteriorly near the orbital apex and then growing forward,⁶ but recent work suggests that muscle origin, belly, and insertion develop simultaneously.⁷² The muscles innervated by cranial nerve III are derived from the first pair of somites at

**FIGURE 7-18**

Sections through developing eyes and optic stalks of human embryos of various stages. **A**, Nine-millimeter embryo (approximately 37 days); 160-degree angle. **B**, Sixteen-millimeter embryo (approximately 48 days); 120-degree angle. **C**, Forty-millimeter embryo (approximately 8 weeks); 72-degree angle. Decrease in angle between optic axes is obvious. *B*, Brain; *E*, eye; *P*, paraxial mesoderm; *M*, maxillary mesoderm; *G*, gasserian ganglion; *CM*, temporal condensation in maxillary mesoderm. (From Mann I: *The development of the human eye*, New York, 1964, Grune & Stratton. Copyright 1964, British Medical Association.)

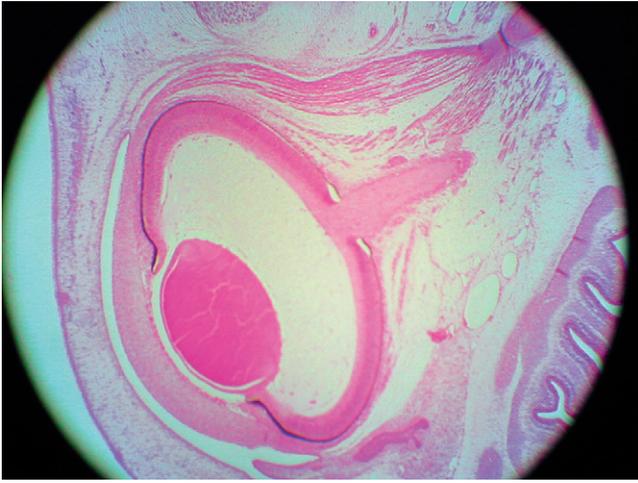


FIGURE 7-19

Light micrograph of 45-mm pig embryo; eyelids are fused, extraocular muscle is evident, and axons are evident in optic nerve.

approximately day 26. The lateral rectus muscle, innervated by cranial nerve VI, develops from the mesenchyme of the maxillomandibular area at about day 27. The superior oblique muscle, innervated by cranial nerve IV, is derived from the second pair of somites at day 29.¹ The newborn exhibits poorly coordinated eye movements during the early years, indicating that the extraocular muscles are not fully developed and early visual experience can influence the development of normal binocular eye movements.⁷³

NASOLACRIMAL SYSTEM

The main lacrimal gland has long been thought to develop from epithelial buds that arise from the temporal portion of the conjunctiva of the superior fornix.⁵ Some investigators question this origin and suggest a neural crest origin.⁷⁴ The lacrimal gland continues to develop after birth and is not fully developed until age 3 or 4 years.⁵

The nasolacrimal drainage system develops from a cord of surface ectodermal cells that becomes buried below the maxillary mesenchyme. This cord may fragment and form the canaliculi, the nasolacrimal duct, and the lacrimal sac, or the canaliculi might be formed from a later epithelial cord.⁵

BLOOD VESSEL PERMEABILITY AND BARRIERS

The blood-retinal and blood-aqueous barriers are recognizable early in development in the tight junctions

formed in the RPE and the capillaries of the ciliary body and iris. Fenestrations that establish vessel permeability in the capillaries of the ciliary processes and the choriocapillaris also are evident early in the gestational period.

REFERENCES

1. Barishak YR: *Embryology of the eye and its adnexae*, New York, 2001, Karger.
2. Duncan MK, Kozmik Z, Cveklova K et al: Overexpression of PAX-6(5a) in lens fibers and cells results in upregulation of (alpha)5(beta)1 integrin expression, *J Cell Sci* 113:3173, 2000.
3. Koroma BM, Yang YM, Sundin OH: The Pax-6 homeobox gene is expressed throughout the corneal and conjunctival epithelia, *Invest Vis Sci* 38(1):108, 1997.
4. Moore KL: *Before we are born: essentials of embryology and birth defects*, ed 5, Philadelphia, 1998, Saunders.
5. Cook CS, Ozanics V, Jakobiec FA: Prenatal development of the eye and its adnexa. In Tasman W, Jaeger EA, editors: *Duane's foundations of clinical ophthalmology*, vol 1, Philadelphia, 1994, Lippincott.
6. Mann I: *Development of the human eye*, New York, 1964, Grune & Stratton.
7. Barishak YR: *Embryology of the eye and its adnexae*. In Straub W, editor: *Developments in ophthalmology*, New York, 1992, Karger.
8. Barber AN: *Embryology of the human eye*, St Louis, 1955, Mosby.
9. Lovasik JV, Kothe AC: Neurophysiological correlates in a case of unilateral iris and chorioretinal coloboma, *J Am Optom Assoc* 60:532, 1989.
10. Morrison DA, FitzPatrick DR, Fleck BW: Iris coloboma with iris heterochromia, *Arch Ophthalmol* 118(11):1590, 2000.
11. Trachimowicz RA: Review of embryology and its relation to ocular disease in the pediatric population, *Optom Vis Sci* 71(3):154, 1994.
12. Smelser GK: Embryology and morphology of the lens, *Invest Ophthalmol* 4:398, 1965.
13. Matsuo T: The genes involved in the morphogenesis of the eye, *Jpn J Ophthalmol* 37(3):215, 1993 (abstract).
14. Harrington L, Klintworth GK, Seror TE et al: Developmental analysis of ocular morphogenesis in alpha A-crystallin/diphtheria toxin in transgenic mice undergoing ablation of the lens, *Dev Biol* 148(2):508, 1991.
15. Coulombre AJ: Regulation of ocular morphogenesis, *Invest Ophthalmol* 8:25, 1969.
16. McKeehan MS: Induction of portions of the chick lens without contact with the optic cup, *Anat Rec* 132:297, 1958.
17. Grainger RM, Henry JJ, Saha MS et al: Recent progress on the mechanisms of embryonic lens formation, *Eye* 6(pt 2):117, 1992.
18. O'Rahilly R: The prenatal development of the human eye, *Exp Eye Res* 2:93, 1975.
19. Coulombre JL, Coulombre AJ: Lens development. IV. Size, shape and orientation, *Invest Ophthalmol* 8:251, 1969.
20. Coulombre JL, Coulombre AJ: Lens development: fiber elongation and lens orientation, *Science* 142:1489, 1963.
21. Amaya L, Taylor D, Russell-Eggitt IR et al: The morphology and natural history of childhood cataracts, *Surv Ophthalmol* 48(2):125, 2003.
22. Nelson LB, Folberg R: Ocular development anomalies. In Tasman W, Jaeger EA, editors: *Duane's foundations of clinical ophthalmology*, vol 1, Philadelphia, 1991, Lippincott.
23. Kanski JJ: *Clinical ophthalmology*, ed 2, Oxford, England, 1989, Butterworth-Heinemann, p 238.
24. Mutlu F, Leopard IH: The structure of the fetal hyaloid system and tunica vasculosa lentis, *Arch Ophthalmol* 71:102, 1964.

25. Jack RL: Ultrastructural aspects of hyaloid vessel development, *Arch Ophthalmol* 87:427, 1972.
26. Zhu M, Madigan MC, Van Driel D et al: The human hyaloid system: cell death and vascular regression, *Exp Eye Res* 70:767, 2000.
27. Warwick R: *Eugene Wolff's anatomy of the eye and orbit*, ed 7, Philadelphia, 1976, Saunders, p 418.
28. Duke-Elder S, Cook C: Normal and abnormal development. In Duke-Elder S, editor: *Embryology*, vol 3, System of ophthalmology, St Louis, 1963, Mosby.
29. Hollenberg MJ, Spira AW: Early development of the human retina, *Can J Ophthalmol* 7:472, 1972.
30. Mund ML, Rodrigues MM, Fine BS: Light and electron microscopic observations on the pigmented layers of the developing human eye, *Am J Ophthalmol* 73:167, 1972.
31. Smelser GK, Ozanics V, Rayborn M et al: The fine structure of the retinal transient layer of Chiewitz, *Invest Ophthalmol* 12:504, 1973.
32. Uga S, Smelser GK: Electron microscopic study of the development of retinal Müllerian cells, *Invest Ophthalmol* 12:295, 1973.
33. Isenmann S, Kretz A, Cellerino A: Molecular determinants of retinal ganglion cell development, survival, and regeneration, *Prog Ret Eye Res* 22(4):483, 2003 (abstract).
34. Oster SE, Sretavan DW: Connecting the eye to the brain: the molecular basis of ganglion cell axon guidance, *Br J Ophthalmol* 87:639, 2003 (abstract).
35. Narayanan K, Wadhwa S: Photoreceptor morphogenesis in the human retina: a scanning electron microscopic study, *Anat Rec* 252:133, 1998.
36. Willbold E, Layer PG: Müller glia cells and their possible roles during retina differentiation in vivo and in vitro, *Histol Histopathol* 13(12):531, 1998.
37. Smelser GK, Ozanics V, Rayborn M et al: Retinal synaptogenesis in the primate, *Invest Ophthalmol* 13:340, 1974.
38. Sharma RK, Ehinger EJ: Development and structure of the retina. In Kaufman PL, Alm A, editors: *Adler's physiology of the eye*, St Louis, 2003, Mosby, p 319.
39. Vrabec F: The temporal raphé of the human retina, *Am J Ophthalmol* 62:926, 1966.
40. Yuodelis C, Hendrickson A: A qualitative and quantitative analysis of the human fovea during development, *Vis Res* 26(6):847, 1986.
41. Jeffery G: The retinal pigment epithelium as a developmental regulator of the neural retina, *Eye* 12:499, 1998.
42. Dorrell MI, Aguilar E, Freidlander M: Retinal vascular development is mediated by endothelial filopodia, a preexisting astrocytic template and specific R-cadherin adhesion, *Invest Ophthalmol Vis Sci* 43(11):3500, 2002.
43. Provis JM: Development of the primate retinal vasculature, *Prog Retin Eye Res* 20(6):799, 2001 (abstract).
44. Patz A, Payne JW: Retrolental fibroplasia. In Duane TD, Jaeger EA, editors: *Clinical ophthalmology*, vol 3, Philadelphia, 1982, Harper & Row.
45. Tisdale AS, Spurr-Michaud SJ, Rodrigues M et al: Development of the anchoring structures of the epithelium in rabbit and human fetal corneas, *Invest Ophthalmol Vis Sci* 29(5):727, 1988.
46. Zinn KM, Mockel-Pohl S: Fine structure of the developing cornea, *Int Ophthalmol Clin* 15(1):19, 1975.
47. Wulle KG: Electron microscopy of the fetal development of the corneal endothelium and Descemet's membrane of the human eye, *Invest Ophthalmol* 11:897, 1972.
48. Wulle KG, Ruprecht KW, Windrath LC: Electron microscopy of the development of the cell junctions in the embryonic and fetal human corneal endothelium, *Invest Ophthalmol* 13:923, 1974.
49. Lesueur L, Arne JL, Mignon-Conte M et al: Structural and ultrastructural changes in the developmental process of premature infants' and children's corneas, *Cornea* 13(4):331, 1994.
50. Bahn CF, Falls HF, Varley GA et al: Classification of corneal endothelial disorders based on neural crest origin, *Ophthalmology* 91:558, 1984.
51. Ozanics C, Rayborn M, Sagun D: Some aspects of corneal and scleral differentiation of the primate, *Exp Eye Res* 22:305, 1976.
52. Wulle KG, Richter J: Electron microscopy of the early embryonic development of the human corneal epithelium, *Albrecht Von Graefes Arch Klin Exp Ophthalmol* 209(1):39, 1978.
53. Heinmann K: The development of the choroid in man: choroidal vascular system, *Ophthalmol Res* 3:257, 1971.
54. Wulle KG: The development of the productive and drainage system of the aqueous humor in the human eye, *Adv Ophthalmol* 26:296, 1972.
55. Loewenfeld IE: *The pupil: anatomy, physiology, and clinical applications*, Boston, 1999, Butterworth-Heinemann.
56. Tamura T, Smelser GK: Development of the sphincter and dilator muscles of the iris, *Arch Ophthalmol* 89:332, 1973.
57. Carlson BM: *Human embryology and developmental biology*, St Louis, 1994, Mosby, p 265.
58. Matsuo N, Smelser GK: Electron microscopic studies on the pupillary membrane: the fine structure of the white strands of the disappearing stage of the membrane, *Invest Ophthalmol* 10:107, 1971.
59. Edelhauser HF, Ubels JL: Cornea and sclera. In Kaufman PL, Alm A, editors: *Adler's physiology of the eye*, St Louis, 2003, Mosby, p 47.
60. Burian HM, Braley AE, Allen L: A new concept of the development of the anterior chamber angle of the human eye, *Arch Ophthalmol* 53:439, 1956.
61. Smelser GK, Ozanics V: The development of the trabecular meshwork in primate eyes, *Am J Ophthalmol* 71:366, 1971.
62. Rodrigues MM, Katz SI, Foidart J-M: Collagen factor VIII antigen and immunoglobulins in the human aqueous drainage channels, *Ophthalmology* 87:337, 1980.
63. Tripathi BJ, Tripathi RC: Neural crest origin of human trabecular meshwork and its implications for the pathogenesis of glaucoma, *Am J Ophthalmol* 107:583, 1989.
64. Tripathi BJ, Tripathi RC: Embryology of the anterior segment of the human eye. In Ritch R, Shields MB, Krupin T, editors: *The glaucomas*, St Louis, 1989, Mosby.
65. Kupfer C, Ross K: The development of outflow facility in human eyes, *Invest Ophthalmol* 10:513, 1971.
66. Hansson HA, Jerndal T: Scanning electron microscopic studies in the development of the iridocorneal angle in human eyes, *Invest Ophthalmol* 10:252, 1971.
67. Coulombre AJ, Coulombre JL: Mechanisms of ocular development, *Int Ophthalmol Clin* 15(1):7, 1975.
68. Sadun AA, Glaser JS: Anatomy of the visual sensory system. In Tasman W, Jaeger EA, editors: *Duane's foundations of clinical ophthalmology*, vol 1, Philadelphia, 1994, Lippincott.
69. Kikkawa DO, Lucarelli MJ, Shovlin JP et al: Ophthalmic facial anatomy and physiology. In Kaufman PL, Alm A, editors: *Adler's physiology of the eye*, Mosby, 2003, St Louis, p 16.
70. Anderson G, Ehlers N, Matthiessen ME et al: Histochemistry and development of the human eyelids, *Acta Ophthalmol (Copenh)* 45:288, 1967.
71. Sires BS, Gausas R, Cook BE et al: Orbit. In Kaufman PL, Alm A, editors: *Adler's physiology of the eye*, St Louis, 2003, Mosby.
72. Sevel D: Reappraisal of the origin of human extraocular muscles, *Ophthalmology* 88:1330, 1981.
73. Porter JD, Andrade FH, Baker RS: The extraocular muscles. In Kaufman PL, Alm A, editors: *Adler's physiology of the eye*, St Louis, 2003, Mosby, p 787.
74. Tripathi BJ, Tripathi RC: Evidence of neuroectodermal origin of the human lacrimal gland, *Invest Ophthalmol Vis Sci* 31:393, 1990.

The skull can be divided into two parts, the cranium and the face. The cranium consists of two parietal bones, the occipital bone, two temporal bones, the sphenoid bone, and the ethmoid bone. The face is made up of two maxillary bones, two nasal bones, the vomer, two inferior conchae, two lacrimal bones, two palatine bones, two zygomatic bones, and the mandible. The single frontal bone is a part of both the cranium and the face.

Generally, the bones of the skull unite at sutures that form immovable joints. The exception is the movable temporomandibular joint, which attaches the mandible to the temporal bones. Air-filled cavities called sinuses are contained within several of the bones.

After a brief description of the bones of the skull, this chapter presents a more detailed presentation of the orbital bones. The reader is advised to have a skull available for reference while reading this chapter, particularly for distinguishing the relationships and articulations between bones.

BONES OF THE CRANIUM

The paired **parietal bones** form the roof and sides of the cranium (Figure 8-1). The parietal bones articulate with each other at the midline in the sagittal suture, with the occipital bone posteriorly in the lambdoid suture, and with the frontal bone anteriorly at the coronal suture. The parietal bone articulates inferiorly with the temporal bone and the greater wing of the sphenoid bone.

The **occipital bone** forms the posterior aspect of the skull and posterior floor of the cranial cavity. A prominence, the external occipital protuberance, or **inion**, is found on the external surface at the posterior midline (Figure 8-2). The large foramen magnum is found in the inferior aspect of the occipital bone. The inner surface of the bone forms the posterior cranial fossa, in which there are depressions where the lobes of the cerebellum lie. Figure 8-3 shows the inner aspect of the cranial floor. The occipital bone articulates with the temporal bones, parietal bones, and sphenoid bone.

CLINICAL COMMENT: INION

The **inion**, located just outer to the posterior pole of the occipital cortex, is a useful landmark in the placement of the electrodes used to record a visual-evoked response (VER). This electrodiagnostic test records responses from the visual cortex. Clinical applications include the determination of visual acuity in a patient unable to respond to the typical eye chart and the assessment of impulse conduction in the patient with suspected multiple sclerosis.

Each of the **temporal bones** is composed of two portions: a large, flat plate, the squamous portion; and a thickened, wedge-shaped area, the petrous portion. The *squamous* portion forms the side of the cranium and articulates with the parietal bone and the sphenoid bone. An anterior projection, the *zygomatic process*, articulates with the zygomatic bone (see Figure 8-1). The *petrous* portion extends within the cranium and houses the middle and inner ear structures. The *mastoid process* and *styloid process* project from the inferior aspect, and between these two processes is the *stylomastoid foramen*, through which the facial nerve exits the skull. The petrous portion articulates with the occipital bone in the floor of the skull. The *carotid canal* runs superiorly and anteriorly through the petrous portion and provides entrance for the internal carotid artery into the cranial cavity.

The single **frontal bone** forms the anterior portion of the cranium, anterior floor of the cranial cavity, and superior part of the face (Figure 8-4). At the top of the skull, the frontal bone articulates with the parietal bones; inferiorly it articulates with the sphenoid bone, ethmoid bone, and lacrimal bones; and inferoanteriorly it articulates with the nasal bones, maxillary bones, and zygomatic bones. The inner surface of the cranial cavity portion of the frontal bone forms the anterior cranial fossa (see Figure 8-3), in which the frontal lobes of the cerebral hemispheres lie. The *frontal sinuses* are located within the anterior portion of the frontal bone.

The **sphenoid bone** is a single bone, the body of which lies in the midline and articulates with the occipital bone and the temporal bones to form the base of the cranium (see Figure 8-3). The sphenoid bone joins the zygomatic bones to form the lateral walls of

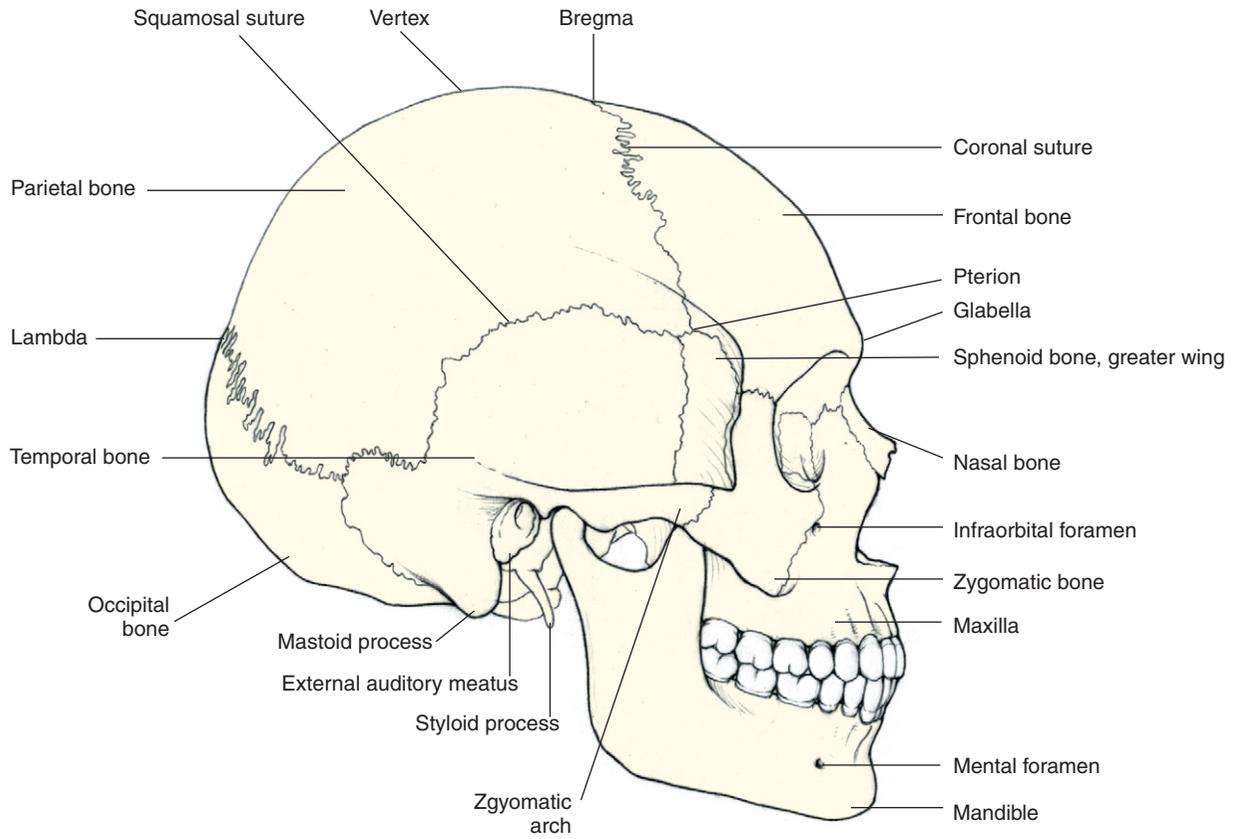


FIGURE 8-1
Lateral view of skull. (From Mathers LH, Chase RA, Dolph J et al: *Clinical anatomy principles*, St Louis, 1996, Mosby.)

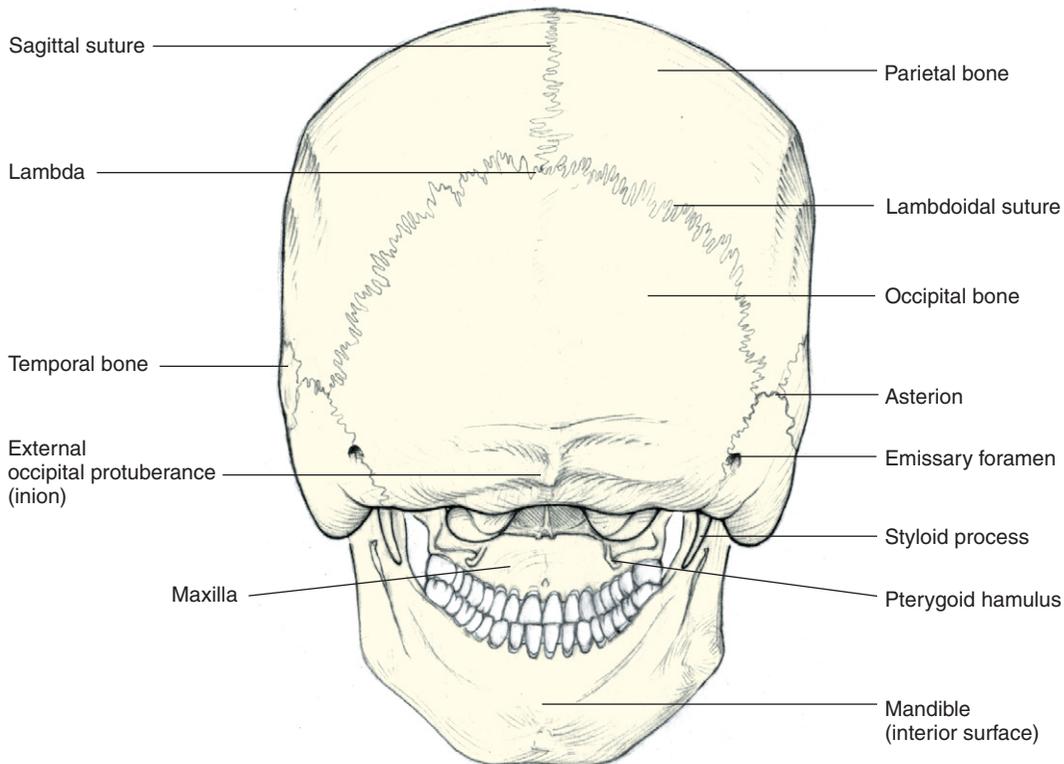


FIGURE 8-2
Posterior view of skull. (From Mathers LH, Chase RA, Dolph J et al: *Clinical anatomy principles*, St Louis, 1996, Mosby.)

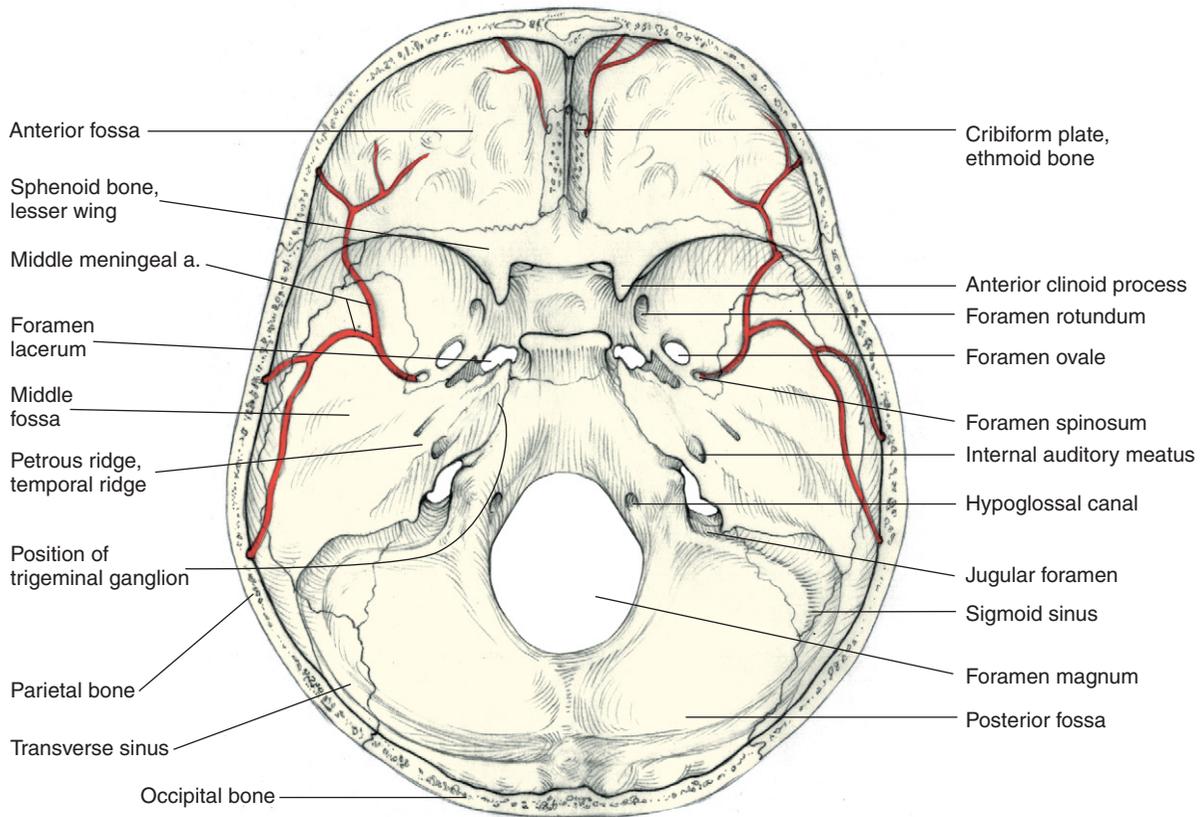


FIGURE 8-3
 Floor of skull. (From Mathers LH, Chase RA, Dolph J et al: *Clinical anatomy principles*, St Louis, 1996, Mosby.)

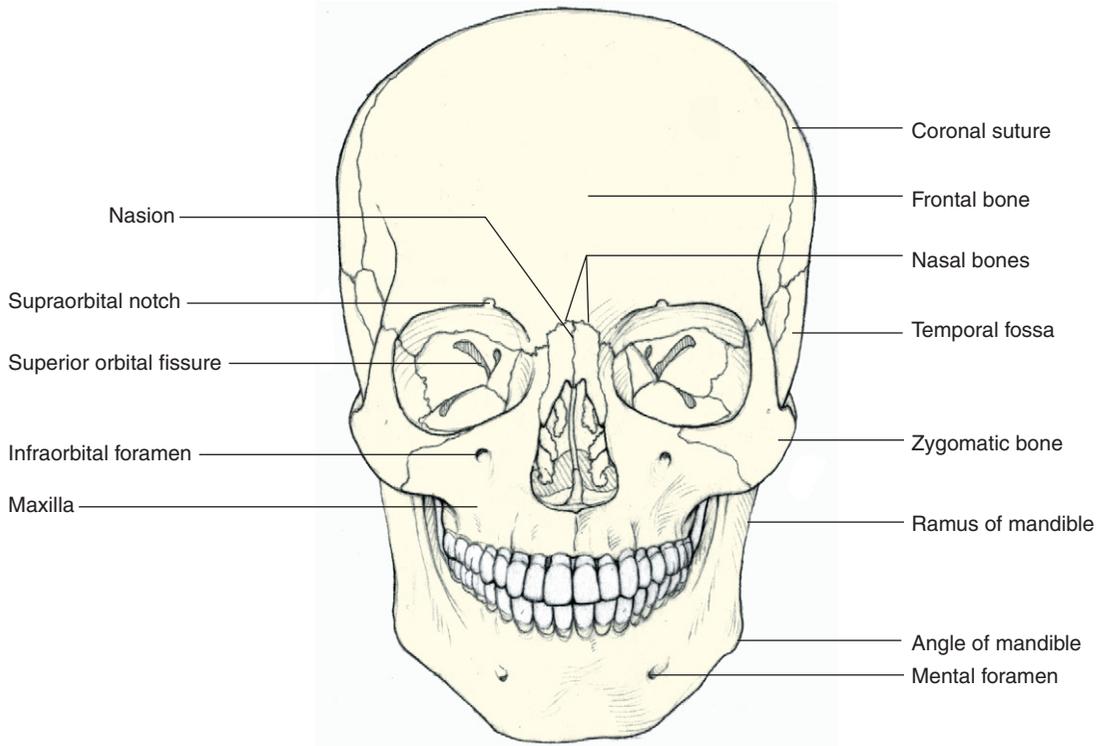
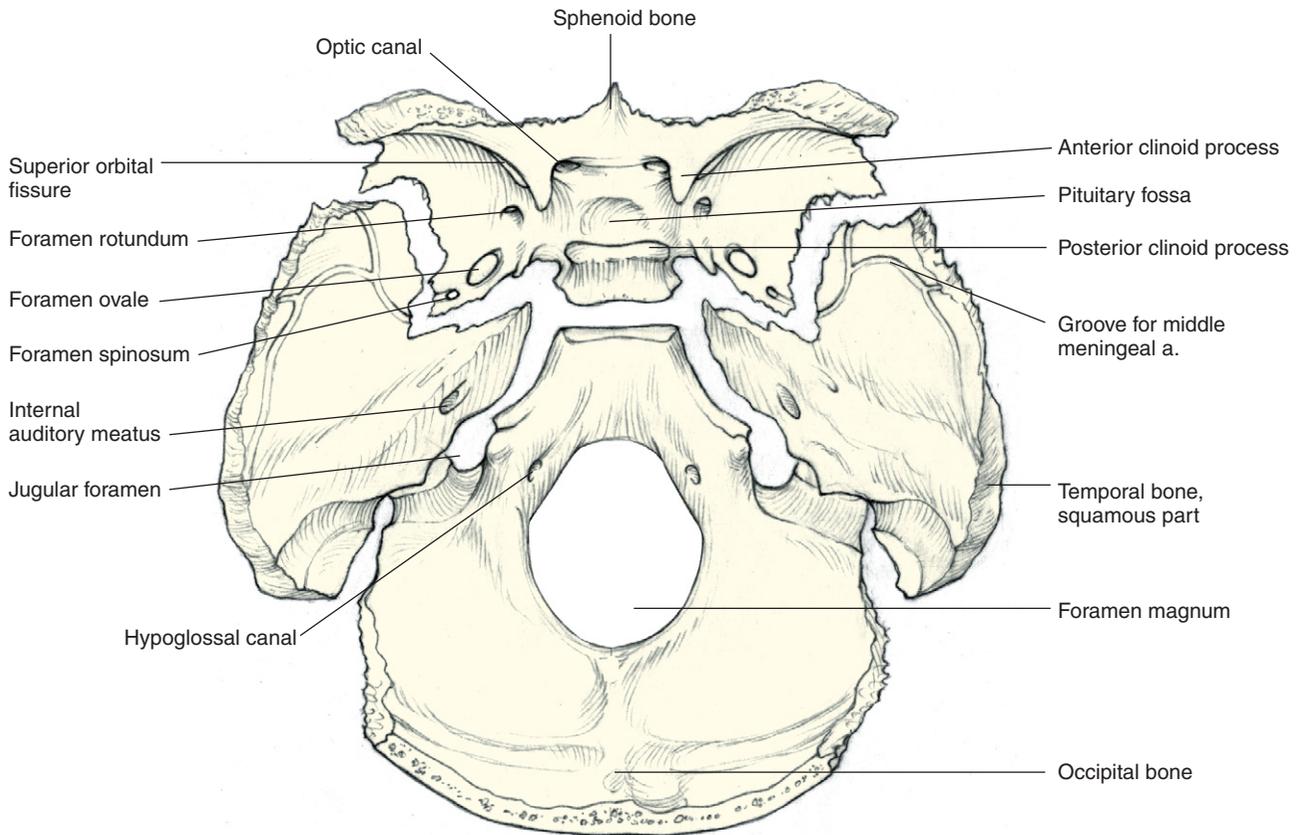


FIGURE 8-4
 Anterior view of skull. (From Mathers LH, Chase RA, Dolph J et al: *Clinical anatomy principles*, St Louis, 1996, Mosby.)

**FIGURE 8-5**

Disarticulated view of base of skull. (From Mathers LH, Chase RA, Dolph J et al: *Clinical anatomy principles*, St Louis, 1996, Mosby.)

the orbits. Anteriorly and inferiorly the sphenoid bone articulates with the maxillary and palatine bones, superiorly with the parietal bones, and anteriorly and superiorly with the ethmoid and frontal bones. The depression on the superior cranial surface of the body of the sphenoid bone, the *hypophyseal fossa* (or the *sella turcica*), houses the pituitary gland; a portion of the body is hollow, forming the *sphenoid sinus* cavity.

Two pairs of wings project from the body of the sphenoid bone. The *lesser wings* project from the anterior aspect of the body and are more superior and smaller than the greater wings (see Figure 8-3). The lesser wings are attached to the body by small roots or struts. The gap between the lesser wing and the sphenoid body forms the *optic foramen (canal)* through which the optic nerve exits the orbit. The lesser wings articulate with the frontal and ethmoid bones.

The *greater wings* project from the lateral aspects of the body and articulate with the frontal bone, the parietal bones, squamous portions of the temporal

bones, and the zygomatic bones. The *pterygoid process* projects from the base of the greater wing and articulates with the vertical stem of the palatine bone; each contributes to a shallow depression, the *pterygo-palatine fossa*. Three important foramina are located in the greater wing (Figure 8-5): the *foramen rotundum*, through which the maxillary nerve passes; the *foramen ovale*, through which the mandibular nerve passes; and the *foramen spinosum*, through which the middle meningeal artery passes.

The single **ethmoid bone** resembles a rectangular box that contains a midline perpendicular plate. This plate bisects the top of the box, the horizontal cribriform plate, which is perforated for the passage of the olfactory nerves. The sides of the box parallel to the perpendicular plate are the orbital plates and are separated from the perpendicular plate by the ethmoid air cells. The ethmoid bone articulates with the sphenoid and frontal bones superiorly and with the vomer inferiorly; the orbital plates also articulate with the maxillary and lacrimal bones.

BONES OF THE FACE

The single **frontal bone** forms the forehead and articulates with the nasal bones, maxillae, and zygomatic bones in formation of the face (see Figure 8-4). The sutures joining adjacent bones of the face generally are named according to the names of the two bones that are connected (e.g., the suture between the frontal bone and the zygomatic bone is the frontozygomatic suture).

The two **maxillae**, or **maxillary bones**, form the upper jaw, the hard palate, the lateral walls of the nasal cavity, and the floor of both orbits (see Figure 8-4). Each maxillary bone articulates with the frontal, nasal, lacrimal, ethmoid, sphenoid, palatine, and zygomatic bones. That portion of the maxillary bone forming the cheek contains the *maxillary sinus*.

The two **nasal bones** form the bridge of the nose and articulate with each other, with the frontal bone, and with the frontal processes of the maxillary bones (see Figure 8-4). The **vomer** is a single bone that forms the posterior part of the nasal septum. It articulates with the palatine and maxillary bones inferiorly and with the ethmoid bone superiorly. The **inferior conchae** are separate bones located along the lateral walls of the nasal cavity.

The **lacrimal bone** (one in each orbit) is the smallest bone of the face and articulates with the maxillary bone, ethmoid bone, and frontal bone.

There are two **palatine bones**. Each is an L-shaped bone that extends from the hard palate at the back of the mouth to the orbit. The horizontal plate is found in the oral cavity; the vertical stem runs along the posterior aspect of the nasal cavity and articulates with the pterygoid process of the sphenoid bone. A small, flattened area at the top of the vertical stem is located in the orbital floor at the posterior edge of the orbital plate of the maxilla.

The paired **zygomatic bones** form the lateral part of the cheekbones and articulate with the zygomatic process of the temporal bones to form the zygomatic arches (see Figure 8-1). The zygomatic bones also articulate with the maxillary bones and with the greater wings of the sphenoid bone.

The **mandible** forms the movable lower jaw. It is a horseshoe-shaped bone consisting of a curved horizontal body and two perpendicular processes, the rami.

THE ORBIT

The orbits are bony cavities on either side of the midsagittal plane of the skull below the cranium. They contain the globes, the extraocular muscles, and orbital nerves, blood vessels, and connective tissue.

The orbit is shaped like a four-sided pyramid, the base of which is at the anterior orbital margin and

the apex at the posterior margin within the skull. The orbital walls are referred to as **roof**, **floor**, and **medial** and **lateral walls**. The medial walls run approximately parallel to each other, whereas the two lateral walls, if extended posteriorly, would form approximately a 90-degree angle with each other^{1,2} (Figure 8-6). The orbit has also been described as pear shaped, having its widest portion 1.5 cm inside the orbital margin.¹ The orbital floor extends to approximately two-thirds the depth of the orbit; the other three sides extend to the apex.

Each orbit is composed of seven bones—the frontal, maxillary, zygomatic, sphenoid, ethmoid, palatine, and lacrimal bones (Figure 8-7). The frontal, sphenoid, and ethmoid are each a single bone and take part in the formation of both orbits.

ORBITAL WALLS

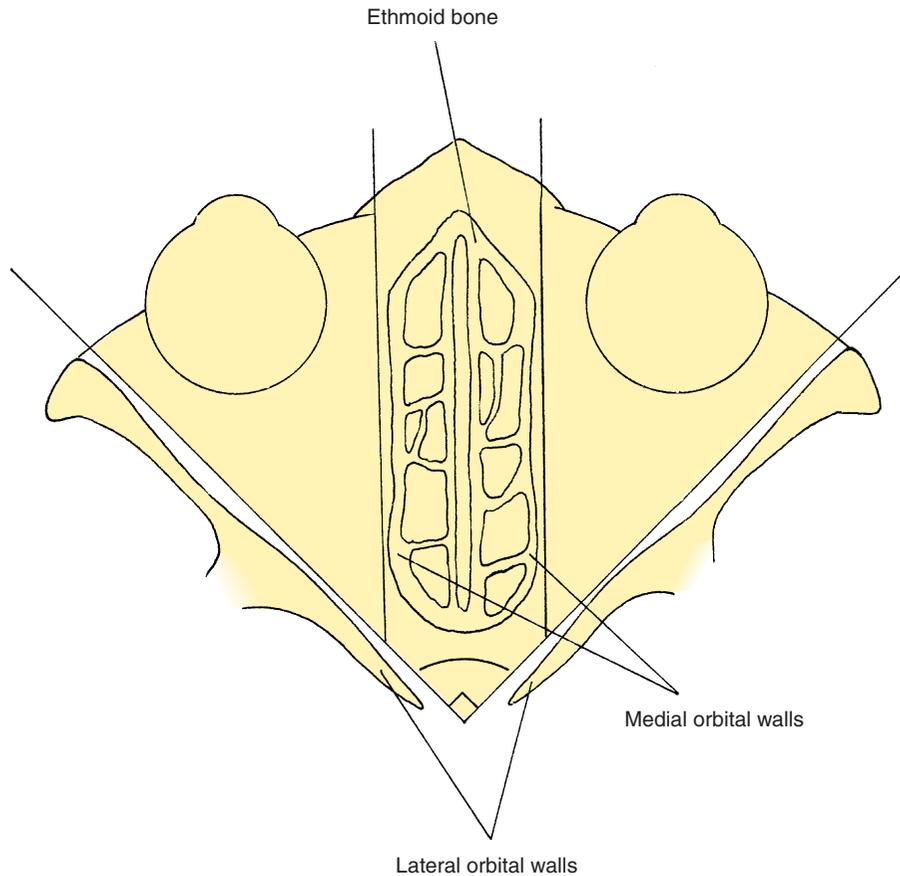
Roof

The roof is triangular and is composed primarily of the orbital plate of the **frontal bone** in front (Figure 8-8). The **lesser wing of the sphenoid** contributes a small posterior portion. The orbital plate of the frontal bone is thin in the area that separates the orbit from the anterior cranial fossa. In an elderly adult, bone in this area may resorb, leaving only the periosteal connective tissue in contact with the dural covering of the frontal lobe of the brain. The small area of the lesser wing of the sphenoid that is involved in this wall runs slightly downward, and an oval foramen, the **optic canal**, lies within it (see Figure 8-7). This optic foramen is located roughly at the apex of the orbit.

The frontal bone forms the ridge of the superior orbital margin. Behind the lateral aspect of this margin is an indentation in the frontal bone: the fossa for the lacrimal gland. A U-shaped piece of cartilage, the **trochlea**, is attached to the orbital plate of the frontal bone approximately 2 mm behind the medial aspect of the superior orbital margin. The tendon of the superior oblique muscle passes through this pulleylike structure.

Floor

The floor is also triangular and is composed of the orbital plate of the **maxillary bone** and the orbital plate of the **zygomatic bone** in front and the small orbital process of the **palatine bone** behind (Figure 8-9). The maxillary bone makes up the largest part of the floor, and most of the remainder is provided by the zygomatic bone. The orbital process of the palatine bone is a small, flattened area at the top of the vertical arm and is located at the most posterior edge of the orbital plate of the maxilla. Often in the adult skull, the suture between

**FIGURE 8-6**

Angular relationship of orbital walls. Medial walls are approximately parallel to each other; if lateral walls were extended an approximate right angle would be formed.

the orbital process of the palatine bone and the maxilla is indistinguishable.

The floor does not reach all the way to the apex and is separated from the lateral wall posteriorly by the **inferior orbital fissure**. The *infraorbital groove* runs across the floor from the inferior orbital fissure and anteriorly is bridged by a thin plate of bone, thus becoming a canal running within the maxillary bone. This canal opens on the facial surface of the maxilla below the inferior orbital margin as the *infraorbital foramen* (see Figure 8-7). The inferior orbital margin is composed of the maxilla and the maxillary process of the zygomatic bone.

CLINICAL COMMENT: BLOW-OUT FRACTURE OF THE ORBIT

The orbital rim is strong and can withstand considerable impact. However, a blow to the orbital rim can cause compression of the orbital contents, and such a sudden increase in intraorbital pressure might cause a fracture in one of the orbital walls. In the classic blow-out fracture, the

orbital rim remains intact. The floor of the orbit is particularly susceptible to such a fracture, which usually occurs in the thin region along the infraorbital canal²⁻⁴ (Figure 8-10). Clinical signs and symptoms accompanying this damage include orbital swelling, ecchymosis, anesthesia of the area innervated by the infraorbital nerve, and diplopia caused by restriction of ocular motility (particularly noted in upward gaze).⁴ Limitations in ocular motility are caused by damage to the inferior extraocular muscles, either from bruising or hematoma or from entrapment of the muscle or adjoining connective tissue within the fracture.^{3,5,6}

Medial Wall

The medial wall is rectangular. From front to back, it is formed by the frontal process of the **maxilla**, the **lacrimal bone**, the orbital plate of the **ethmoid**, and a part of the **body of the sphenoid** (Figure 8-11). A ridge on the frontal process of the maxilla that forms the anterior part of the medial orbital margin also forms the *anterior lacrimal crest*, which demarcates one border of the fossa for the lacrimal sac. The lacrimal bone, a small bone approximately the size of a thumbnail, together with

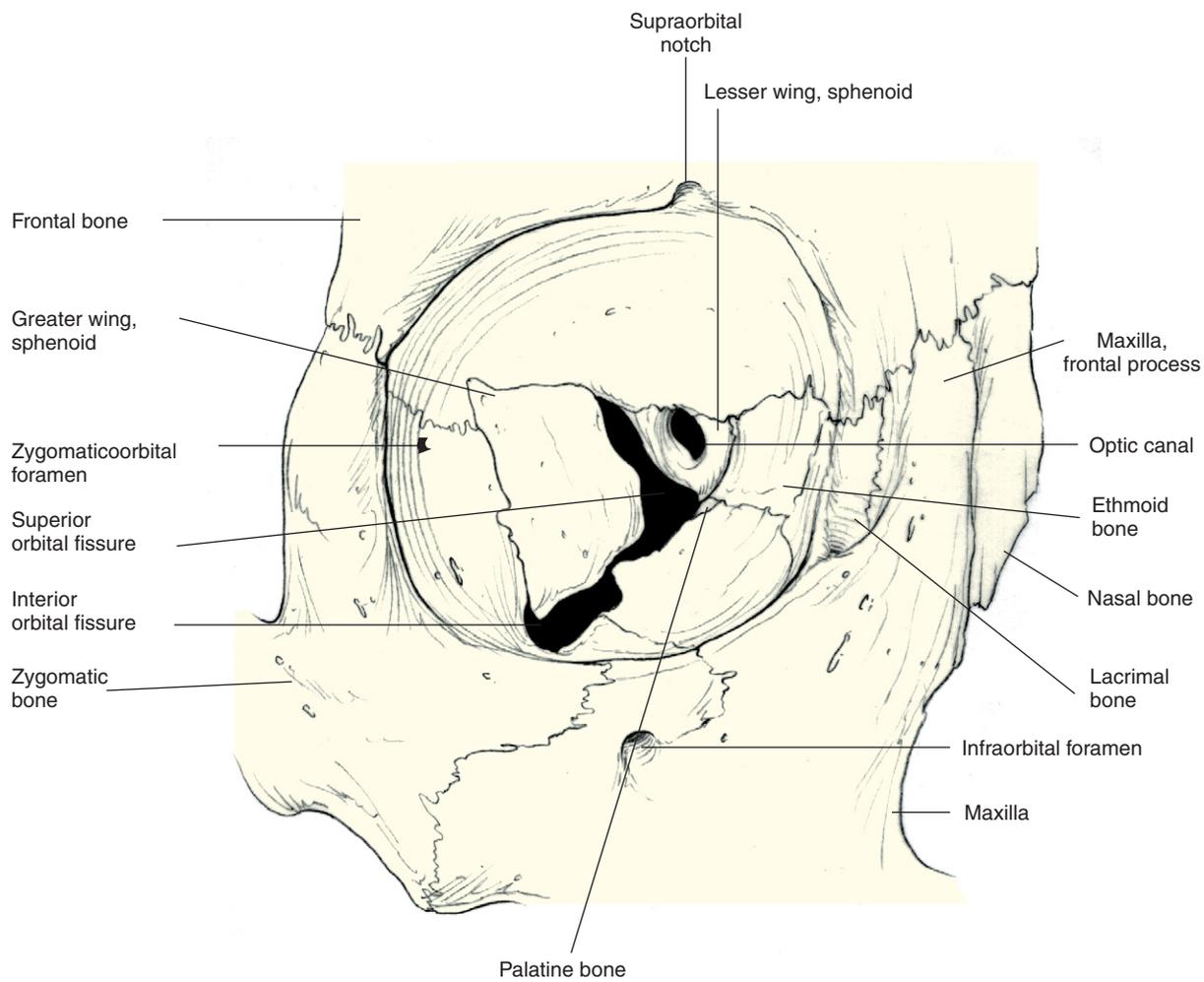


FIGURE 8-7

Anterior view of bones of orbit. (From Mathers LH, Chase RA, Dolph J et al: *Clinical anatomy principles*, St Louis, 1996, Mosby.)

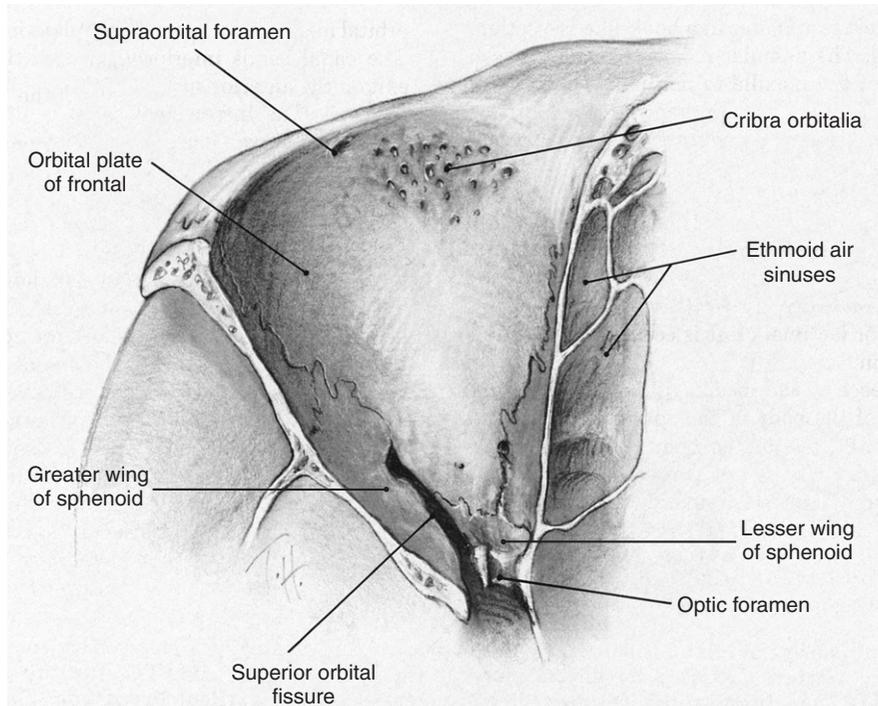


FIGURE 8-8
Bones of orbital roof. (From Doxanas MT, Anderson RL: *Clinical orbital anatomy*, Baltimore, 1984, Williams & Wilkins.)

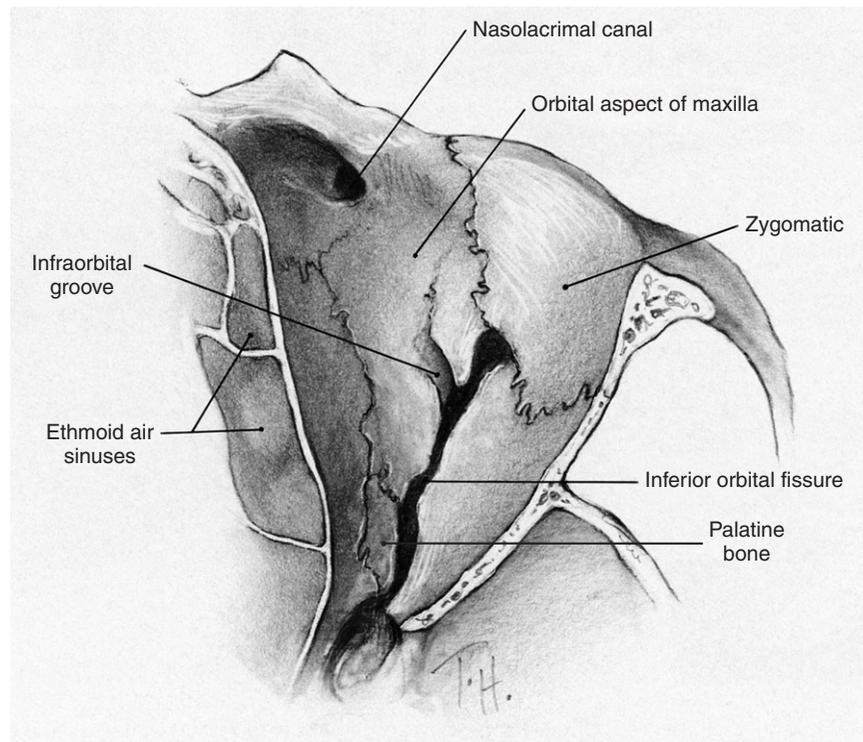
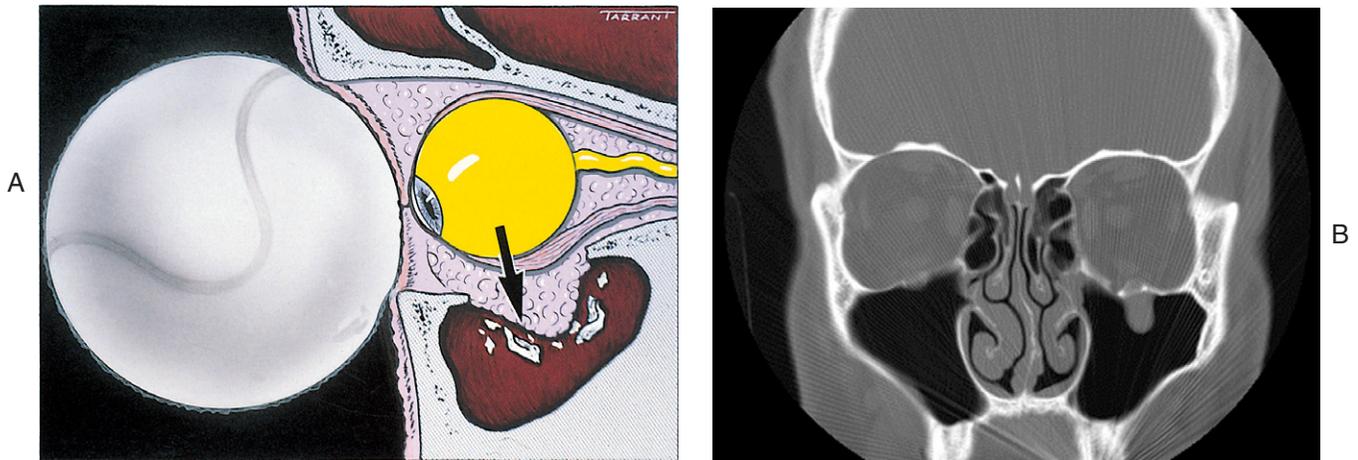
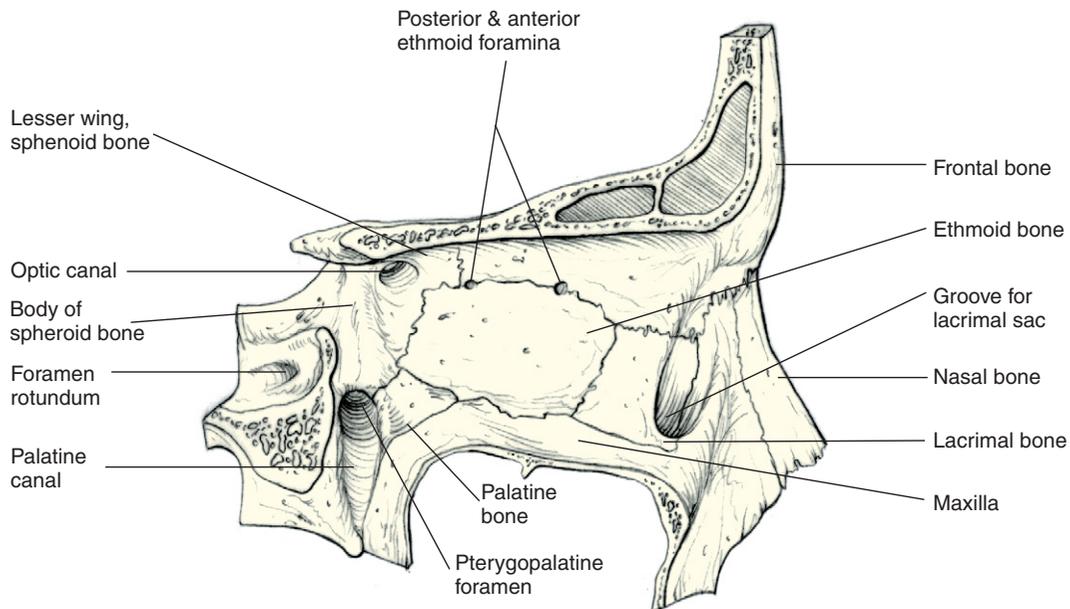


FIGURE 8-9
Bones of orbital floor. (From Doxanas MT, Anderson RL: *Clinical orbital anatomy*, Baltimore, 1984, Williams & Wilkins.)

Blowout fracture

**FIGURE 8-10**

A, Mechanism of blow-out fracture. Arrow indicates that the force damages the weakest orbital wall, the floor. **B**, Coronal computed tomography (CT) scan showing blow-out fracture of left orbital floor. (**A** from Kanski JJ: *Clinical ophthalmology: a systematic approach*, ed 5, Oxford, England, 2003, Butterworth-Heinemann; **B** courtesy Dr. Weon Jun, Portland VA Medical Center, Portland, Ore.)

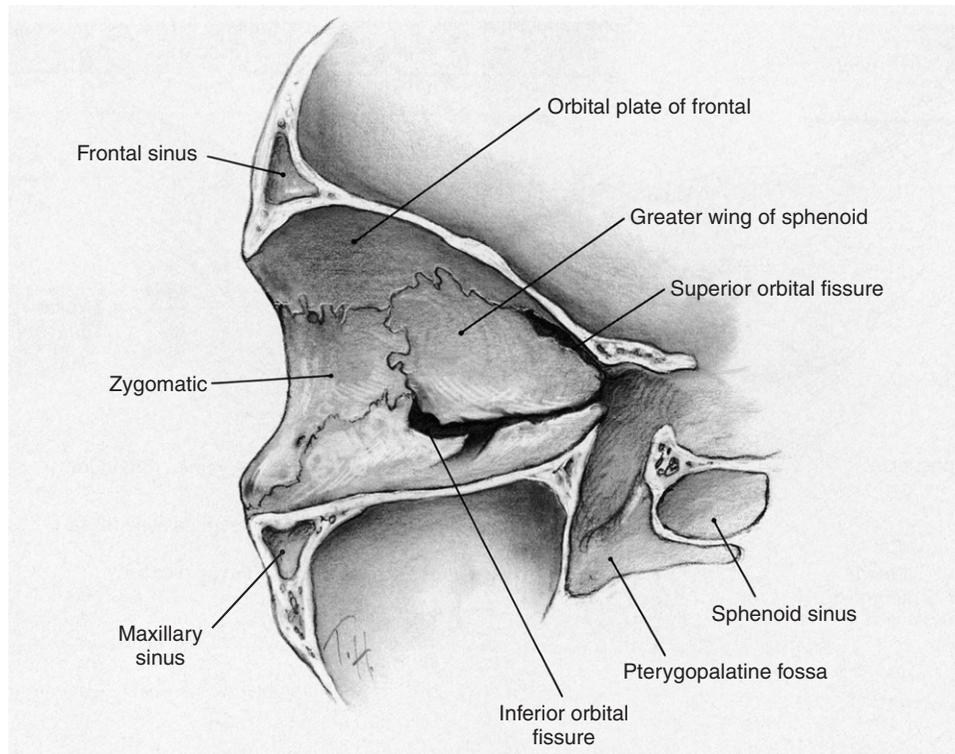
**FIGURE 8-11**

Bones of medial orbital wall. (From Mathers LH, Chase RA, Dolph J et al: *Clinical anatomy principles*, St Louis, 1996, Mosby.)

the frontal process of the maxillary bone, forms the wall of this fossa. The lower portion of the fossa is a groove that is continuous inferiorly with the *nasolacrimal canal*, which continues into the nasal cavity. A ridge in the lacrimal bone forms the *posterior lacrimal crest* and is

continuous superiorly with the prominence of the frontal bone, forming the posterior part of the medial margin of the orbit.

The ethmoid bone forms most of the medial wall. The orbital plate of the ethmoid sometimes is said to be

**FIGURE 8-12**

Bones of lateral orbital wall. (From Doxanas MT, Anderson RL: *Clinical orbital anatomy*, Baltimore, 1984, Williams & Wilkins.)

“paper thin” (*lamina papyracea*); thus the medial wall is the thinnest of the orbital walls. The small part of the sphenoid bone present in this wall is part of the body and is located at the posterior end adjacent to the wall of the optic canal. The floor is joined to the medial wall at the sutures connecting the bones of the two walls, and the anterior and posterior ethmoidal canals are located within the frontoethmoidal suture at the junction of the roof and medial wall.

Lateral Wall

The lateral wall is roughly triangular and is composed of the **zygomatic bone** in front and of the **greater wing of the sphenoid bone** behind (Figure 8-12). The zygomatic bone separates the orbit from the temporal fossa. One or more foramina may be present in the zygomatic bone as a conduit for nerves and vessels between the orbit and facial areas. The *lateral* or *marginal orbital tubercle* (*Whitnall's tubercle*) is a small, bony prominence located on the orbital surface of the zygomatic bone and is the attachment site for the aponeurosis of the superior palpebral levator muscle, the lateral palpebral ligament, and the lateral check ligament.⁷

The greater wing of the sphenoid separates the orbit from the middle cranial fossa. The roof is separated from the lateral wall in back by the **superior orbital fissure** and in front by the frontozygomatic and frontosphenoidal sutures. The **inferior orbital fissure** separates the posterior part of the floor from the lateral wall (see Figure 8-7).

ORBITAL MARGINS

Although dimensions of the orbit vary widely, the average horizontal diameter of the orbital margin is 4 cm, the average vertical diameter is 3.5 cm, and the average depth is 4.5 cm.^{1,2,8} The frontal bone forms the superior orbital margin. The highest point of this arch is located one-third the way along the margin from the superior medial corner of the orbit. The *supraorbital notch* (see Figure 8-7) is located just medial to the center of the superior orbital margin and is the conduit for the supraorbital vessels and nerves. This notch can be palpated easily. In 25% of orbits the supraorbital notch is enclosed to form a foramen.^{2,9}

At the superior medial corner is a less well-defined groove, the *supratrochlear notch*, through which pass the nerve and vessels of the same name. The supratrochlear

notch remains a notch or groove in the majority of orbits, becoming a foramen in just 3%.⁹

The lateral orbital margin is the orbital region most exposed to possible injury and therefore is the strongest area of the orbital margin. It is formed by the zygomatic process of the frontal bone superiorly and by the frontal process of the zygomatic bone inferiorly.

The inferior orbital margin usually is formed equally by the maxillary bone and the zygomatic bone. The

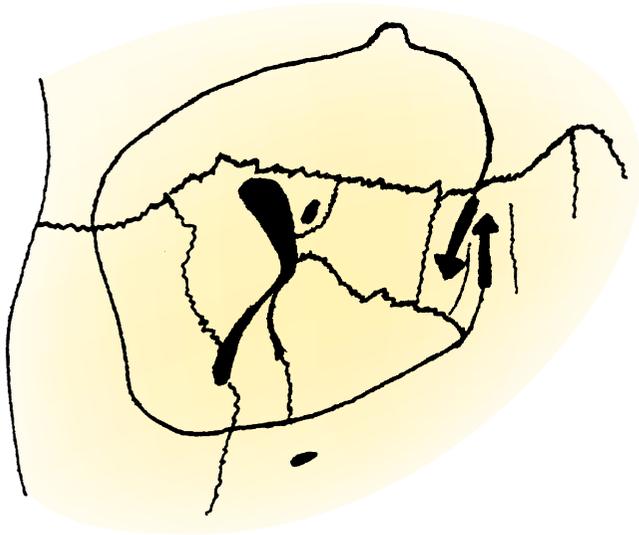


FIGURE 8-13

Orbital margin. Arrows indicate spiral shape formed at nasal margin.

zygomaticomaxillary suture can often be easily palpated through the skin along the inferior orbital edge. The *infraorbital foramen* (the opening from the infraorbital canal) is found in the anterior surface of the maxillary bone below the inferior orbital margin.

The frontal process of the maxillary bone articulates with the frontal bone and forms part of the medial rim of the orbital margin. This process articulates posteriorly with the lacrimal bone and anteriorly with the nasal bone. The medial margin is not continuous. Starting from the inferior nasal aspect, which is the anterior lacrimal crest, the orbital margin forms a spiral (Figure 8-13). The posterior lacrimal crest completes the superior curve of the medial orbital margin.

ORBITAL FORAMINA AND FISSURES

A number of foramina and fissures exist between the orbit and the middle cranial fossa, sinuses, and face to allow the entrance and exit of vessels and nerves that supply the globe and orbital structures. The **optic foramen** or the **optic canal** (see Figure 8-7) is formed by a bridge of bone called the “optic strut” extending from the lesser wing to the sphenoid body.¹⁰ The canal lies just lateral to the body of the sphenoid. The canal often causes an indentation into the bone of the sphenoid sinus.¹¹ It provides communication between the orbital cavity and the middle cranial fossa and is separated from the medial posterior edge of the superior orbital fissure by a strip of bone. The optic nerve exits and the ophthalmic artery enters the orbit through this canal (Figure 8-14).

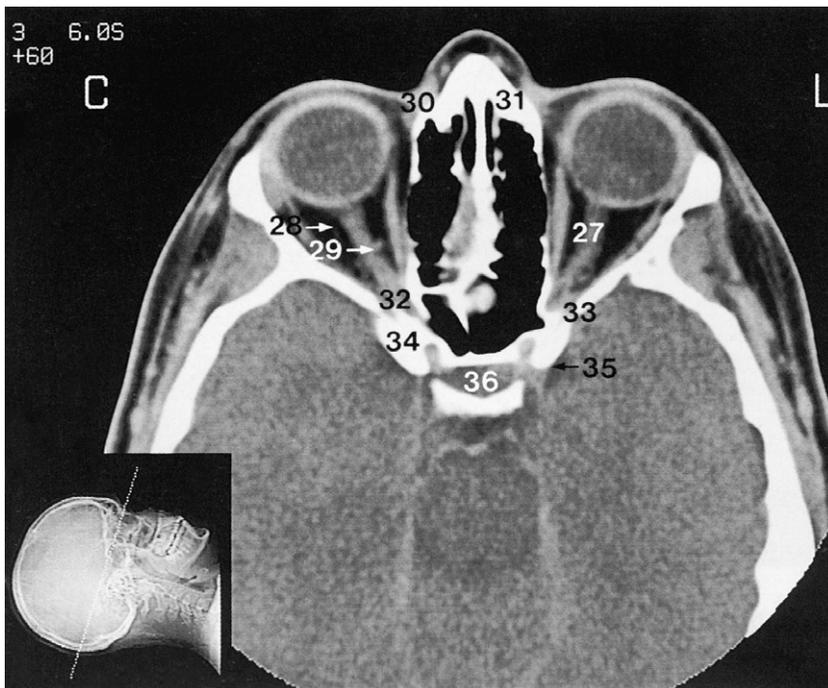
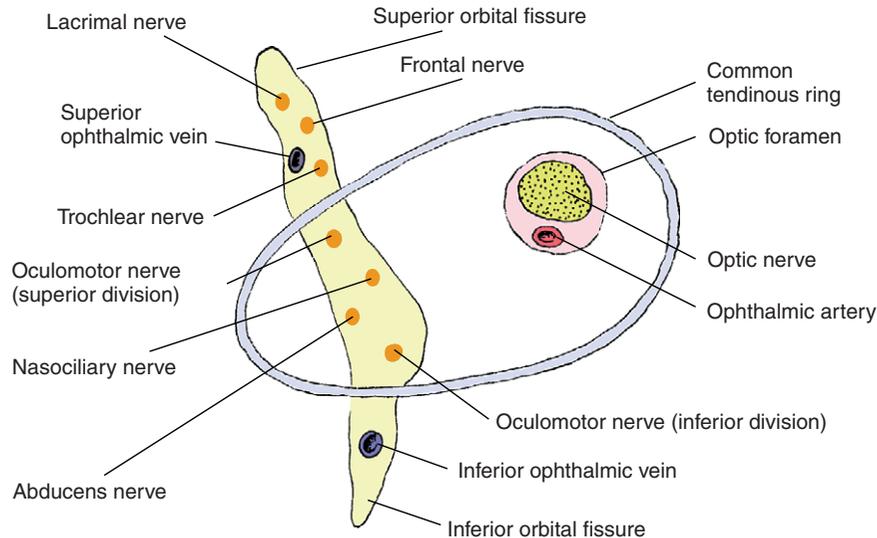


FIGURE 8-14

Horizontal section through the orbits. CT scan through long axis of orbit in horizontal plane. 27, Optic nerve; 28, long posterior ciliary artery; 29, ophthalmic artery; 30, angular vein; 31, frontal process of maxilla; 32, optic canal; 33, superior orbital fissure; 34, lesser wing of sphenoid; 35, anterior clinoid process; 36, pituitary gland. (From Mathers LH, Chase RA, Dolph J et al: *Clinical anatomy principles*, St Louis, 1996, Mosby.)

**FIGURE 8-15**

Nerves and vessels that enter orbit through superior orbital fissure within, above, and below the common tendinous ring.

CLINICAL COMMENT: OPTIC NERVE DAMAGE

The dura mater lining the optic canal is adherent to both the dura of the optic nerve and the periosteum of the canal. This close confinement of the nerve within the bony passage predisposes the nerve to compression and damage by even very small lesions or tumors of the bony canal.¹²

The **superior orbital fissure** is the gap between the lesser wing and the greater wing of the sphenoid bone and is located between the roof and the lateral wall (see Figure 8-7). As with the optic canal, this fissure is a communication between the orbital cavity and the middle cranial fossa. The fissure usually is widest medially, becoming narrower toward the lateral portion. Approximately midway on the lower aspect is a small sharp spur (the lateral rectus spine) that serves as the attachment for the lateral rectus muscle. A circular band of connective tissue, the **common tendinous ring** (or **annulus of Zinn**), is located anterior to the fissure and the optic canal. This ring is the origin for the four rectus muscles. Figure 8-15 shows the relationships among the superior orbital fissure, the tendinous ring, and the various nerves passing through them. The lacrimal nerve, frontal nerve, trochlear nerve, and superior ophthalmic vein pass through the superior orbital fissure *above* the circular tendon. The superior and inferior divisions of the oculomotor nerve, the nasociliary nerve, and the abducens nerve pass through the fissure *and* the ring tendon. The optic nerve and the ophthalmic artery pass through the optic canal *and* the tendinous ring.

The **inferior orbital fissure** lies between the floor of the orbit and the lateral wall (see Figure 8-7). It allows passage of vessels and nerves between the orbit and the pterygopalatine and temporal fossae. This fissure often is narrowest in its center. The foramen rotundum opens into the pterygopalatine fossa and transmits the maxillary division of the trigeminal nerve to the inferior orbital fissure. Branches of the maxillary nerve, including the infraorbital nerve, join vessels passing through the inferior orbital fissure. Most of these structures continue into the infraorbital groove in the maxillary bone. The inferior ophthalmic vein exits the orbit through the inferior orbital fissure *below* the ring tendon.

PARANASAL SINUSES

The paranasal sinuses are mucosa-lined, air-filled cavities located in four of the orbital bones. These hollow spaces decrease the weight of the skull and act as a resonator for the voice. The paranasal sinuses communicate with the nasal cavity through small apertures.

The orbit is surrounded on three sides by sinuses (Figure 8-16): the **frontal sinus** above, the **ethmoid** and **sphenoid sinus** cavities medial to, and the **maxillary sinus** below the orbit. Of these, the maxillary sinus is largest. The roof of the maxillary sinus is the orbital plate of the maxilla; this plate, only 0.5 to 1 mm thick, separates the sinus from the orbital contents.¹ The sphenoid sinus is within the body of the sphenoid and, in some individuals, continues into the lesser wing and may surround the optic canal.¹ The ethmoid sinus sometimes continues into the lacrimal bone or into the

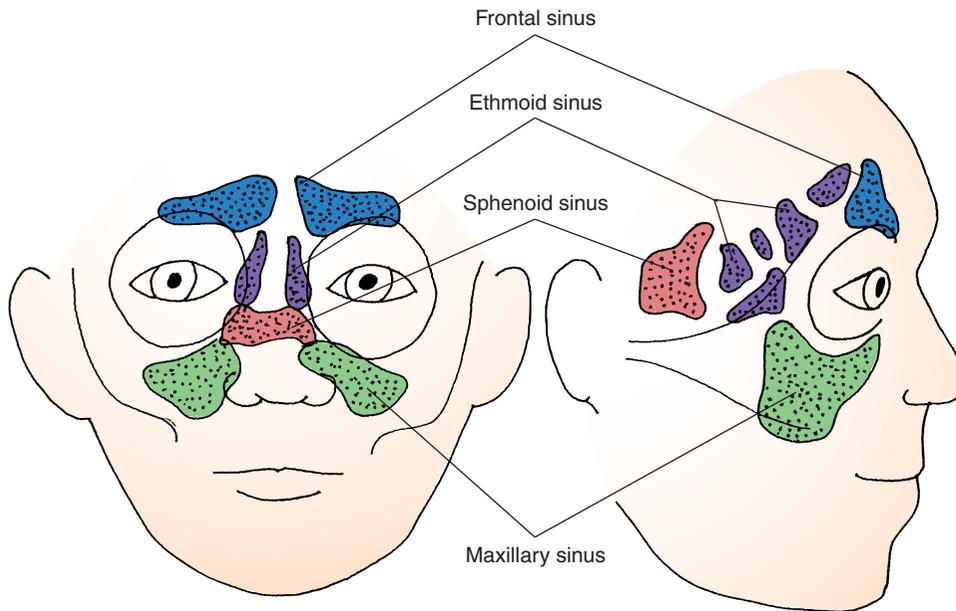


FIGURE 8-16
Location of sinus cavities within orbital walls.

frontal process of the maxilla.¹³ In a high percentage of orbits, the thin bone of both the sphenoid and the ethmoid sinuses makes contact with the dural sheath of the optic nerve.^{14,15} Table 8-1 shows the location of each of the sinus cavities.

CLINICAL COMMENT: ORBITAL CELLULITIS

*The thin walls of the sinus cavities are poor barriers to the passage of infection from the air cavities into the orbit. If pathogens from a sinusitis penetrate the thin, bony barrier, a serious infection involving the orbital contents might ensue. A major infection that involves the orbital connective-tissue contents is called **orbital cellulitis**, and one of its major causes is sinusitis.^{2,3,16,17} Signs and symptoms include sudden onset of pain, edema, proptosis, and a decrease in ocular motility. Orbital cellulitis is a serious medical situation because of the relatively easy access to the brain and must be treated aggressively; hospitalization may be required.^{3,16} Orbital cellulitis also is a possible sequela of a blow-out fracture, which can (but rarely does) provide a pathologic avenue between the sinus cavities and the orbit that results in orbital infection.¹⁸*

CONNECTIVE TISSUE OF ORBIT

The connective tissue of the orbit is arranged in a complex network that serves to line, cover, and compartmentalize orbital structures; to anchor soft tissue structures to bone; and to compartmentalize areas. Although this network is continuous, the segments are described here individually according to their position and function.

Table 8-1 Paranasal Sinuses

Sinus	Location
Frontal	In frontal bone, on each side of midline superior to orbits
Ethmoid	Several air cells on both sides of perpendicular plate of ethmoid bone, medial to orbits
Sphenoid	In body of sphenoid bone, posterior and medial to orbits
Maxillary	In each maxillary bone, inferior to orbits

Periorbita

The **periorbita**, also called the **orbital periosteum** or **orbital fascia**, covers the bones of the orbit (Figure 8-17). This dense connective tissue membrane serves as an attachment site for muscles, tendons, and ligaments and is a support structure for the blood supply to the orbital bones. The periorbita is attached only loosely to the underlying bone except at the orbital margins, the sutures, and the edges of fissures and foramina. At the orbital margins it is continuous with the periosteal covering of the bones of the face; at the edges of the superior orbital fissure, the optic canal, and the ethmoid canals, the periorbita is continuous with the periosteal layer of the dura mater. At the anterior portion of the optic canal the periorbita splits such that a portion becomes continuous with the dura of the optic nerve and another portion reflects forward to take part in the formation of the common tendinous ring. At the

Rights were not granted to include this figure in electronic media.
Please refer to the printed publication.

FIGURE 8-17

Fascial system of orbit shown in vertical section through vertical meridian of eyeball, with the latter in primary position, eyelids closed. (From Kronfeld PC: *The human eye*, Rochester, NY, 1943, Bausch & Lomb Press.)

inferior orbital fissure the periorbita is continuous with the periosteum of the skull. At the lacrimal crests a sheet of periorbita covers the lacrimal sac, and the periorbita is continuous with the tissue lining the nasolacrimal canal. Another portion of the periorbita covers the lacrimal gland.

Orbital Septum

At the orbital margins the periorbita is continuous with a connective tissue sheet known as the **orbital septum**, also termed the **palpebral fascia** or **septum orbitale**. This dense connective tissue sheet is circular and runs from the entire rim of the orbit to the tarsal plates,

which are embedded in the eyelids. This strong barrier helps prevent facial infections from entering the orbit; it also maintains orbital fat in its place. Figures 8-17 and 8-18 show the relationships between orbital structures and these connective tissue structures. At the lateral margin the orbital septum lies in front of the lateral palpebral ligament and the check ligament for the lateral rectus muscle.⁷ At the superior orbital margin the orbital septum passes in front of the trochlea and bridges the supraorbital and supratrochlear notches. At the medial margin the orbital septum, which attaches behind the posterior lacrimal crest, lies in front of the check ligament for the medial rectus muscle; it lies behind the medial palpebral ligament, Horner's muscle, and the lacrimal

Rights were not granted to include this figure in electronic media.
Please refer to the printed publication.

FIGURE 8-18

Fascial system of orbit shown in horizontal section. Plane of section lies slightly above horizontal meridian of eyeball, which is assumed to be in primary position, eyelids closed. (From Kronfeld PC: *The human eye*, Rochester, NY, 1943, Bausch & Lomb Press.)

sac (see Figure 8-18), isolating the lacrimal sac (which communicates with the nasal cavity) from the orbit proper.

CLINICAL COMMENT: PRESEPTAL CELLULITIS

Preseptal cellulitis is an inflammatory condition that affects the tissue of the eyelid. If an infection of an eyelid gland becomes more serious and involves the tissue around the gland, preseptal cellulitis occurs. The disease can be limited by the location of the orbital septum, which provides some barrier to prevent spread into the orbit and development of orbital cellulitis.

Tenon's Capsule

Tenon's capsule (bulbar fascia) is a sheet of dense connective tissue that encases the globe.¹⁹ It lies between the conjunctiva and the episclera and merges with them anteriorly in the limbal area. Tenon's capsule is pierced by the optic nerve, the vortex veins, the ciliary vessels and nerves, and the extraocular muscles. At the muscle insertions Tenon's capsule forms sleeve-like sheaths that cover the tendons.^{2,20} Posteriorly, Tenon's capsule merges with the dural sheath of the optic nerve. This dense connective tissue capsule acts as a barrier to prevent the spread of orbital infections into the globe.

Suspensory Ligament (of Lockwood)

The **suspensory ligament (of Lockwood)** (see Figure 8-17) is a hammocklike sheet of dense connective tissue that runs from its attachment on the lacrimal bone at the medial orbital wall to the zygomatic bone at the lateral wall. Tissue from several structures—Tenon’s capsule, the sheaths of the two inferior extraocular muscles, and the inferior eyelid aponeurosis—contributes to the formation of this ligament. The suspensory ligament helps to support the globe, particularly in the absence of the bones of the orbital floor.

Orbital Muscle of Müller

The **orbital muscle of Müller** is a small, smooth muscle embedded in the periorbita and covering part of the inferior orbital fissure.^{6,21} Its function in humans is unknown.

Orbital Septal System

A complex web of interconnecting connective tissue septa organize the orbital space surrounding the globe into radial compartments (Figure 8-19). Collagenous

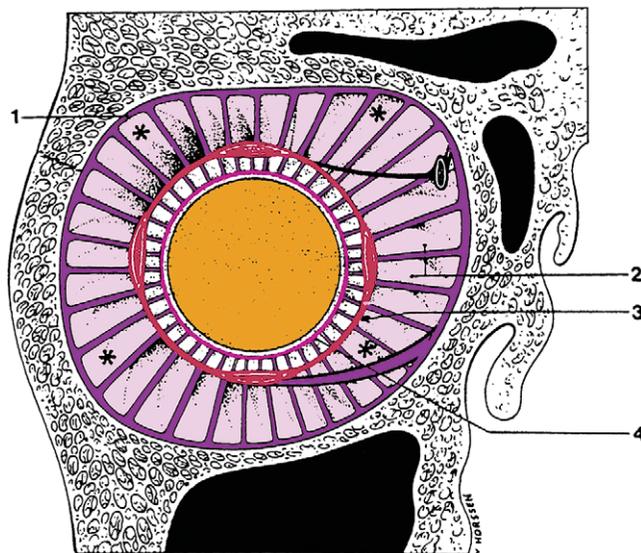


FIGURE 8-19

Anterior orbital connective tissue septa: 1, periorbita; 2, fibrous septa; 3, common muscle sheath around eye; 4, Tenon’s capsule. Asterisks indicate areas where smooth muscle tissue was found. (From Koornneef L: *Arch Ophthalmol* 95:1269, 1977.)

strands connect the periorbita to Tenon’s capsule and intermuscular membranes. This connective tissue system of “slings” anchors and supports the extraocular muscles and blood vessels attaching them to adjacent orbital walls.²² The slings associated with each of the muscles maintain correct positioning of the muscles during eye movements. Varying degrees of connectivity occur throughout the orbit (see Chapter 10).

Orbital Fat

The spaces not occupied by ocular structures, connective tissue, nerves, or vessels become filled with adipose tissue. Usually, four adipose tissue compartments are located within the muscle cone surrounding the optic nerve and separating it from the extraocular muscles.^{6,23} A ring of adipose tissue separates the muscles from the walls of the orbit, and adipose is the predominant tissue near the orbital apex.⁶ Because of the close association of the orbital contents, a space-occupying lesion will cause outward displacement of the globe.

CLINICAL COMMENT: EXOPHTHALMOS

Protrusion of the globe is termed **exophthalmos**, or **proptosis** (Figure 8-20). It can be caused by a number of pathologic conditions, including inflammation, edema, tumors, and injuries.¹⁶ The most common type is thyroid ophthalmopathy (dysthyroid orbitopathy, Graves’ disease), which can cause hypertrophy of the extraocular muscles; in some patients the muscles become enlarged to eight times their normal size.³ Thyroid ophthalmopathy also causes proliferation of orbital fat and connective tissue and lymphoid infiltration.³ Because the orbital tissue is encased in immovable bony walls, this increase in volume of the orbital contents produces protrusion of the globe and simulates eyelid retraction. At the first sign of proptosis, investigation is necessary to determine the causative factor.

AGING CHANGES IN THE ORBIT

In elderly adults the orbital septum often weakens, particularly in the medial inferior area, and herniation of fat and loose connective tissue can occur. The walls of the paranasal sinuses thin, and with age these walls may actually contain perforations that pass into the orbit.



FIGURE 8-20

A, Asymmetric signs in ophthalmic Graves' disease, proptosis of the left eye. **B**, CT scan showing proptosis of the right eye. (**A** from Kanski JJ: *Clinical ophthalmology: a systematic approach*, ed 5, Oxford, England, 2003, Butterworth-Heinemann; **B** courtesy Dr. Weon Jun, Portland VA Medical Center, Portland, Ore.)

REFERENCES

1. Warwick R: *Eugene Wolff's anatomy of the eye and orbit*, ed 7, Philadelphia, 1976, Saunders, pp 1, 8, 15, 19.
2. Doxanas MT, Anderson RL: *Clinical orbital anatomy*, Baltimore, 1984, Williams & Wilkins, pp 20, 25, 117.

3. Kanski JJ: *Clinical ophthalmology*, ed 3, London, 1994, Butterworth-Heinemann, pp 33, 52.
4. Forrest LA, Schuller DE, Strauss RH: Management of orbital blow-out fractures, *Am J Sports Med* 17(2):217, 1989.
5. Taher AA: Diplopia caused by orbital floor blowout fracture, *Oral Surg Oral Med Oral Pathol* 75(4):433, 1993.
6. Koornneef L: Orbital connective tissue. In Jakobiec FA, editor: *Ocular anatomy, embryology, and teratology*, Philadelphia, 1982, Harper & Row, p 835.
7. Rosenstein T, Talebzadeh N, Pogrel MA: Anatomy of the lateral canthal tendon, *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 89(1):24, 2000.
8. Reeh MJ, Wobig JL, Wirtschafter JD: *Ophthalmic anatomy*, San Francisco, 1981, American Academy of Ophthalmology, p 11.
9. Webster RC, Gaunt JM, Hamdan US et al: Supraorbital and supratrochlear notches and foramina: anatomical variations and surgical relevance, *Laryngoscope* 96(3):311, 1986.
10. Sires BS, Gausas R, Cook BE Jr et al: Orbit. In Kaufman PL, Alm A, editors: *Adler's physiology of the eye*, St Louis, 2003, Mosby, p 11.
11. Goldberg RA, Hannai K, Toga AW: Microanatomy of the orbital apex, *Ophthalmology* 99(9):1447, 1992.
12. Lang J, Kageyama I: The ophthalmic artery and its branches, measurements, and clinical importance, *Surg Radiol Anat* 12(2):83, 1990.
13. Blaylock WK, Moore CA, Linberg JV: Anterior ethmoid anatomy facilitates dacryocystorhinostomy, *Arch Ophthalmol* 108(12):1774, 1990.
14. Bansberg SE, Harner SG, Forbes G: Relationship of the optic nerve to the paranasal sinuses as shown by computed tomography, *Otolaryngol Head Neck Surg* 96(4):331, 1987.
15. Cheung DK, Attia EL, Kirkpatrick DA et al: An anatomic and CT scan study of the lateral wall of the sphenoid sinus as related to the transnasal transethmoid endoscopic approach, *J Otolaryngol* 22(2):63, 1993.
16. Berkow R, editor: *The Merck manual*, ed 14, Rahway, NJ, 1982, Merck, p 1984.
17. Mills RP, Kartush JM: Orbital wall thickness and the spread of infection from the paranasal sinuses, *Clin Otolaryngol* 10(4):209, 1985.
18. Silver HS, Fucci MJ, Flanagan JC et al: Severe orbital infection as a complication of orbital fracture, *Arch Otolaryngol Head Neck Surg* 118(8):845, 1992.
19. Tenon J-R: Anatomical observations on some parts of the eye and eyelids, *Strabismus* 11(1):63, 2003 (Translated by JJ Naus and RR Blanken).
20. Eggers HM: Functional anatomy of the extraocular muscles. In Tasman W, Jaeger EA, editors: *Duane's foundations of clinical ophthalmology*, vol 1, Philadelphia, 1994, Lippincott.
21. Rodriguez-Vazquez JE, Merida-Velasco JR, Jimenez-Collado J: Orbital muscle of Müller: observations on human fetuses measuring 35-150 nm, *Acta Anat (Basel)* 139:300, 1990.
22. Dutton JJ: Clinical and surgical orbital anatomy, *Ophthalmol Clin North Am* 9(4):527, 1996.
23. Wolfram-Gabel R, Kahn JL: Adipose body of the orbit, *Clin Anat* 15(3):186, 2002.

Ocular Adnexa and Lacrimal System

The ocular adnexa includes the structures situated in proximity to the globe. This chapter discusses the eyebrows, structures of the eyelids, the conjunctiva, and the lacrimal system, which consists of a secretory system, for tear production, and an excretory system, for tear drainage.

EYEBROWS

The **eyebrows** consist of thick skin covered by characteristic short, prominent hairs extending across the superior orbital margin, usually arching slightly but sometimes merely running horizontally. Generally, in men the brows run along the orbital margin, whereas in women the brows run above the margin.¹ The first body hairs produced during embryologic development are those of the eyebrow.²

The muscles located in the forehead—the frontalis, procerus, corrugator superciliaris, and orbicularis oculi—produce eyebrow movements, an important element in facial expression (Figure 9-1). The **frontalis** muscle originates high on the scalp and inserts into connective tissue near the superior orbital rim. The fibers are oriented vertically and raise the eyebrow, causing a look of surprise or attention. The **corrugator** originates on the frontal bone and inserts into skin superior to the medial eyebrow. It is characterized as the muscle of trouble or concentration, and its fibers are oriented obliquely; it moves the brow medially, toward the nose, creating vertical furrows between the brows. The **procerus**, the muscle of menace or aggression, originates on the nasal bone and inserts into the medial side of the frontalis: it pulls the medial portion of the eyebrow inferiorly and produces horizontal furrows over the bridge of the nose.^{2,3} The orbicularis oculi (described later) lowers the entire brow. The fibers of these muscles blend with one another and are difficult to separate.² All are innervated by the facial nerve, cranial nerve VII.

EYELIDS

The **eyelids**, or **palpebrae**, are folds of skin and tissue that, when closed, cover the globe. The eyelids have four major functions: (1) cover the globe for protection,

(2) move the tears toward drainage at the medial canthus on closure, (3) spread the tear film over the anterior surface of the eye on opening, and (4) contain structures that produce the tear film. On closure the upper eyelid moves down to cover the cornea, whereas the lower eyelid rises only slightly. When the eyes are closed gently, the eyelids should cover the entire globe.

CLINICAL COMMENT: LAGOPHTHALMOS

Lagophthalmos refers to incomplete closure of the eyelids (Figure 9-2). Its cause may be physiologic, mechanical (e.g., scarring), or paralytic. Lagophthalmos is most evident during sleep, when drying of the inferior cornea may result. Scratchy, irritated eyes are evident on awakening, and punctate keratitis can occur.⁴⁻⁶ Clinical assessment of the inferior cornea will show varying degrees of epithelial disruption, manifested as punctate staining with fluorescein dye.

PALPEBRAL FISSURE

The **palpebral fissure** is the area between the open eyelids. Although numerous variations exist in the positional relationship of the lid margins to the limbus, generally the upper lid just covers the superior limbus when one's eyes are open and looking straight ahead. The lower lid position is more variable, usually lying within 1 mm of the inferior limbus.⁷⁻⁹

The upper and lower eyelids meet at the corners of the palpebral fissure in the lateral and medial canthi. The **lateral canthus** is located approximately 5 to 7 mm medial to the bony orbital margin and lies directly on the globe.⁹ The **medial canthus** is at the medial orbital margin but is separated from the globe by a reservoir for the pooling of tears, the **lacrimal lake**. The floor of the lacrimal lake is the **plica semilunaris** (Figure 9-3). This narrow, crescent-shaped fold of conjunctiva, located in the medial canthus, allows for lateral movement of the eye without stretching the bulbar conjunctiva. The **caruncle** is a small, pink mass of modified skin located just medial to the plica. It is covered with epithelium that contains goblet cells and fine hairs and their associated sweat and sebaceous glands.

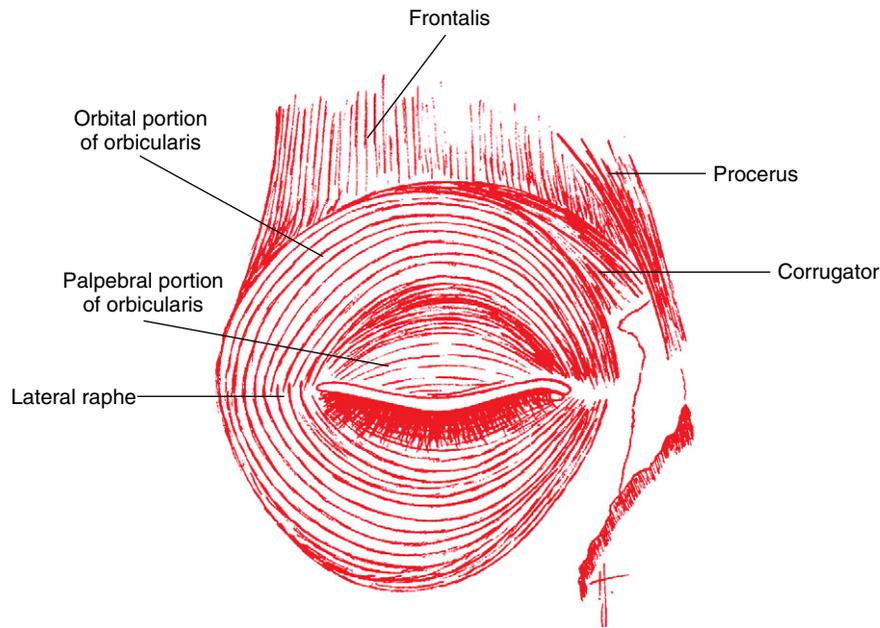


FIGURE 9-1
Forehead muscles that control the eyebrows.



FIGURE 9-2
Lagophthalmos: inability to oppose the eyelids on attempted lid closure. In this patient, left seventh cranial nerve palsy caused a lower lid paralytic ectropion and lagophthalmos. (From Krachmer JH, Palay DA: *Cornea color atlas*, St Louis, 1995, Mosby.)

EYELID TOPOGRAPHY

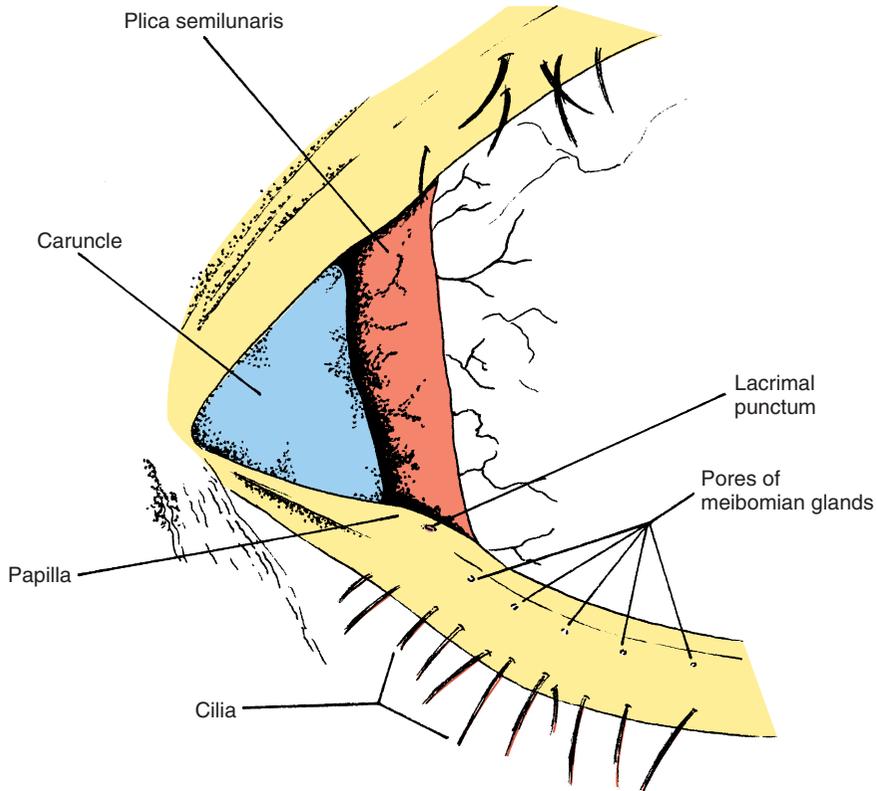
The upper eyelid extends to the eyebrow and is divided into the tarsal and the orbital (or preseptal) parts. The **tarsal portion** lies closest to the lid margin, rests on the globe, and contains the tarsal plate. The skin is thin, and the underlying loose connective tissue is devoid of adipose tissue. The **orbital portion** extends from the tarsus to the eyebrow, and a furrow, the **superior**

palpebral sulcus, separates the tarsal portion from the orbital portion (Figure 9-4). This sulcus separates the pretarsal skin, which is tightly adherent to the underlying tissue, from the preseptal skin, which is only loosely adherent to its underlying tissue, which contains a cushion of fat. In the eyelids of those of Eastern Asian descent, the orbital septum fuses with the levator aponeurosis below the upper tarsal border, allowing the fat to descend further into the lid¹⁰ and eliminating the superior palpebral sulcus.^{2,11-13}

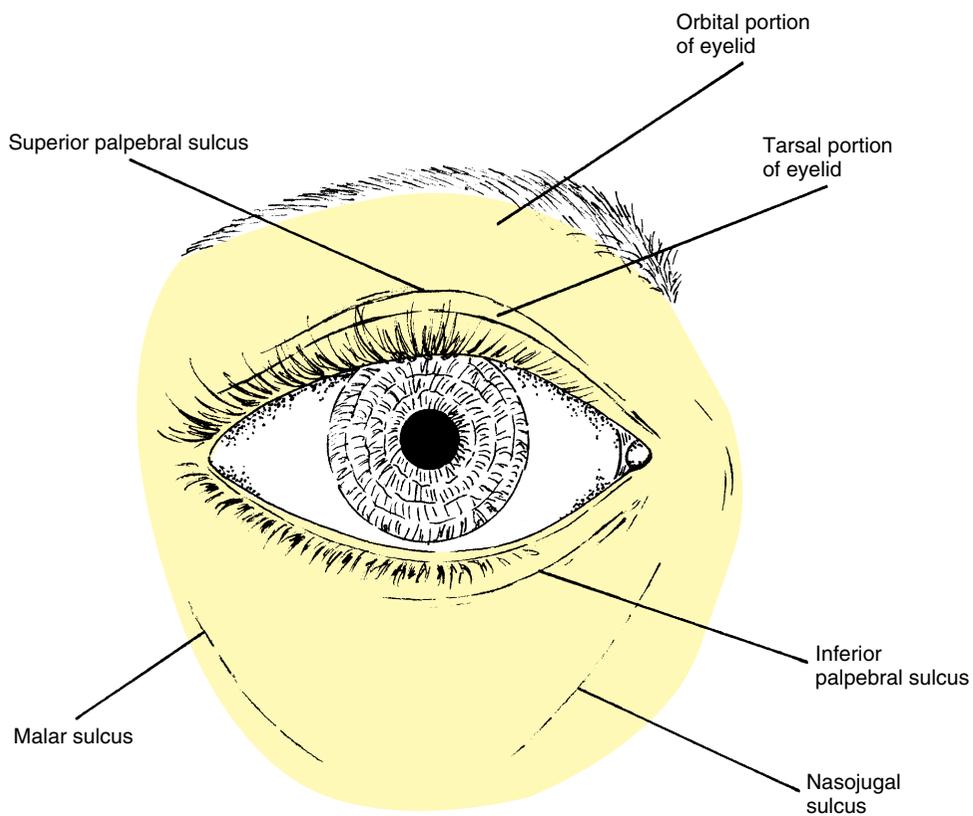
In the lower eyelid the **inferior palpebral sulcus**, which separates the lower lid into tarsal and orbital parts, is often not very distinct. The tarsal portion rests against the globe, and the orbital portion extends from the lower border of the tarsus onto the cheek, extending just past the inferior orbital margin to the nasojugal and malar sulci (see Figure 9-4). These furrows occur at the attachment of the skin to the underlying connective tissue and become more prominent with age.

EYELID MARGIN

The eyelid margin rests against the globe and contains the eyelashes and the pores of the meibomian glands. The **cilia** (eyelashes) are arranged at the lid margin in a double or triple row, with approximately 150 in the upper eyelid and 75 in the lower lid.¹⁴ The lashes curl upward on the upper and downward on the lower lid. Replacement lashes grow to full size in approximately

**FIGURE 9-3**

Structures located in left medial canthus.

**FIGURE 9-4**

Surface anatomy of the right eyelid.

10 weeks, and each lash is replaced approximately every 5 months.⁹ The eyelashes are richly supplied with nerves, causing them to be sensitive to even the slightest unexpected touch, which will elicit a protective response—a blink.

CLINICAL COMMENT: ABNORMALITIES AFFECTING THE CILIA

Various epithelial diseases can cause madarosis (loss of eyelashes) or trichiasis (misdirected growth of eyelashes), in which the eyelashes grow toward rather than away from the palpebral fissure. Contact with the cornea can cause irritation and painful abrasions and can lead to ulceration.⁴ The problem lashes can be removed by epilation.

The pores of the meibomian glands are located posterior to the cilia (see Figure 9-3), and the transition from skin to conjunctiva, the *muco-cutaneous junction*, occurs just posterior to these openings.¹⁵ A groove called the *gray line* runs along the eyelid margin between the cilia insertions and the pores of the meibomian glands. This groove is the location of a surgical plane that divides the lid into anterior and posterior portions.²

The eyelid margin can be divided into two parts: the medial one sixth is the *lacrimal portion*, and the lateral five sixths is the *ciliary portion*. The division occurs at the *lacrimal papilla*, a small elevation containing the *lacrimal punctum*, the opening that carries the tears into the nasolacrimal drainage system (see Figure 9-3). Usually, no cilia or meibomian pores are found medial to the punctum, in the lacrimal portion of the lid margin.

CLINICAL COMMENT: EPICANTHUS

Epicanthus is a vertical fold of skin at the nasal canthus, arising in the medial area of the upper eyelid and terminating in the nasal canthal area. It is common in the newborn and may cause the appearance of esotropia (Figure 9-5). A parent of an infant with epicanthus might worry that the child's eyes are crossed; however, a cover test will identify a true esotropia. As the bridge of the nose develops, epicanthus gradually disappears. A form of epicanthus arising from the tarsal fold and extending into the medial canthal area is common in those of Eastern Asian descent.²

EYELID STRUCTURES

Orbicularis Oculi Muscle

The striated fibers of the **orbicularis oculi** muscle are located below the subcutaneous connective tissue layer and encircle the palpebral fissure from the eyelid margin to overlap onto the orbital margin. The muscle can be divided into two regions, palpebral and orbital.



FIGURE 9-5

Epicanthal fold may give rise to pseudoesotropia. (From Kanski JJ, Nischal KK: *Ophthalmology: clinical signs and differential diagnosis*, St Louis, 1999, Mosby.)

Palpebral Portion. The palpebral portion of the orbicularis oculi muscle occupies the area of the eyelid that rests on the globe and is closest to the eyelid margin. It sometimes is divided further into pretarsal and preseptal parts. The palpebral portion is composed of semicircles of muscle fibers that run from the medial orbital margin and the medial palpebral ligament¹⁶ to the lateral palpebral raphe, where the superior and inferior fibers interdigitate with one another (see Figure 9-1). The lateral palpebral raphe overlies the lateral palpebral ligament.

Some fibers arise from deeper attachments on the posterior lacrimal crest. This section of the palpebral part of the orbicularis, the **muscle of Horner** or **lacrimal part (pars lacrimalis)**, encircles the lacrimal canaliculi.^{9,11,16,17} Contraction of the orbicularis assists in moving tears through the canaliculi into the nasolacrimal drainage system.¹⁸ Another section of the palpebral orbicularis, the **muscle of Riolan** or **ciliary part (pars ciliaris)**, lies near the lid margin on both sides of the meibomian gland openings; it maintains the lid margins close to the globe.¹⁹

CLINICAL COMMENT: ECTROPION AND ENTROPION

*Eversion of the eyelid margin is called **ectropion** (Figure 9-6), the common cause of which is loss of muscle tone, a normal part of the aging process. As the lid margin falls away from its position against the globe, the lacrimal punctum is no longer in position to drain the tears from the lacrimal lake. Epiphora, an overflow of tears onto the cheek, may occur, causing maceration of the delicate skin in this area.*

Continued

**FIGURE 9-6**

Severe involuntional (senile) ectropion. (From Kanski JJ: *Clinical ophthalmology: a systematic approach*, ed 5, Oxford, England, 2003, Butterworth-Heinemann.)

*Inversion of the lid margin is called **entropion** and may result from spasm of the orbicularis oculi muscle that causes the lid margin to turn inward (Figure 9-7). This inward turning puts the eyelashes in contact with the globe and, unless relieved, can cause corneal abrasion. Scarring of the lid after trauma or disease may also cause entropion. Both ectropion and entropion are more common in the lower lid and can be corrected surgically, if necessary. The anatomic relationship of the muscular and connective tissue components is an important consideration when repair is done.²⁰⁻²²*

Orbital Portion. The orbital portion of the orbicularis oculi muscle is attached superiorly to the orbital margin, medial to the supraorbital notch. The fibers encircle the area outer to the palpebral portion and attach inferiorly to the orbital margin, medial to the infraorbital foramen.² These concentric circular fibers extend throughout the rest of the lid and over the orbital rim.

Orbicularis Action. The orbicularis oculi muscle is innervated by cranial nerve VII (the facial nerve). Contraction of the palpebral portion closes the eyelid gently, and the palpebral orbicularis is the muscle of action in an involuntary blink and a voluntary wink; relaxation of the levator muscle follows.²³ Spontaneous involuntary blinking renews the precorneal tear film. A reflex blink is protective and may be elicited by a number of stimuli—a loud noise; corneal, conjunctival, or ciliary touch; or the sudden approach of an object. When the orbital portion of the orbicularis contracts, the eye is closed tightly, and the areas surrounding the

**FIGURE 9-7**

Involuntional (senile) entropion. (From Kanski JJ: *Clinical ophthalmology: a systematic approach*, ed 5, Oxford, England, 2003, Butterworth-Heinemann.)

lids—the forehead, temple, and cheek—are involved in the contraction. Such eyelid closure is often a protective mechanism against ocular pain or after injury and is called *reflex blepharospasm*. If the lids are closed tightly in a strong contraction, forces compressing the orbital contents can significantly increase the intraocular pressure.²⁴

The antagonist to the palpebral portion of the orbicularis is the levator muscle. The antagonist to the orbital portion is the frontalis muscle.

Superior Palpebral Levator Muscle

The superior palpebral levator muscle, the retractor of the upper eyelid, is located within the orbit above the globe and extends into the upper lid. It originates on the lesser wing of the sphenoid bone above and in front of the optic foramen, and its sheath blends with the sheath of the superior rectus muscle. As the levator approaches the eyelid from its posterior origin at the orbital apex, a ligament, the **superior transverse ligament (Whitnall's ligament)** may act as a fulcrum, changing the anteroposterior direction of the levator to superoinferior.^{10,12,25-28} (Figure 9-8).

Levator Aponeurosis. As it enters the eyelid the levator becomes a fan-shaped tendinous expansion, the **levator aponeurosis**. Unlike a typical tendon, the aponeurosis spreads out into an extensive sheet posterior to the orbital septum. The fibers of the aponeurosis penetrate the orbital septum and extend into the upper lid, fanning out across its entire width. These tendinous fibers pass through the submuscular connective tissue; the posterior fibers insert into the lower anterior surface

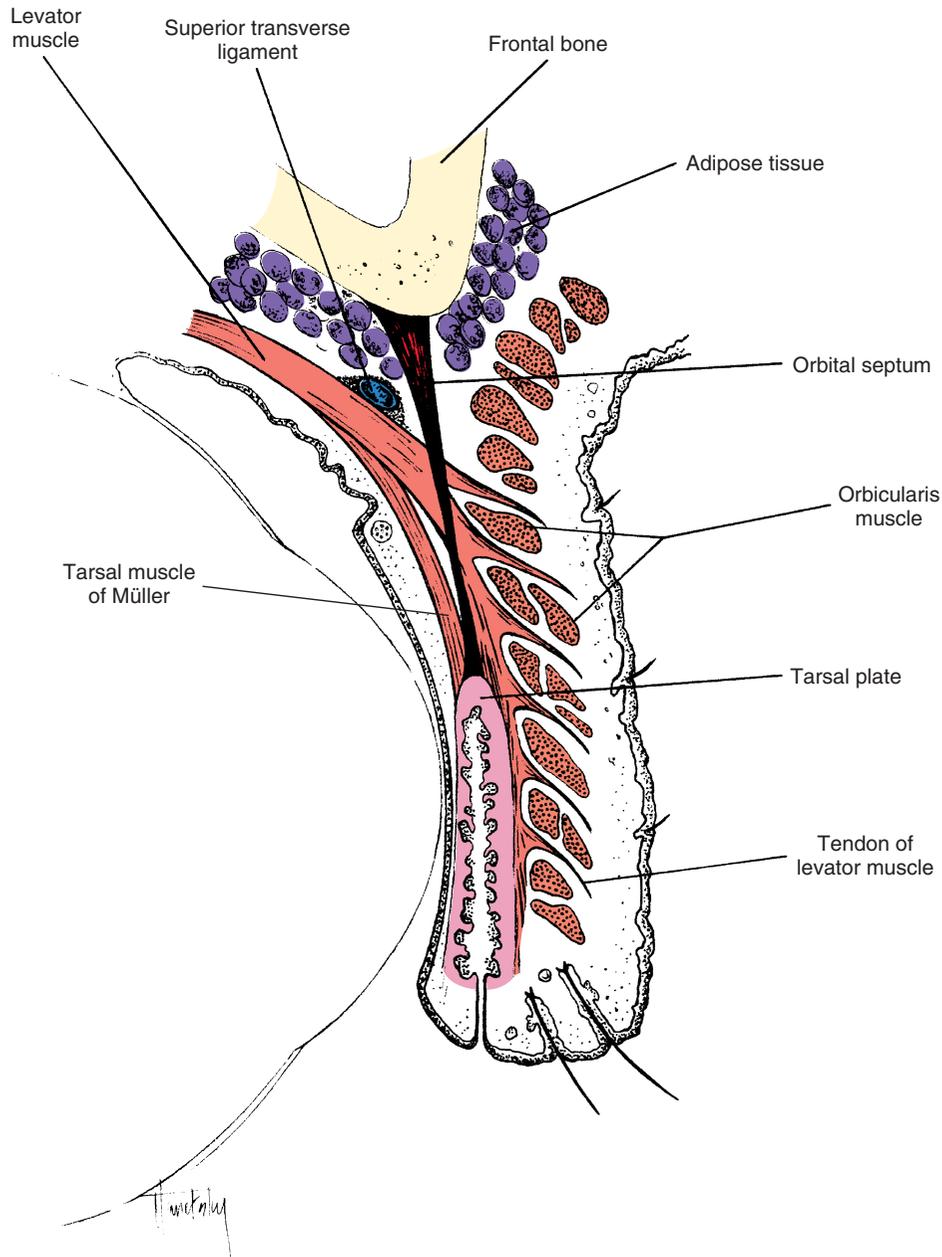
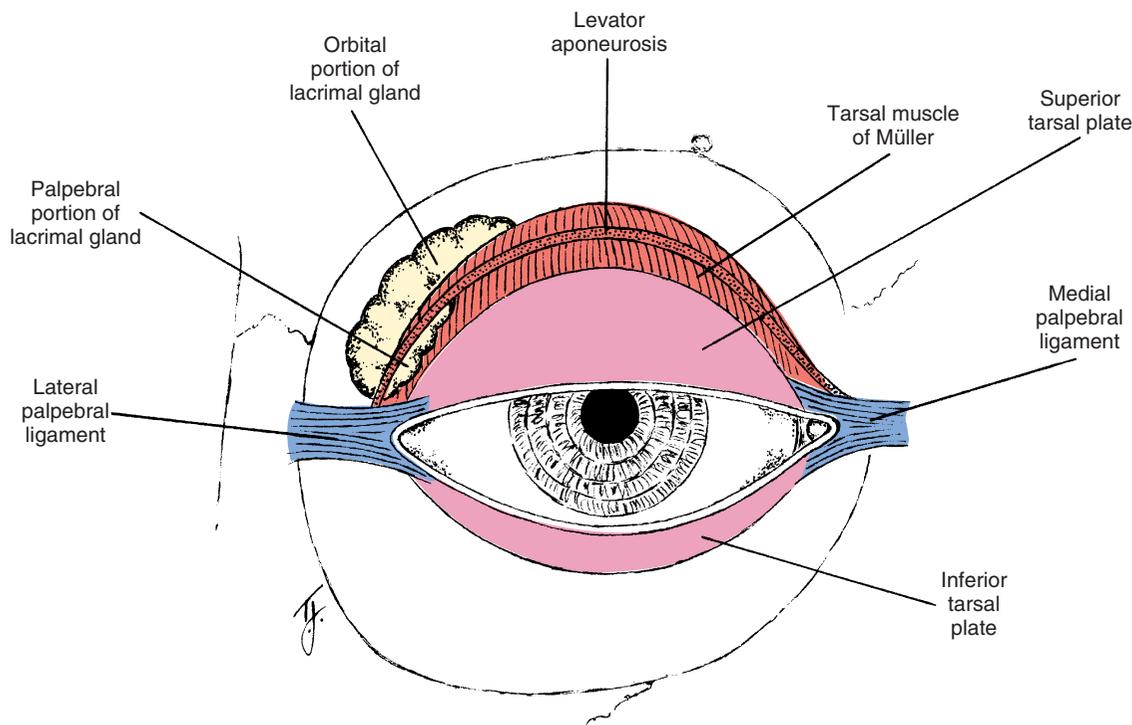


FIGURE 9-8
Sagittal section of upper eyelid.

of the tarsal plate, and the anterior fibers run between the muscle bundles of the orbicularis to insert primarily into the skin of the eyelid, although some insert into the intermuscular septa of the orbicularis^{9,11,25-28} (see Figure 9-8). This attachment of the fibers from the levator aponeurosis anchors the skin to the underlying tissues in the pretarsal area of the eyelid and creates the palpebral sulcus. In those of Eastern Asian descent the orbital septum attaches to the tarsal plate more inferiorly, and the aponeurotic fibers do not attach as extensively to the cutaneous tissue.^{2,11}

The two side extensions of the aponeurosis are referred to as **horns**. The lateral horn helps to support the lacrimal gland by holding it against the orbital roof, dividing the gland into orbital and palpebral lobes (Figure 9-9). The lateral horn then attaches to the lateral palpebral ligament and lateral orbital tubercle. The medial horn is attached to the medial palpebral ligament and medial orbital rim.

Levator Action. Contraction of the levator muscle causes elevation of the eyelid. The connection between

**FIGURE 9-9**

Orbital area viewed from in front, with skin, subcutaneous tissue, and orbital septum removed.

the sheath of the levator and sheath of the superior rectus coordinates eyelid position with eye position so that as the eye is elevated, the lid is raised.^{27,28} The levator is innervated by the superior division of the oculomotor nerve, cranial nerve III.

The eyelids are closed by relaxation of the levator and contraction of the orbicularis oculi muscles. The tonic activity of the levator and the relaxation of the orbicularis holds the eyelid open. In a blink, tonic activity of the levator is suspended, and with a burst of activity the orbicularis rapidly lowers the lid, followed by a cessation of orbicularis activity and resumption of levator tonicity.²⁹

Retractor of Lower Eyelid

The retractor of the lower lid is the **capsulopalpebral fascia (lower eyelid aponeurosis)**.^{2,10} The capsulopalpebral fascia, an anterior extension from the sheath of the inferior rectus muscle and the suspensory ligament, inserts into the inferior edge of the tarsal plate.^{11,27,28} This insertion coordinates lid position with globe movement. The lower eyelid is depressed on globe depression, and the lower eyelid elevates slightly on upward movement of the globe.⁸ The capsulopalpebral

fascia also fuses with the orbital septum and sends some fibers to insert into the inferior fornix.^{2,21,28}

Tarsal Muscle (of Müller)

The **superior tarsal muscle (muscle of Müller)** is composed of smooth muscle and originates on the posteroinferior aspect of the levator muscle. These smooth muscle fibers begin to appear within the striated muscle at the point at which the muscle becomes aponeurotic.^{2,9,27,28} The superior tarsal muscle inserts on the superior edge of the tarsal plate (see Figures 9-8 and 9-9).

Contraction of Müller's muscle can provide 2 mm of additional lid elevation.¹⁰ A similar smooth muscle, the **inferior tarsal muscle**, is found in the lower eyelid. It arises from the inferior rectus muscle sheath and inserts into the lower conjunctiva and lower border of the tarsal plate.^{2,9,24} Investigators disagree about whether the inferior tarsal muscle actually inserts into the tarsal plate^{2,9,27} or inserts into the tissue below the tarsal plate.³⁰ Both tarsal muscles are innervated by sympathetic fibers that widen the palpebral fissure when activated (as in situations associated with fear or surprise).^{9,28}

CLINICAL COMMENT: PTOSIS

Ptosis is a condition in which the upper eyelid droops or sags. It can be caused by weakness or paralysis of the levator or Müller's muscle. If Müller's muscle alone is affected, a less noticeable form of ptosis occurs than when the levator is involved.³¹ An individual with ptosis might attempt to raise the lid by using the frontalis muscle, which results in elevation of the eyebrow and wrinkling of the forehead (Figure 9-10).

Tarsal Plate

Each eyelid contains a **tarsal plate (tarsus)** that gives the lid rigidity and structure and shapes it to the curvature of the globe. The tarsal plate in the upper lid is approximately 11 mm high, and the inferior tarsal plate is approximately 5 mm high.⁹ The anterior surface is adjacent to the submuscular connective tissue. The posterior surface is adherent to the palpebral conjunctiva. The orbital border of the tarsus is attached to the orbital septum, whereas the marginal border lies at the lid margin. The sides of the tarsal plates are attached to the bony orbital margin by the palpebral or tarsal ligaments (see Figure 9-9).

CLINICAL COMMENT: EYELID EVERSION

When attempting to evert the upper lid, one should place the cotton-tipped applicator or fingertip above the superior edge of the tarsal plate. The novice will experience difficulty in everting the eyelid if the applicator is placed in the middle of the tarsal plate.



FIGURE 9-10

Unilateral ptosis. Note elevation of brow. (From Kanski JJ, Nischal KK: *Ophthalmology: clinical signs and differential diagnosis*, St Louis, 1999, Mosby.)

Palpebral Ligaments

The palpebral or tarsal ligaments are bands of dense connective tissue connecting the tarsal plates to the orbital rim and holding the tarsal plates in position against the globe during eye and lid movements. The **medial palpebral ligament** runs from the medial edge of each tarsal plate to the medial orbital rim, where it divides into two limbs. One limb attaches to the posterior lacrimal crest and the other to the anterior lacrimal crest. Both limbs lie *anterior* to the orbital septum³² (see Figure 8-18).

The **lateral palpebral ligament** is located *posterior* to the orbital septum and attaches the lateral edges of the tarsal plates to the lateral orbital margin at the lateral orbital tubercle³³ (see Figure 8-18). Fibrous connections between the lateral palpebral ligament and the check ligament for the lateral rectus muscle allow a slight lateral displacement of the lateral canthus with extreme abduction.³⁴

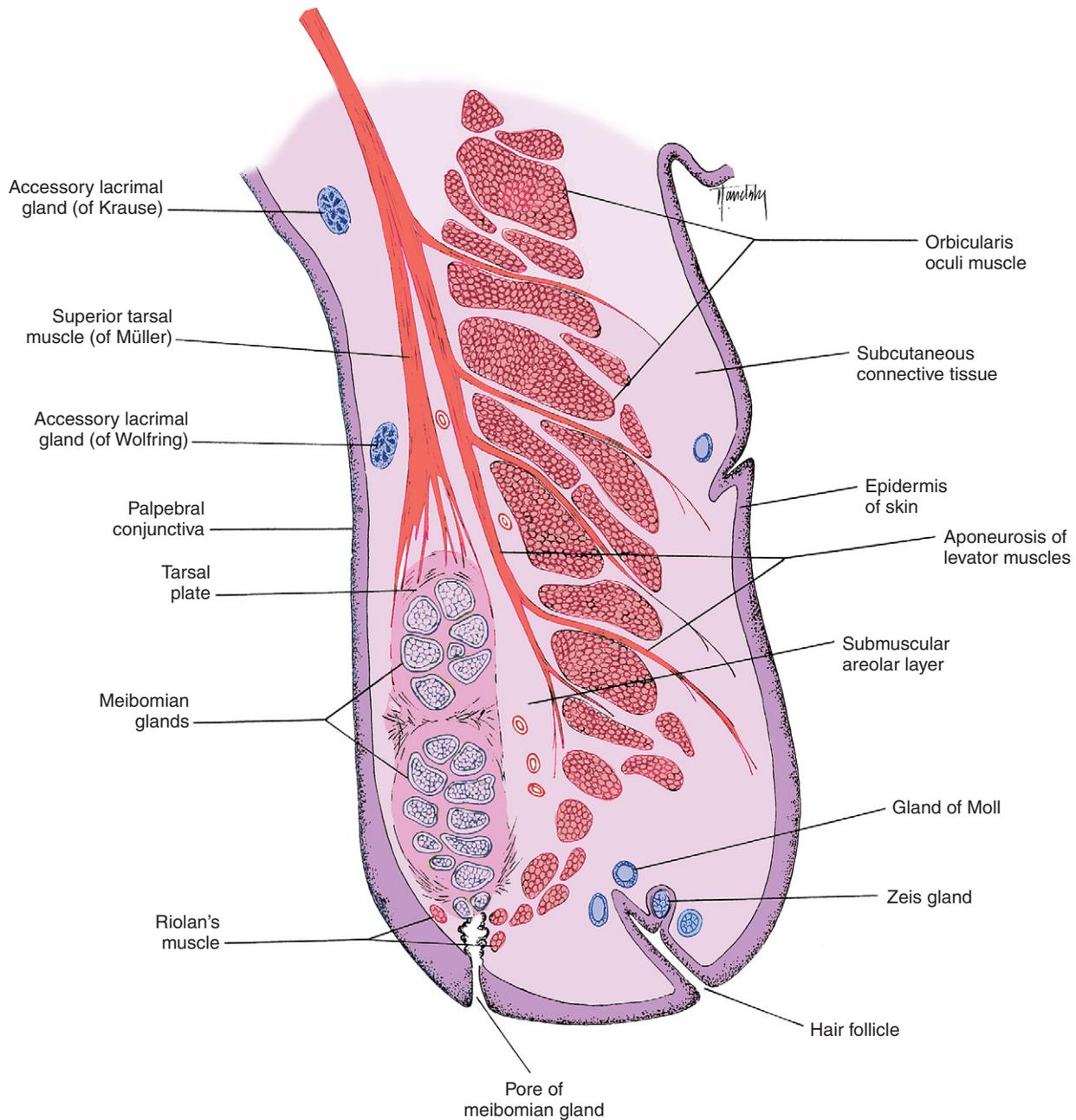
The upper borders of both the medial and the lateral ligaments are joined to the expansion of the levator tendon, and their lower borders are joined to an expansion of the ligament of Lockwood.⁹ The connective tissue structures at the canthi have been described as a retinaculum that is made up of the palpebral ligaments, the horns of the levator aponeurosis, the suspensory ligament, the check ligaments, and the superior transverse ligament.²

Glands of the Lids

The **meibomian glands (tarsal glands)** are sebaceous glands embedded in the tarsal plate. These long, multilobed glands resemble a large bunch of grapes and are arranged vertically such that their openings are located in a row along the lid margin posterior to the cilia (Figure 9-11). Approximately 30 to 40 meibomian glands are found in the upper lid and 20 to 30 in the lower lid.¹⁴ On eyelid eversion the vertical rows of the meibomian glands can sometimes be seen as yellow streaks through the palpebral conjunctiva. These glands secrete the outer lipid layer of the tear film.

The **sebaceous glands of Zeis** secrete sebum into the hair follicle of the cilia, coating the eyelash shaft to keep it from becoming brittle.⁹

The **glands of Moll** are modified sweat glands located near the lid margin. Their ducts empty into the hair follicle, into the Zeis gland duct, or directly onto the lid margin. Similar glands found in the axillae are scent organs, but the purpose of the Moll glands in the eyelid is unclear.^{9,14} Histochemical studies have identified markers for substances in Moll glands that suggest a role in immune defense.³⁵

**FIGURE 9-11**

Sagittal section of eyelid, illustrating palpebral muscles and glands.

The **accessory lacrimal glands of Krause** are located in the stroma of the conjunctival fornix, and the **accessory lacrimal glands of Wolfring** are located along the orbital border of the tarsal plate^{2,9} (see Figure 9-11). These glands are oval and display numerous acini. In the upper fornix, 20 to 40 glands of Krause are found, although only six to eight such glands appear in the lower fornix.² The glands of Wolfring are less numerous. The secretion of the accessory lacrimal glands appears

similar to that of the main lacrimal gland and contributes to the aqueous layer of the tear film.

HISTOLOGIC FEATURES

Skin

The skin of the eyelid contains many fine hairs, sebaceous glands, and sweat glands. It is the thinnest

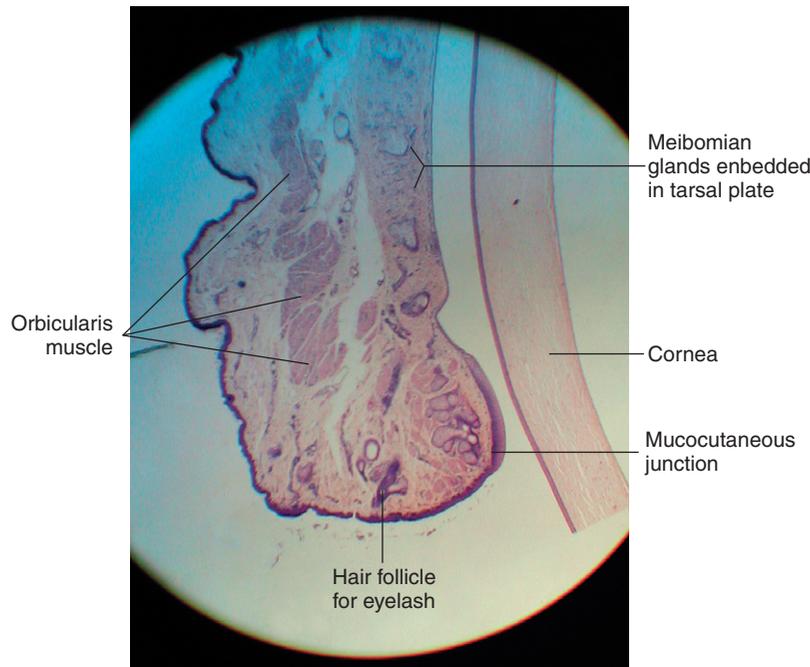


FIGURE 9-12
Light micrograph of upper lid and cornea section.

skin in the body, easily forms folds and wrinkles, and is almost transparent in the very young.² The epidermal layer consists of a basal germinal layer, a granular layer, and a superficial layer that is cornified. The underlying dermis is abundant in elastic fibers. A very sparse areolar connective tissue layer, the **subcutaneous tissue**, lies below the dermis. This thin layer is devoid of adipose tissue in the tarsal portion. A pad of fat often is located in this region in the orbital portion that separates the orbicularis from the skin.⁹

CLINICAL COMMENT: FLUID ACCUMULATION

The loose connective tissue layer of the eyelid can be separated easily from the underlying tissue and is the site of accumulation of blood or edema in injuries or accumulation of exudates in inflammatory conditions. The thinness of the skin and the fine underlying adjacent tissue allow this area to be greatly distensible, as evidenced in patients with periorbital cellulitis or ecchymosis (a black eye). This skin recovers rapidly after distention because of the elasticity of the dermis. With advancing age, however, the skin loses its elasticity, and stretching will cause exaggerated skin folds.

Muscles

The **orbicularis oculi** lies deep to the subcutaneous layer. These striated muscle bundles run throughout the

eyelid. In a sagittal section of the lid prepared for microscopic examination, the orbicularis bundles are cut in cross section (Figure 9-12). Along the lid margin, small muscle bundles located on both sides of the meibomian gland represent a specific part of the orbicularis, the **ciliary part (Riolan's muscle)**, which holds the lid margin against the globe (see Figure 9-11).

Posterior to the orbicularis lies another layer of loose connective tissue, the **submuscular areolar layer**, which separates the muscle from the tarsal plate. Between this layer and the tarsal plate is a potential space, the pretarsal space, that contains the vessels of the palpebral arcades. The preseptal space is located between the orbicularis and the orbital septum; directly above is the preseptal cushion of fat.⁹

Tendinous fibers of the **levator aponeurosis** run through the submuscular tissue layer between the orbicularis and the superior tarsal muscle to insert into the tarsal plate and the skin of the lid (see Figure 9-11). It is this insertion of fibers that anchors the skin so firmly in the tarsal portion of the lid. There is no such attachment of the aponeurosis in the preseptal area. The smooth muscle fibers of the **superior tarsal muscle** are located above the superior tarsal plate and insert into its upper edge. Both the aponeurosis and the superior tarsal muscle are cut longitudinally in a microscope slide of a sagittal section of the lid.



FIGURE 9-13
Light micrograph of conjunctival epithelium showing goblet cells.

Tarsal Plates

The **tarsal plates** are composed of dense connective tissue. The collagen fibrils of this tissue are of uniform size and run both vertically and horizontally to surround the meibomian glands.

Palpebral Conjunctiva

The **palpebral conjunctiva** is composed of two layers, a stratified **epithelial layer** and a connective tissue stromal layer, the **submucosa**. The epithelial layer of the conjunctiva is continuous with the skin epithelium at the mucocutaneous junction of the lid margin (see Figure 9-12). As the conjunctiva lines the lid, squamous cells are replaced by cuboidal and columnar cells, forming a stratified columnar mucoepithelial layer, the granular and keratinized layers having been discontinued.^{14,36} At the **mucocutaneous junction**, the epithelial layer is approximately five cells thick and is the location of stem cells that repopulate the palpebral conjunctival epithelium.³⁷ Over much of the upper lid

the conjunctival epithelium is two or three cells thick, whereas over much of the lower lid, the epithelium is three or four cells thick.⁹ This stratified columnar epithelium continues throughout the fornices into the bulbar conjunctiva, where it changes to a stratified squamous layer near the limbus, becoming continuous with the corneal epithelium.

Goblet cells, which produce the innermost mucous layer of the tear film, are scattered throughout the stratified columnar conjunctival epithelium (Figure 9-13). These cells are most numerous in the inferior nasal aspect of the tarsal conjunctiva.³⁸ Their number decreases with advancing age and increases in inflammatory conditions. A goblet cell produces mucin droplets that accumulate, causing the cell to swell and become goblet shaped. The surface of the cell finally ruptures, releasing mucus. Parasympathetic and sympathetic nerves have been associated with goblet cells and may play a role in their secretion.³⁹ Invaginations of conjunctival epithelium, often located near the fornix, are called **crypts of Henle**. Goblet cells release their mucus into the cavity formed by these invaginations, and the mucus may become

trapped if the opening to the crypt is narrow. This accumulation of mucoid material may account for the application of the misnomer “glands” of Henle to describe these structures.

CLINICAL COMMENT: VITAMIN A DEFICIENCY

Vitamin A deficiency has been associated with a loss of goblet cells and keratinization of the epithelium. In dry-eye disorders showing a decrease in the number of goblet cells, treatment with vitamin A therapy can induce the reappearance of goblet cells.⁴⁰

The **submucosa (stroma, substantia propria)** of the **palpebral conjunctiva** is very thin in the tarsal portion of the eyelid but becomes increasingly thick in the orbital portion. It is composed of loose, vascularized connective tissue that can be subdivided into an outer lymphoid layer and a deep fibrous layer. In addition to the normal connective tissue components (collagen fibrils, fibroblasts, ground substance, and a few fine elastic fibers), the lymphoid layer contains macrophages, mast cells, polymorphonuclear leukocytes, eosinophils, and accumulations of lymphocytes. Immunoglobulin A (IgA) is found in the lymphoid layer, making the conjunctiva an immunologically active tissue.⁴¹⁻⁴³

The deep fibrous layer connects the conjunctiva to underlying structures and contains a random network

of collagen fibrils and numerous fibroblasts, blood vessels, nerves, and accessory lacrimal glands. This fibrous layer merges and is continuous with the dense connective tissue of the tarsal plate. The conjunctiva is so richly supplied with blood vessels that a pale palpebral conjunctiva may be a clinical sign of anemia.

CLINICAL COMMENT: CONJUNCTIVAL CYSTS AND CONCRETIONS

*Clear **conjunctival cysts**, either intraepithelial or subepithelial, are filled with mucoid material and are found most often in the palpebral conjunctiva.⁴⁴ **Conjunctival concretions** are small, yellow-white nodules about the size of a pinhead and most often located in the tarsal conjunctiva. They are composed of finely granular material and membranous debris, products of cellular degeneration. These nodules are hard but contain no calcific deposits.⁴⁵ Concretions are found more often in elderly patients and can be removed if they produce foreign body irritation.⁴³*

Glands

The **meibomian glands** are large sebaceous glands occupying the length of the tarsal plate. Each consists of 10 to 15 lobes or acini attached to a large central duct.^{46,47} The duct is arranged vertically such that the opening is located at the edge of the tarsal plate corresponding to the eyelid margin (Figure 9-14).



FIGURE 9-14

Light micrograph of meibomian glands embedded in tarsal plate. Duct and pore are shown.



FIGURE 9-15

Light micrograph of lid margin. Zeis gland is located next to hair follicle; duct is evident.

Meibomian glands are *holocrine* glands; their secretion is produced by the decomposition of the entire cell. Each acinus is surrounded by a layer of myoepithelial cells and is filled with actively dividing cells. These cells become large and polyhedral and are filled with sebaceous granules. As each cell degenerates, the nucleus begins to diminish in size, and the cell wall disintegrates. Cells in varying stages of decomposition pack each sacculus. Decomposed cells move down the duct to the opening, at which point the secretion forms the outermost lipid layer of the tear film.^{15,46,47} The predominant innervation of meibomian glands is parasympathetic.⁴⁸

Histologically, the sebaceous **Zeis glands** are similar to the meibomian glands. The Zeis glands, however, are composed of just one or two acini and are associated with the eyelash follicle (Figure 9-15). Generally, two Zeis glands are present per follicle. They release sebum into the follicle, thereby preventing the cilia from becoming dry and brittle.⁴⁶

Glands of Moll are modified sweat glands and also are located near the eyelash follicle. They consist of a

spiral that begins as a large cavity, the neck of which becomes narrow as it forms a duct. The large lumen often appears empty and is surrounded by a layer of cuboidal to columnar secretory cells (Figure 9-16).⁴⁶ Myoepithelial cells surround these cells. The Moll gland is an *apocrine* gland; its secretion is composed not of the whole cell but of parts of the cellular cytoplasm. The duct might empty into the duct of a Zeis gland, or it might open directly onto the lid margin between cilia.³⁵

Accessory lacrimal glands are groups of secretory cells with a truncated-pyramid shape arranged in an oval pattern around a central lumen³⁶ (Figure 9-17). The acini are surrounded, sometimes incompletely, by a row of myoepithelial cells.² Animal studies suggest that the ducts of Wolfring glands have a tortuous course and open onto the palpebral conjunctiva.⁴⁹ These are *merocrine* glands—that is, the cell remains intact and secretes a product—and they have the same histologic makeup as the main lacrimal gland.⁴⁹ The accessory lacrimal glands are densely innervated, as is the main lacrimal gland.⁵⁰

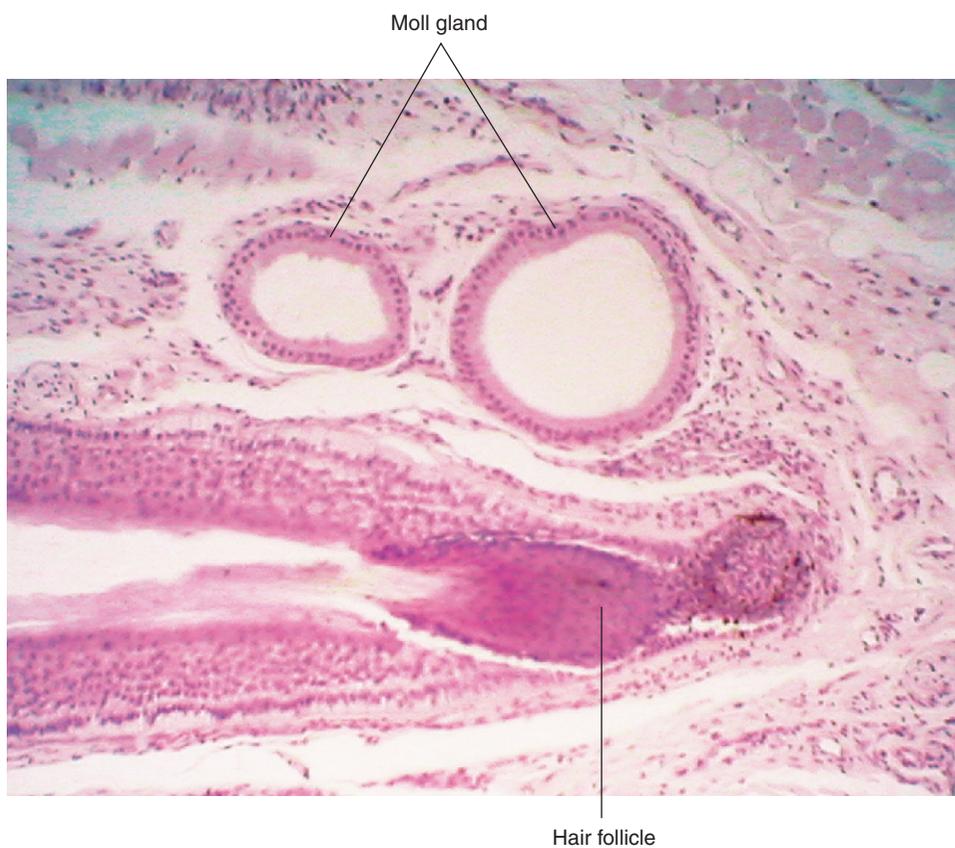


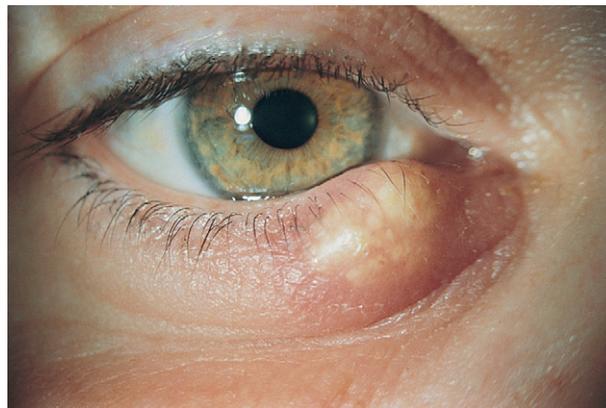
FIGURE 9-16
Light micrograph of hair follicle for cilia. Two Moll glands are seen.



FIGURE 9-17
Light micrograph of lower lid. Accessory lacrimal gland is seen distal to tarsal plate, which has meibomian gland within it.

**FIGURE 9-18**

External hordeolum. (From Kanski JJ: *Clinical ophthalmology: a systematic approach*, ed 5, Oxford, England, 2003, Butterworth-Heinemann.)

**FIGURE 9-19**

Painless chalazion. (From Kanski JJ, Nischal KK: *Ophthalmology: clinical signs and differential diagnosis*, St Louis, 1999, Mosby.)

CLINICAL COMMENT: COMMON EYELID CONDITIONS

A **hordeolum** is an acute inflammation of an eyelid gland, usually caused by staphylococci.⁴ An infected Zeis or Moll gland is called an **external hordeolum**, or **common stye**, and usually comes to a head on the skin of the eyelid (Figure 9-18). A localized infection of a meibomian gland usually drains from the inside surface of the lid and thus is called an **internal hordeolum**. Mild cases usually resolve with hot compress treatment, but more severe cases might require antibiotic treatment.

A **chalazion** is a localized, noninfectious, and sometimes painless swelling of a meibomian gland, often caused by an obstructed duct (Figure 9-19). The gland may extrude its secretion into surrounding tissue, setting up a granulomatous inflammation. Medical or surgical therapy sometimes is necessary.⁵¹

INNERVATION OF EYELIDS

The ophthalmic and maxillary divisions of the trigeminal nerve provide sensory innervation of the eyelids. The upper lid is supplied by the supraorbital, supratrochlear, infratrochlear, and lacrimal nerves, branches of the ophthalmic division. The supply to the lower lid is by the infratrochlear branch of the ophthalmic nerve and the infraorbital nerve, a branch of the maxillary division (Figure 9-20). Motor control of the orbicularis muscle is through the temporal and zygomatic branches of the facial nerve, and that of the levator muscle is through the superior division of the oculomotor nerve. The tarsal smooth muscles are innervated by sympathetic fibers from the superior cervical ganglion.

BLOOD SUPPLY OF EYELIDS

The blood vessels are located in a series of arcades or arches in each eyelid. The marginal palpebral arcade lies near the lid margin, and the peripheral palpebral arcade lies near the orbital edge of the tarsal plate (Figure 9-21). The vessels forming these arcades are branches from the medial and lateral palpebral arteries. The medial and lateral palpebral arteries are branches of the ophthalmic and lacrimal arteries, respectively. Normal variations occur in the blood supply, and the most common variation is a lack of the peripheral arcade in the lower lid.

CONJUNCTIVA

The **conjunctiva** is a thin, translucent mucous membrane that runs from the limbus over the anterior sclera, forms a cul-de-sac at the superior and inferior fornices, and turns anteriorly to line the eyelids. It ensures smooth movement of the eyelids over the globe. The conjunctiva can be divided into three sections that are continuous with one another: (1) the tissue lining the eyelids is the **palpebral conjunctiva**, or **tarsal conjunctiva**; (2) the **bulbar conjunctiva** covers the sclera; and (3) the **conjunctival fornix** is the cul-de-sac connecting palpebral and bulbar sections (Figure 9-22). The *limbus* is the location of stem cells for bulbar conjunctiva and the *mucocutaneous junction* is the site of stem cells for palpebral conjunctiva.⁵²

At the mucocutaneous junction of the lid margin, the nonkeratinized squamous palpebral conjunctival

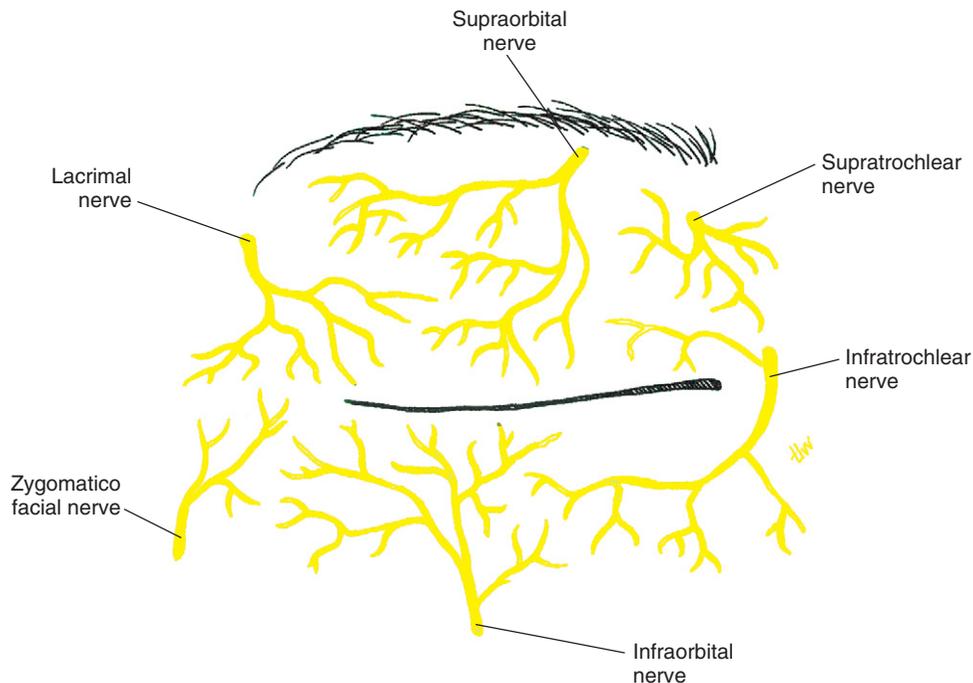


FIGURE 9-20
Palpebral innervation.

epithelium is continuous with the keratinized squamous epithelium of the epidermis of the eyelid. The conjunctiva forming the fornices is attached loosely to the fascial extensions of the levator, tarsal, and extraocular muscles, providing coordination of conjunctival movement with movement of the globe and lids. The fornices are present superiorly, inferiorly, and laterally, easing movement of the globe without creating undue stretching of the conjunctiva. The lateral fornix is the deepest and extends posterior to the equator of the globe.

The bulbar conjunctiva is translucent, allowing the sclera to show through, and is colorless except when its blood vessels are engorged. Bulbar conjunctiva is loosely adherent to the underlying tissue up to within 3 mm of the cornea, where it becomes tightly adherent and merges with the underlying Tenon's capsule and sclera.

HISTOLOGIC FEATURES

The conjunctiva is composed of two layers, a stratified epithelial layer and a connective tissue stromal layer, the submucosa.

Conjunctival Epithelium

At the limbus the stratified squamous conjunctival epithelium is continuous with the corneal epithelium.

The surface of the superficial conjunctival cells and their microvilli and microplicae are covered with a glycocalyx similar to that of the corneal surface.^{53,54} Melanin granules often are found in the cytoplasm of conjunctival epithelial cells, especially near the limbus; these are particularly prevalent in individuals with heavily pigmented skin. Goblet cells, which produce the mucous component of the tear film, also are located in the epithelium.

Subsurface vesicles, found below the outer membrane of the superficial conjunctival cell, may be an additional source of mucous material. As these vesicles fuse with the epithelial cell membrane, chains extend outward and may form a chemical bond with the mucous layer secreted by the goblet cells. These chains increase the adherence of the tear film to the globe. These vesicle membranes may contribute to the microvilli present on the surface epithelial cells.⁵⁵

Conjunctival Submucosa

The **submucosa** underlying the epithelium is a stromal (substantia propria) layer composed of vascularized, loose connective tissue containing the same components as in palpebral conjunctival stroma.

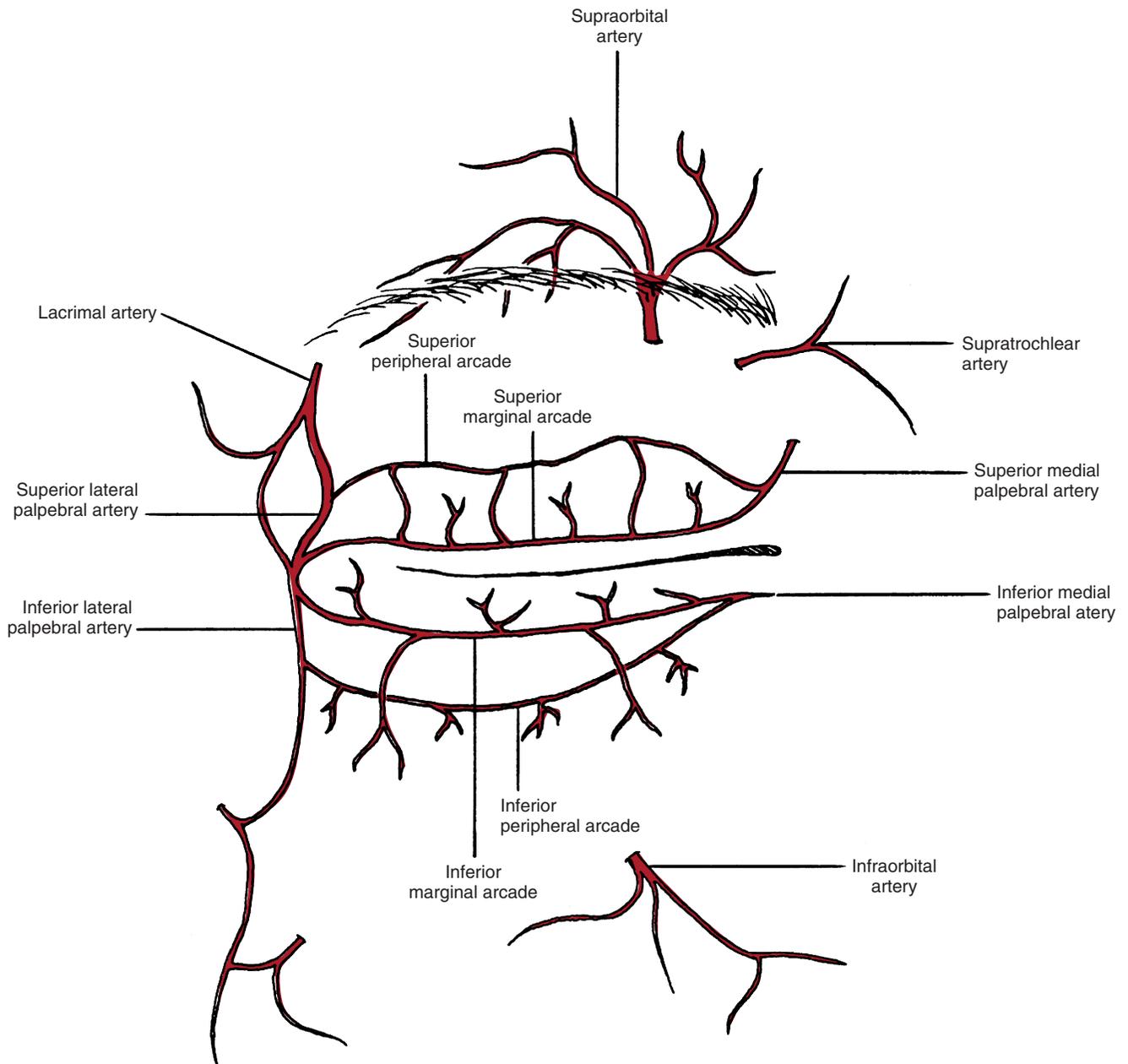


FIGURE 9-21
Palpebral blood supply.

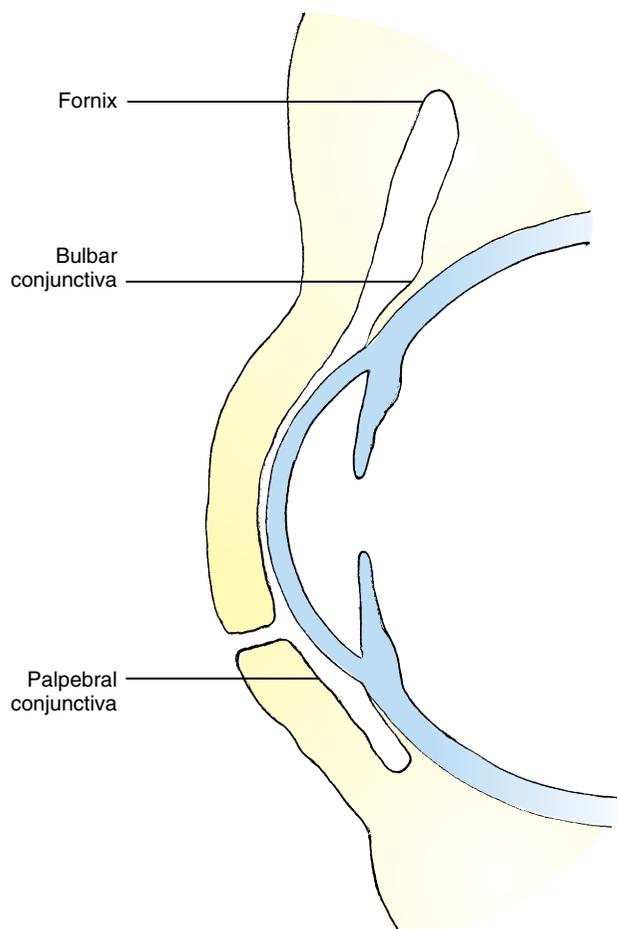


FIGURE 9-22
Three partitions of conjunctiva.

PLICA SEMILUNARIS

The **plica semilunaris** is a crescent-shaped fold of conjunctiva located at the medial canthus (see Figure 9-3). (It might be a remnant of the nictitating membrane seen in lower vertebrates.) The epithelium is 8 to 10 cells thick and contains numerous goblet cells, and the stroma is highly vascularized, containing smooth muscle and adipose tissue.⁵⁶ Because there is no deep fornix at the medial side as there is at the lateral side, the evident function of the plica is to allow full lateral movement of the eye without tissue stretching.

CARUNCLE

The function of the **caruncle**, a mound of tissue that overlies the medial edge of the plica semilunaris (see Figure 9-3), is poorly understood. The caruncle is similar to conjunctiva in that it contains nonkeratinized epithelium and accessory lacrimal glands, but it also has

skin elements: hair follicles and sebaceous and sweat glands.^{56,57} The sebaceous glands are a likely source for the occasional accumulation of matter in the medial canthus of the healthy eye.

CONJUNCTIVAL BLOOD VESSELS

The palpebral conjunctiva receives its blood supply from the palpebral arcades. Branches from the arcades anastomose on both sides of the tarsal plate; vessels from the posterior network supply the palpebral conjunctiva in both upper and lower lids.

The fornices are supplied by branches from the peripheral arcades, which then branch again and enter the bulbar conjunctiva, forming a plexus of vessels, the posterior conjunctival arteries. These anastomose with the plexus of anterior conjunctival arteries formed by branches from the anterior ciliary arteries. Conjunctival veins parallel the arteries but are more numerous. They drain into the palpebral and ophthalmic veins.

CONJUNCTIVAL LYMPHATICS

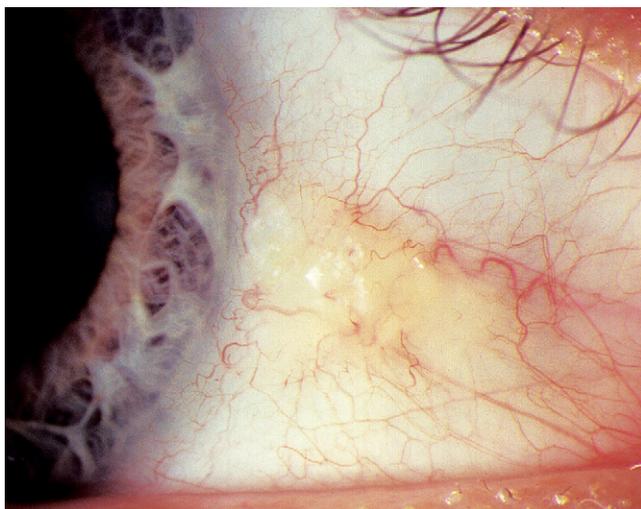
The conjunctival lymphatic vessels are arranged in superficial and deep networks within the submucosa. These vessels drain into the lymphatics of the eyelids; those from the lateral aspect empty into the parotid lymph node, and those from the medial aspect empty into the submandibular lymph node (see Figure 11-13).

CONJUNCTIVAL INNERVATION

Sensory innervation of the bulbar conjunctiva is through the long ciliary nerves. Sensory innervation of the superior palpebral conjunctiva is provided by the frontal and lacrimal branches of the ophthalmic nerve. Innervation of the inferior palpebral conjunctiva is provided by the lacrimal nerve and the infraorbital branch of the maxillary nerve. All sensory information is carried in the trigeminal nerve.

CLINICAL COMMENT: BIOMICROSCOPIC EXAMINATION

The normal bulbar conjunctiva is clear and displays a fine network of blood vessels. The blood flow in an individual vessel can be seen under proper magnification. The conjunctival surface is not as smooth as the cornea, and thus a small amount of fluorescein pooling might be evident in the normal eye. The palpebral conjunctiva is examined by everting the eyelids and should appear bright pink in color. The blood vessel network is evident, and arteries can be seen that run at right angles to the lid margins. The meibomian gland ducts, if seen, will appear as fine yellow lines.

**FIGURE 9-23**

Pinguecula. (From Krachmer JH, Palay DA: *Cornea color atlas*, St Louis, 1995, Mosby.)

**FIGURE 9-24**

Pterygium. (From Krachmer JH, Palay DA: *Cornea color atlas*, St Louis, 1995, Mosby.)

CLINICAL COMMENT: CONJUNCTIVITIS

Conjunctivitis is any inflammation of the conjunctiva and may be caused by a variety of factors. Among the common causative agents are bacterial or viral invasion and allergic reaction. In inflammatory conditions, fluids often accumulate in the loose stromal tissue; this conjunctival edema is called **chemosis**. Dilation and engorgement of the conjunctival blood vessels also occur with inflammation and irritation; this vascular change is known as conjunctival **injection**. Both chemosis and injection are present to varying degrees in diseases and irritations of the conjunctiva. In viral conjunctivitis the preauricular lymph node often is prominent on the involved side.

CLINICAL COMMENT: PINGUECULAE AND PTERYGIA

A **pinguecula** consists of an opaque, slightly elevated mass of modified conjunctival tissue in the interpalpebral area, usually at the 3-o'clock or 9-o'clock position. Pingueculae may vary considerably in size and appearance but usually are round or oval and yellowish (Figure 9-23). Two histologic changes occur in the submucosal layers, whereas the epithelial layers remain unchanged. The first submucosal change is hyalinization, which occurs in a zone just below the epithelium. This zone contains degenerating collagen along with a granular material that probably results from the breakdown of connective tissue components.^{58,59} The second submucosal change in development of pinguecula is the formation of abnormal elastic fibers. Precursors of elastic fibers and abnormally immature forms of newly synthesized elastic fibers are found beneath the zone of hyalinization. These fibers degenerate, and elastic myofibrils are greatly reduced, which prevents normal

assembly of elastic fibers.^{58,59} Fibroblasts in these regions show extensive alteration.

A **pterygium** is a fibrovascular overgrowth of bulbar conjunctiva onto cornea and is usually progressive. As with pinguecula, pterygium occurs in the 3- or 9-o'clock position of the interpalpebral area (Figure 9-24). The triangular pterygium may be gray in appearance, and its apex (often called the head) invades the cornea. This leading edge is composed of a zone of limbal epithelial tissue arising from altered basal stem cells. A zone of cells follows the head, migrating along corneal basement membrane and dissolving Bowman's layer.^{58,60} Fibrovascular tissue with the same abnormal characteristics seen in pingueculae underlie the epithelium of a pterygium.⁶⁰⁻⁶² An extensive network of blood vessels is evident.⁵⁸

Pingueculae and pterygia show many of the same connective tissue changes but are different diseases. If mutational changes occur in the limbal epithelium at the corneal edge of a pinguecula, it may become a pterygium.⁶² Exposure to irritants such as wind and dust might initiate hyperplasia and may be a precursor of both these degenerative changes. Molecular damage produced by chronic solar radiation, particularly high-energy ultraviolet rays, is the primary causal factor in pterygium, with irritants being predisposing factors.^{60,63-65}

Pingueculae rarely are treated unless inflamed. Pterygia are surgically removed (1) when the apex approaches the visual axis, (2) if significant corneal astigmatism is induced, or (3) for cosmetic concerns. Complete removal is difficult because the altered cells appear as normal cornea, and the abnormal cell can only be discerned histologically.⁶¹ Thus, pterygia often recur. Patients with either condition should be advised of the relationship of these conditions to irritants and sun exposure, and ultraviolet-filtering protective lenses should be prescribed, as well as artificial tears and ocular lubricants as needed.

TENON'S CAPSULE

Below the conjunctival stroma is a thin, fibrous sheet called **Tenon's capsule (fascia bulbi)**. Tenon's capsule serves as a fascial cavity within which the globe can move. It protects and supports the globe and attaches it to the orbital connective tissue.

The collagen fibrils that form Tenon's capsule are arranged in a three-dimensional network of longitudinal, horizontal, and oblique groups.⁶⁶ In young people, Tenon's capsule contains collagen fibrils of uniform shape and diameters of 70 to 110 nm; in older individuals there is greater variation in fibril shape, and diameters vary from 30 to 160 nm.^{66,67} Few fibroblasts and some elastic fibers are present, but in a very small ratio compared with the number of collagen fibrils.⁶⁷

TEAR FILM

The **tear film**, which covers the anterior surface of the globe, has several functions: (1) keeps the surface moist and serves as a lubricant between the globe and eyelids; (2) traps debris and helps remove sloughed epithelial cells and debris; (3) is the primary source of atmospheric oxygen for the cornea; (4) provides a smooth refractive surface necessary for optimum optical function;⁶⁸ (5) contains antibacterial substances (lysozyme, beta-lysin, lactoferrin, IgA) to help protect against infection;⁶⁹ and (6) helps to maintain corneal hydration by changes in tonicity that occur with evaporation.⁷⁰

The tear film is composed of three layers. The outermost is a **lipid layer** containing waxy esters, cholesterol, and free fatty acids, primarily produced by the meibomian glands with a small contribution from the Zeis glands. The lipid layer retards evaporation and provides lubrication for smooth eyelid movement. The middle or **aqueous layer** contains inorganic salts, glucose, urea, enzymes, proteins, glycoproteins, and most of the antibacterial substances.² It is secreted by the main and accessory lacrimal glands. The innermost or **mucous layer** is adsorbed by the glycocalyx of the ocular surface cells and acts as an interface that facilitates adhesion of the aqueous layer of the tears to the ocular surface.^{71,72} It is produced and secreted by the conjunctival goblet cells.

According to some sources, the tear film is 7 to 10 μm thick, with the aqueous layer accounting for 90% of the thickness.^{9,73} However, recent measurements using laser interferometry suggest that the full thickness of the mucous layer was not recognized in the past using conventional measuring methods. The tear layer thickness may actually be in the range of 34 to 45 μm , and the mucous layer might be the thickest.^{74,75}

LACRIMAL SECRETORY SYSTEM

The secretory system includes the main lacrimal gland, the accessory lacrimal glands, meibomian and Zeis glands, and the conjunctival goblet cells. The main **lacrimal gland** is located in a fossa on the temporal side of the orbital plate of the frontal bone, just posterior to the superior orbital margin.

The lacrimal gland is divided into two portions, palpebral and orbital, by the aponeurosis of the levator muscle (see Figure 9-9). The superior orbital portion is larger and almond shaped. The superior surface lies against the periorbita of the lacrimal fossa, the inferior surface rests against the aponeurosis, the medial edge lies against the levator, and the lateral edge lies on the lateral rectus muscle. The palpebral lobe is one-third to one-half the size of the orbital lobe and is subdivided into two or three sections.³⁶ If the upper lid is everted, the lacrimal gland can be seen above the edge of the upper tarsal plate. Ducts from both portions of the gland exit through the palpebral lobe.

The lacrimal gland consists of lobules made up of numerous acini. Each acinus is an irregular arrangement of secretory cells around a central lumen surrounded by an incomplete layer of myoepithelial cells.⁷⁶ (Histologically, the main lacrimal gland is identical to the accessory lacrimal glands.) A network of ducts connects the acini and drains into one of the main excretory ducts. There are approximately 12 of these ducts, which empty into the conjunctival sac in the superior fornix.⁴² The accessory glands are located in the subconjunctival tissue from the fornix area to near the tarsal plate. Basic secretion maintains the normal volume of the aqueous portion of the tears, and reflex secretion increases the volume in response to a stimulus. Both main and accessory glands play a role in basic and reflex secretion.

The lacrimal gland is supplied by the lacrimal artery, a branch of the ophthalmic artery. Sensory innervation is through the lacrimal nerve, a branch of the ophthalmic division of the trigeminal nerve. The gland receives vasomotor sympathetic innervation and secretomotor parasympathetic innervation.⁷⁷ Reflex tearing occurs with stimulation of branches of the ophthalmic nerve or in response to external stimuli, such as intense light; the afferent pathway is through the trigeminal nerve, and the parasympathetic pathway is through the facial nerve.

Disagreement still exists regarding the relative contributions of the main and accessory lacrimal glands. In the traditional view, accessory glands provide basic secretion, and the main lacrimal gland is primarily active during reflex or psychogenic stimulation.⁷⁷ A more recent view holds that all lacrimal glands produce the aqueous layer and that production is stimulus driven, with the rate of production ranging from low levels in sleep to high levels under conditions of stimulation.⁷⁸

CLINICAL COMMENT: TEAR FILM ASSESSMENT

A number of clinical conditions can cause changes in the composition or stability of the tear film. Dry-eye syndrome has complex symptoms that may be caused by a deficiency or alteration of any of the layers of the tear film or by an abnormal interaction between the layers.⁷⁹ Aqueous deficiencies are common, and normal aging can cause a decrease of aqueous tear production. Patients with rheumatoid arthritis often develop Sjögren's syndrome, which includes dry-eye symptoms caused by aqueous layer deficiency and dry-mouth symptoms.^{80,81} Meibomianitis causes abnormalities of the lipid layer that result in evaporation of the tears. Conditions with deficient secretion of mucus are associated with reduced goblet cell populations, such as chemical burns, Stevens-Johnson syndrome, and ocular pemphigoid.^{82,83} Complaints associated with dry eye include scratchy and foreign body sensations.

Various clinical tests are used to assess the extent of tear abnormalities. The Schirmer test is a clinical measure of the adequacy of the aqueous portion of the tears. A special piece of filter paper is inserted over the inferior eyelid margin. Normally the strip should be moistened by at least 5 mm after 5 minutes.^{69,84} This test can be done with or without topical anesthesia; the test without topical anesthesia measures both reflex and basic secretion, and the test with anesthetic measures only basic secretion. The phenol red thread test, which uses a thread treated with a pH indicator, is replacing the Schirmer test in many practices.

In another clinical assessment method, fluorescein dye is instilled into the lower cul-de-sac and spreads throughout the tear film. After a blink the thin lipid upper layer begins to break down, and dry spots appear. The time between the completion of the blink and the first appearance of a dry spot is termed the tear film breakup time (TBUT). Normally the TBUT is greater than 10 seconds and longer than the time between blinks.^{2,83-85} A short TBUT can occur if irregularities or disturbances in the corneal surface prevent complete tear film adherence or if abnormalities exist in the lipid layer.⁸⁶

CLINICAL COMMENT: DRY EYE

Alteration in any of the layers of the tear film or in normal lid anatomy and closure can result in depletion of the tear film. The tear film can be augmented by the application of ocular lubricants, consisting of artificial tears during the day and ointments at night. More serious dry-eye problems can be treated with procedures that decrease tear drainage; punctal plugs are a temporary solution, and electrocautery can produce permanent closure of the punctum. Recent clinical studies suggest that a subclinical inflammatory condition contributing to dry eye may be successfully treated with topical antiinflammatory agents such as cyclosporin A.⁸⁷⁻⁹⁰

TEAR FILM DISTRIBUTION

The lacrimal gland fluid is secreted into the lateral part of the upper fornix and descends across the anterior

surface of the globe. Each blink reforms and maintains the tear film.

At the posterior edge of both upper and lower eyelid margins, there is a meniscus of tear fluid. The meniscus at the lower lid is more easily seen. The upper tear meniscus is continuous with the lower meniscus at the lateral canthus, whereas at the medial canthus the tear menisci lead directly to the puncta and drain into them.⁹¹ The **lacrimal lake**, a tear reservoir, is located in the medial canthus. The plica semilunaris makes up the floor of the lake, and the caruncle is located at its medial side.

NASOLACRIMAL DRAINAGE SYSTEM

Some tear fluid is lost by evaporation and some by reabsorption through conjunctival tissue, but approximately 75% is passed through the nasolacrimal drainage system.⁶⁹ The **nasolacrimal drainage system** consists of the puncta, canaliculi, lacrimal sac, and nasolacrimal duct, which empties into the nasal cavity (Figure 9-25).

Puncta and Canaliculi

A small aperture, the **lacrimal punctum**, is located in a slight tissue elevation, the **lacrimal papilla**, at the junction of the lacrimal and ciliary portions of the eyelid margin. Both upper and lower lids have a punctum. The puncta are turned toward the globe and normally can be seen only if the eyelid edge is everted slightly. Each punctum opens into a tube, the **lacrimal canaliculus**.

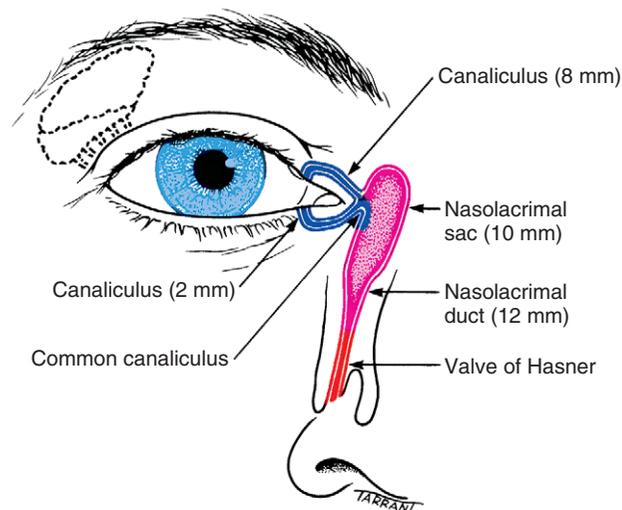


FIGURE 9-25

Anatomy of lacrimal drainage system. (From Kanski JJ: *Clinical ophthalmology*, ed 3, Oxford, England, 1995, Butterworth-Heinemann.)

The canaliculi are tubes in the upper and lower lids that join the puncta to the lacrimal sac. The walls of the canaliculi contain elastic tissue and are surrounded by fibers from the lacrimal portion of the orbicularis muscle (Horner's muscle). The first portion of the canaliculus is vertical and extends approximately 2 mm; a slight dilation, the ampulla, is at the base of this portion of the canaliculus.^{9,14,92} The canaliculus then turns horizontally to run along the lid margin for approximately 8 mm (see Figure 9-25). The canaliculi join to form a single common canaliculus that pierces the periorbita covering the lacrimal sac and enters the lateral aspect of the sac.⁹³ The angle at which the canaliculus enters the sac produces a physiologic valve that prevents reflux.^{2,92-95}

Lacrimal Sac and Nasolacrimal Duct

The **lacrimal sac** lies within a fossa in the anterior portion of the medial orbital wall. This fossa is formed by the frontal process of the maxillary bone and the lacrimal bone. The sac is surrounded by fascia, continuous with the periorbita, which runs from the anterior to the posterior lacrimal crest. The two limbs of the medial palpebral ligament straddle the sac to attach to the posterior and anterior crests.⁹⁶ The orbital septum and the check ligament of the medial rectus muscle lie behind the lacrimal sac (see Figure 8-18).

The lacrimal sac empties into the **nasolacrimal duct** just as it enters the nasolacrimal canal in the maxillary bone. The duct is approximately 15 mm long and terminates in the inferior meatus of the nose. At this point the **valve of Hasner** is found. This fold of mucosal tissue prevents retrograde movement of fluid up the duct from the nasal cavity.^{9,17,92}

TEAR DRAINAGE

During closure the eyelids meet first at the temporal canthus; closure then moves toward the medial canthus, where the tears pool in the lacrimal lake. The tear menisci are pushed toward the lacrimal puncta into which they drain. Theories explaining tear drainage report that the state of the lacrimal sac is either distended or compressed by contraction of the orbicularis muscle. According to Jones and Marquis,⁹⁷ contraction of the lacrimal part of the orbicularis compresses the canaliculi, forcing the tears into the lacrimal sac. Coincidentally, contraction of the muscle pulls on the fascial sheath attached to the lacrimal sac,^{16,97} which causes lateral displacement of the lateral wall, expanding the sac and creating negative pressure within it—in effect, pulling tears in from the canaliculus. On relaxation of the orbicularis, the lacrimal sac collapses, and the tears are driven into the nasolacrimal duct. In addition, the

canaliculi open and act as siphons to pull tears in through the puncta.⁹⁷ The tears drain into the nasolacrimal duct mainly by gravity, where most are absorbed by the mucosal lining before the remaining tears enter the inferior meatus.²

A number of studies, however, have measured an increase in pressure within the lacrimal sac during lid closure.⁹⁸ Using high-speed photography, Doane⁹¹ observed that during eye blink the medial eyelids meet halfway through the blink, occluding the puncta. According to this theory, the canaliculi and lacrimal sac are compressed, forcing all fluids into the nasolacrimal duct. As the eyelids open, compression of the canaliculi decreases, but the puncta remain occluded, creating a negative pressure in the canaliculi. When the puncta finally are opened, the negative pressure pulls the tears in immediately after the blink.^{2,99}

The primary difference in these two theories is the state of the lacrimal sac. In the first scenario the sac is dilated, whereas in the second case the sac is compressed with orbicularis contraction. Capillary attraction plays a role in moving tears into the puncta and down into the canaliculi between blinks.⁶⁹

AGING CHANGES IN ORBITAL ADNEXA AND LACRIMAL SYSTEM

The eyebrow position heightens in both genders with increasing age.⁹⁹

The aging process is apparent in the eyelids as tissue atrophies, the skin loses elasticity, and wrinkles appear. With age the distance between the center of the pupil and the lower eyelid margin increases due to sagging of the lower lid; this change is greater in males than females.⁹⁹ More pronounced changes in lid margin position, including ectropion and entropion (previously described), increase in incidence with changes in the orbicularis muscle tone.

Tearing may be caused by eversion of the lower punctum due to eyelid position or by stenosis of the passages in the lacrimal drainage system; both occur more frequently in elderly persons. The basal rate of tear secretion diminishes after age 40, contributing to dry eye, the incidence of which increases with age.^{100,101} The many causative factors include loss of glandular tissue, and symptoms of dry eye can be mild or severe.

REFERENCES

1. McCord CD, Doxanas MT: Browplasty and bropepsy: an adjunct to blepharoplasty, *Plast Reconstr Surg* 86(2):248, 1990.
2. Doxanas MT, Anderson RL: *Clinical orbital anatomy*, Baltimore, 1984, Williams & Wilkins, p 89.

3. Tarbet KJ, Lemke BN: Clinical anatomy of the upper face, *Int Ophthalmol Clin* 37(3):11, 1999.
4. Bartlett JD, Jaanus SD: *Clinical ocular pharmacology*, ed 3, Boston, 1995, Butterworth-Heinemann, p 583.
5. Katz J, Kaufman HE: Corneal exposure during sleep (nocturnal lagophthalmos), *Arch Ophthalmol* 95:449, 1977.
6. Sturrock GD: Nocturnal lagophthalmos and recurrent erosion, *Br J Ophthalmol* 60:97, 1976.
7. Jelks GW, Jelks EB: The influence of orbital and eyelid anatomy on the palpebral aperture, *Clin Plast Surg* 18(1):183, 1991.
8. Fox SA: The palpebral fissure, *Am J Ophthalmol* 62:73, 1966.
9. Warwick R: *Eugene Wolff's anatomy of the eye and orbit*, ed 7, Philadelphia, 1976, Saunders, p 181.
10. Stewart JM, Carter SR: Anatomy and examination of the eyelids, *Int Ophthalmol Clin* 42(2):1, 2002.
11. Dailey RA, Wobig JL: Eyelid anatomy, *J Dermatol Surg Oncol* 18:1023, 1993.
12. Goldberg RA, Wu JC, Jesmanowicz A et al: Eyelid anatomy revisited, *Arch Ophthalmol* 110(11):1598, 1992.
13. Jeong S, Lemke BN, Dortzbach RK et al: The Asian upper eyelid, *Arch Ophthalmol* 117:907, 1999.
14. Jakobiec FA, Iwamoto T: The ocular adnexa: lids, conjunctiva, and orbit. In Fine BS, Yanoff M, editors: *Ocular histology*, ed 2, New York, 1979, Harper & Row, p 290.
15. Jester JV, Nicolaides N, Smith RE: Meibomian gland studies: histologic and ultrastructural investigations, *Invest Ophthalmol Vis Sci* 20(4):537, 1981.
16. Ahl NC, Hill JC: Horner's muscle and the lacrimal system, *Arch Ophthalmol* 100:488, 1982.
17. Fernandez-Valencia R, Pellico LG: Functional anatomy of the human saccus lacrimalis, *Acta Anat (Basel)* 139:54, 1990.
18. Shinohara H, Kominami R, Yasutaka S et al: The anatomy of the lacrimal portion of the orbicularis oculi muscle (tensor tarsi or Horner's muscle), *Okajimas Folia Anat Jpn* 77(6):225, 2001 (abstract).
19. Lipham WJ, Tawfik HA, Dutton JJ: A histologic analysis and three-dimensional reconstruction of the muscle of Riolan, *Arch Ophthalmol* 18(2):93, 2002.
20. Morax S, Herdan ML: The aging eyelid, *Schweiz Rundsch Med Prax* 9(48):1506, 1990 (abstract).
21. Dryden RM, Leibsohn J, Wobig J: Senile entropion: pathogenesis and treatment, *Arch Ophthalmol* 96:1883, 1978.
22. Fox SA: Primary congenital entropion, *Arch Ophthalmol* 56:839, 1956.
23. Kikkawa DO, Lucarelli MJ, Shovlin JP et al: Ophthalmic facial anatomy and physiology. In Kaufman, Alm, editors: *Adler's physiology of the eye*, ed 10, St Louis, 2003, Elsevier.
24. Hart WM Jr: The eyelids. In WM Hart Jr, editor: *Adler's physiology of the eye*, ed 9, St Louis, 1992, Mosby.
25. Wobig JL: Surgical technique for ptosis repair, *Aust NZ J Ophthalmol* 17(2):125, 1989.
26. Anderson RL, Beard C: The levator aponeurosis: attachments and their clinical significance, *Arch Ophthalmol* 95:1437, 1977.
27. Kuwabara T, Cogan DG, Johnson CC: Structure of the muscles of the upper eyelid, *Arch Ophthalmol* 93:1189, 1975.
28. Wobig JL: The eyelids. In Reeh MJ, Wobig JL, Wirtschafter JD, editors: *Ophthalmic anatomy*, San Francisco, 1981, American Academy of Ophthalmology, p 38.
29. Evinger C, Manning KA, Sibony PA: Eyelid movements: mechanisms and normal data, *Invest Ophthalmol Vis Sci* 32:387, 1991.
30. Hawes MJ, Dortzbach RK: The microscopic anatomy of the lower eyelid retractors, *Arch Ophthalmol* 100:1313, 1982.
31. Small RG, Sabates NR, Burrows D: The measurement and definition of ptosis, *Ophthalm Plast Reconstr Surg* 5(3):171, 1989.
32. Anderson RL: Medial canthal tendon branches out, *Arch Ophthalmol* 95:2051, 1977.
33. Rosenstein T, Talebzadeh N, Pogrel MA: Anatomy of the lateral canthal tendon, *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 89(1):24, 2000.
34. Gioia VM, Linberg JV, McCormick SA: The anatomy of the lateral canthal tendon, *Arch Ophthalmol* 105:529, 1987.
35. Stoeckelhuber M, Stoeckelhuber BM, Welsch U: Human glands of Moll: histochemical and ultrastructural characterization of the glands of Moll in the human eyelid, *J Invest Dermatol* 121(1):28, 2003.
36. Iwamoto T, Jakobiec FA: Lacrimal glands. In Tasman W, Jaeger EA, editors: *Duane's foundations of clinical ophthalmology*, vol 1, Philadelphia, 1994, Lippincott.
37. Wirtschafter JD, Ketcham JM, Weinstock RJ et al: Mucocutaneous junction as the major source of replacement palpebral conjunctival epithelial cells, *Invest Ophthalmol Vis Sci* 40(13):3138, 1999.
38. Kessing SV: Investigations of the conjunctival mucin, *Acta Ophthalmol (Copenh)* 44:439, 1966.
39. Diebold Y, Rios JD, Hodges RR et al: Presence of nerves and their receptors in mouse and human conjunctival goblet cells, *Invest Ophthalmol Vis Sci* 42(10):2270, 2001.
40. Sullivan WR, McCulley JP, Dohlman CH: Return of goblet cells after vitamin A therapy in xerosis of the conjunctiva, *Am J Ophthalmol* 75:720, 1973.
41. Hogan MJ, Alvarado JA: *Histology of the human eye*, Philadelphia, 1971, Saunders, p 112.
42. Allensmith MR, Greiner JV, Baird RS: Number of inflammatory cells in the normal conjunctiva, *Am J Ophthalmol* 86:250, 1978.
43. Jakobiec FA, Iwamoto T: Ocular adnexa: introduction to lids, conjunctiva, and orbit. In Tasman W, Jaeger EA, editors: *Duane's foundations of clinical ophthalmology*, vol 1, Philadelphia, 1994, Lippincott.
44. Srinivasan BD, Jakobiec FA, Iwamoto T et al: Epibulbar mucogenic subconjunctival cysts, *Arch Ophthalmol* 96:857, 1978.
45. Chin GN, Chi EY, Bunt A: Ultrastructure and histochemical studies of conjunctival concretions, *Arch Ophthalmol* 98:720, 1980.
46. Weingeist TA: The glands of the ocular adnexa. In Zinn KM, editor: *Ocular structure for the clinician*, Boston, 1973, Little, Brown, p 243.
47. Sirigu P, Shen RL, Pinto-da-Silva P: Human meibomian glands: the ultrastructure of acinar cells as viewed by thin section and freeze-fracture transmission electron microscopes, *Invest Ophthalmol Vis Sci* 33(7):2284, 1992.
48. LeDoux MS, Zhou Q, Murphy RB et al: Parasympathetic innervation of the meibomian glands in rats, *Invest Ophthalmol Vis Sci* 42(11):2434, 2001.
49. Bergmanson JP, Doughty MJ, Blocker Y: The acinar and ductal organization of the tarsal accessory lacrimal gland of Wolfring in rabbit eyelid, *Exp Eye Res* 68(4):411, 1999.
50. Seifert P, Stuppi S, Spitznas M: Distribution pattern of nervous tissue and peptidergic nerve fibers in accessory lacrimal glands, *Cur Eye Res* 16:298, 1997.
51. Kanski JJ: *Clinical ophthalmology*, ed 3, London, 1994, Butterworth-Heinemann.
52. Pe'er J, Zajicek G, Greifner H et al: Streaming conjunctiva, *Anat Rec* 245(1):36, 1996.
53. Gipson IK, Yankauckas M, Spurr-Michaud SJ et al: Characteristics of a glycoprotein in the ocular surface glycocalyx, *Invest Ophthalmol Vis Sci* 33:218, 1992.
54. Nichols B, Dawson CR, Togni B: Surface features of the conjunctiva and cornea, *Invest Ophthalmol Vis Sci* 24:570, 1983.
55. Dilly PN: On the nature and the role of the subsurface vesicles in the outer epithelial cells of the conjunctiva, *Br J Ophthalmol* 69:477, 1985.

56. Fine BS, Yanoff M: *Ocular histology*, ed 2, Hagerstown, Md, 1979, Harper & Row, p 310.
57. Shields CL, Shields JA: Tumors of the caruncle, *Int Ophthalmol Clin* 33(3):31, 1993.
58. Austin P, Jakobiec FA, Iwamoto T: Elastodysplasia and elastodystrophy as the pathologic bases of ocular pterygia and pinguecula, *Ophthalmology* 90:96, 1983.
59. Li ZY, Wallace RN, Streeten BW et al: Elastic fiber components and protease inhibitors in pinguecula, *Invest Ophthalmol Vis Sci* 32(5):1573, 1991.
60. Dushku N, John MK, Schultz GS et al: Pterygia pathogenesis, *Arch Ophthalmol* 119:695, 2001.
61. Dushku N, Reid TW: P53 expression in altered limbal basal cells of pingueculae, pterygia, and limbal tumors, *Cur Eye Res* 16:1179, 1997.
62. Dushku N, Reid TW: Immunohistochemical evidence that human pterygia originate from an invasion of vimentin-expressing altered limbal epithelial basal cells, *Cur Eye Res* 13:473, 1994.
63. Taylor HR, West SK, Rosenthal FS et al: Corneal changes associated with chronic UV radiation, *Arch Ophthalmol* 107:1481, 1989.
64. Mackenzie FD, Hirst LW, Battistutta D et al: Risk analysis in the development of pterygia, *Ophthalmology* 99(7):1056, 1992.
65. Young RW: The family of sunlight-related eye diseases, *Optom Vis Sci* 71(2):125, 1994.
66. Shauly Y, Miller B, Lichtig C: Tenon's capsule: ultrastructure of collagen fibrils in normals and infantile esotropia, *Invest Ophthalmol Vis Sci* 33:651, 1992.
67. Meyer E, Ludatscher RN, Miller B et al: Connective tissue of the orbital cavity in retinal detachment: an ultrastructural study, *Ophthalmic Res* 24:365, 1992.
68. Reiger G: The importance of the precorneal tear film for the quality of optical imaging, *Br J Ophthalmol* 76:157, 1992.
69. Lemp MA, Wolfley DE: The lacrimal apparatus. In Hart WM Jr, editor: *Adler's physiology of the eye*, ed 9, St Louis, 1992, Mosby.
70. Mishima S, Maurice DM: The effect of normal evaporation from the eye, *Exp Eye Res* 1:46, 1961.
71. Lemp MA, Holly FJ, Iwata S: The precorneal tear film, *Arch Ophthalmol* 83:89, 1970.
72. Watanabe H, Fabricant M, Tisdale AS et al: Human corneal and conjunctival epithelia produce a mucin-like glycoprotein for the apical surface, *Invest Ophthalmol Vis Sci* 36(2):337, 1995.
73. Ehlers N: The thickness of the precorneal tear film, *Acta Ophthalmol (Copenh)* 8(suppl 81):92, 1965.
74. Prydal JI, Artal P, Woon H et al: Study of human precorneal tear film thickness and structure using laser interferometry, *Invest Ophthalmol Vis Sci* 33(6):2006, 1992.
75. Prydal JI, Campbell FW: Study of precorneal tear film thickness and structure by interferometry and confocal microscopy, *Invest Ophthalmol Vis Sci* 33(6):1996, 1992.
76. Egeberg J, Jenson OA: The ultrastructure of the acini of the human lacrimal gland, *Acta Ophthalmol (Copenh)* 47:400, 1969.
77. Jones LT: Anatomy of the tear system, *Int Ophthalmol Clin* 13(1):3, 1973.
78. Jordan A, Baum JL: Basic tear flow, does it exist? *Ophthalmology* 95:1, 1980.
79. Khurana AK, Chaudhary R, Ahluwalia BK et al: Tear film profile in dry eye, *Acta Ophthalmol (Copenh)* 69(1):79, 1991.
80. Friedlaender MH: Ocular manifestations of Sjögren's syndrome: keratoconjunctivitis sicca, *Rheum Dis Clin North Am* 18(3):591, 1992.
81. Roberts DK: Keratoconjunctivitis sicca, *J Am Optom Assoc* 62(3):187, 1991.
82. Ralph RA: Conjunctival goblet cell density in normal subjects and in dry eye syndromes, *Invest Ophthalmol* 14(4):299, 1975.
83. Lemp MA, Dohlman CH, Kuwabara T et al: Dry eye secondary to mucous deficiency, *Trans Am Acad Ophthalmol Otolaryngol* 75:1223, 1971.
84. Cho P, Yap M.: Schirmer test: a review, *Optom Vis Sci* 70(2):152, 1993.
85. Lemp MA, Hamil JR: Factors affecting tear film breakup in normal eyes, *Arch Ophthalmol* 89:103, 1973.
86. Mai G, Yang S: Relationship between corneal dellen and tear film breakup time, *Yen Ko Hsueh Pao* 7(1):43, 1991 (abstract).
87. Cross WD, Lay LF Jr, Walt JG et al: Clinical and economic implications of topical cyclosporin A for the treatment of dry eye, *Manag Care Interface* 15(9):44, 2002.
88. Calonge M: The treatment of dry eye, *Surv Ophthalmol Suppl* 2:S227, 2001.
89. Stevenson D, Tauber J, Reis BL: Efficacy and safety of cyclosporin A ophthalmic emulsion in the treatment of moderate-to-severe dry eye disease: a dose-ranging, randomized trial. The Cyclosporin A Phase 2 Study Group, *Ophthalmology* 107(5):967, 2000.
90. Sall K, Stevenson OD, Mundorf TK et al: Two multicenter, randomized studies of the efficacy and safety of cyclosporine ophthalmic emulsion in moderate-to-severe dry eye disease. The Cyclosporin A Phase 3 Study Group, *Ophthalmology* 107(4):631, 2000.
91. Doane MG: Blinking and the mechanics of the lacrimal drainage system, *Ophthalmology* 88(8):844, 1981.
92. Wobig JL. The lacrimal apparatus. In Reeh MJ, Wobig JL, Wirtschafter JD, editors: *Ophthalmic anatomy*, San Francisco, 1981, American Academy of Ophthalmology, p 55.
93. Yazici B, Yazici Z: Frequency of the common canaliculus, *Arch Ophthalmol* 118:1381, 2000.
94. Doane MG: Interactions of eyelids and tears in corneal wetting and the dynamics of the normal human eyeblink, *Am J Ophthalmol* 89:507, 1981.
95. Tucker NA, Tucker SM, Linberg JV: The anatomy of the common canaliculus, *Arch Ophthalmol* 114:1231, 1996.
96. Milder B, Demorest BH: Dacryocystography, the normal lacrimal apparatus, *Arch Ophthalmol* 51:181, 1954.
97. Jones LT, Marquis MM: Lacrimal function, *Am J Ophthalmol* 73:658, 1972.
98. Lucarelli MJ, Dartt DA, Cook BE et al: The lacrimal system. In Kaufman PL, Alm A, editors: *Adler's physiology of the eye*, ed 10, St Louis, 2003, Elsevier.
99. Van den Bosch WA, Leenders I, Mulder P: Topographic anatomy of the eyelids, and the effects of sex and age, *Br J Ophthalmol* 83:347, 1999.
100. Lin PY, Tsai SY, Cheng CY et al: Prevalence of dry eye among an elderly Chinese population in Taiwan, *Ophthalmology* 110(6):1096, 2003.
101. Schaumberg DA, Sullivan DA, Buring JE et al: Prevalence of dry eye syndrome among US women, *Am J Ophthalmol* 136(2):318, 2003.

The muscles of the globe can be divided into two groups: the involuntary intrinsic muscles and the voluntary extrinsic muscles. The intrinsic muscles—the ciliary muscle, the iris sphincter, and the iris dilator—are located within the eye; these muscles control the movement of internal ocular structures. The extrinsic muscles—the six extraocular muscles—attach to the sclera and control movement of the globe.

This chapter begins with a brief review of the microscopic and macroscopic anatomy of striated muscle, then discusses eye movements and describes the characteristics and actions of each extraocular muscle. (The smooth intrinsic muscles are discussed in Chapter 3.)

MICROSCOPIC ANATOMY OF STRIATED MUSCLE

Striated muscle is surrounded by a connective tissue sheath known as the *epimysium*; continuous with this sheath is a connective tissue network, the *perimysium*, which infiltrates the muscle and divides it into bundles. The individual muscle fiber within the bundle is surrounded by a delicate connective tissue enclosure, the *endomysium* (Figure 10-1). The individual muscle fiber is comparable to a cell; however, each fiber is multinucleated, with the nuclei arranged in the periphery of the fiber. The plasma cell membrane surrounding each muscle fiber, the *sarcolemma*, forms a series of invaginations into the cell, the *transverse tubules* (*T tubules*), which allow ions to spread through the cell in response to an action potential. The cell cytoplasm, *sarcoplasm*, contains the normal cellular structures and the special muscle fibers, the myofibrils.

Myofibrils comprise two types, thick and thin. The thick myofibrils are composed of hundreds of *myosin* subunits. Each subunit is a long, slender filament with two globular heads attached by arms at one end. These filaments lie next to each other and form the “backbone” of the myofibril, with the heads projecting outward in a spiral (Figure 10-2, A). The thin myofibrils are formed by the protein *actin* arranged in a double-helical filament, with a molecular complex of *troponin* and *tropomyosin* lying within the grooves of the double helix (Figure 10-2, B).

The alternating light and dark bands characteristic of striated muscle are produced by the manner in which these two types of myofibrils are arranged. The light band is the I (isotropic) band, and the dark band is the A (anisotropic) band. These names describe the birefringence to polarized light exhibited by the two areas.¹

The I band contains two sets of actin filaments connected to each other at the Z line, a dark stripe bisecting the I band. Only actin myofibrils are found in the I band. The A band contains both myosin and actin; the central lighter zone of the A band—the H zone—contains only myosin. Overlapping actin and myosin filaments form the outer darker edges of the A band (Figure 10-3).

The *sarcomere* extends from Z line to Z line and is the contractile unit of striated muscle. With muscle contraction, a change in configuration occurs; the H zone width decreases as the actin filaments slide past the myosin filaments. The sarcomere is shortened; as this occurs along the muscle, muscle length is decreased.

SLIDING RATCHET MODEL OF MUSCLE CONTRACTION

The precise biomolecular process of muscle contraction is not fully understood; however, the sliding ratchet model of muscle contraction provides a reasonable explanation.²⁻⁴ The initiation of a muscle contraction occurs when a nerve impulse causes the release of acetylcholine into the neuromuscular junction. Biochemical changes in the muscle tissue result in a configurational change in the troponin-tropomyosin complex, allowing an active site on the actin protein to be available for binding with a myosin head. Coincidentally, adenosine triphosphate (ATP) attached to the myosin head is broken down and released, allowing the cross-bridge to bind with the active actin site. Once this bond is formed, the head tilts toward the shaft of the myosin filament, pulling the actin filament along with it.

The junction between the actin and myosin is broken by the attachment of a new ATP molecule to the myosin head. The head then rights itself, and the cross-bridge is ready to bind with the next actin site along the chain. This ratchet type of movement occurs along the length of the fiber, moving the filaments past one another with

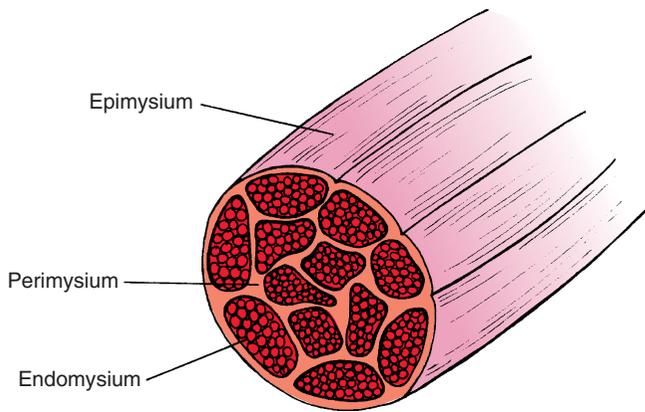


FIGURE 10-1
Connective tissue network of striated muscle.

the overall effect of shortening the sarcomere and the entire muscle.

STRUCTURE OF THE EXTRAOCULAR MUSCLES

The extraocular muscles have a denser blood supply, and their connective tissue sheaths are more delicate and richer in elastic fibers than is skeletal muscle.⁵ Fewer muscle fibers are included in a motor unit in extraocular muscle than are found in skeletal muscle elsewhere. Striated muscle of the leg can contain several hundred muscle fibers per motor unit;⁶ in the extraocular muscles, each axon innervates 3 to 10 fibers.⁷ Precise fine motor control and quick accurate movement of the extraocular muscles occur because of this dense innervation. Singly innervated fibers have the classic end plate (*en plaque*) seen in skeletal muscle; multiply

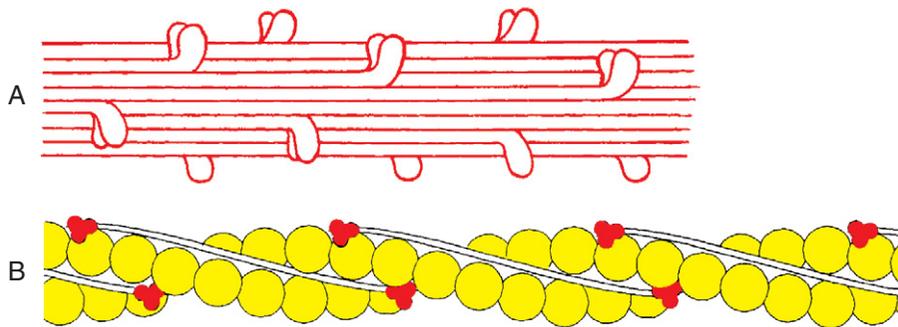


FIGURE 10-2
Myosin and actin myofibrils. **A**, Myosin fibril is composed of two-headed filaments, with heads arranged in a spiral. **B**, Actin myofibril is composed of double-helix filament to which troponin-tropomyosin complex is attached.

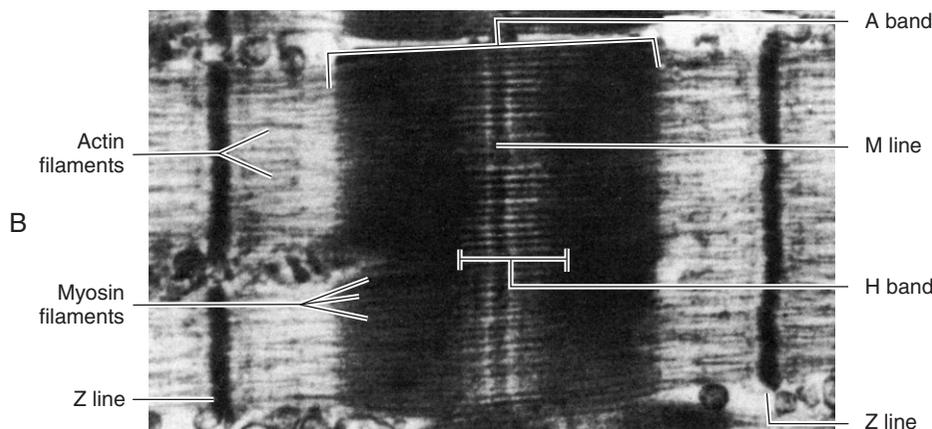
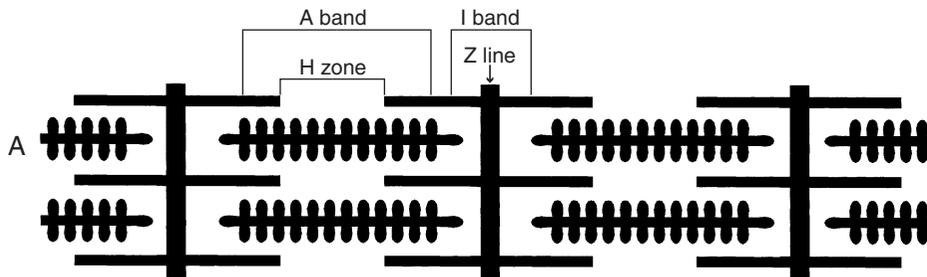


FIGURE 10-3
A, Arrangement of thick and thin filaments in sarcomere. **B**, Photomicrograph of striated muscle, with parts of sarcomere indicated. (**B** from Krause WJ, Cutts JH: *Concise text of histology*, Baltimore, 1981, Williams & Wilkins.)

innervated fibers have a neuromuscular junction resembling a bunch of grapes (*en grappe*).^{8,9}

The extraocular muscles have a range of fiber sizes, with the fibers closer to the surface generally having smaller diameters (5-15 μm) and those deeper within the muscle generally having larger diameters (10-40 μm).¹⁰⁻¹³ They can be divided into groups based on characteristics such as location, size, morphology, neuromuscular junction type, or various biochemical properties.^{5,11,12,14,15} The fibers range from typical twitch fibers at one end of the spectrum to typical slow fibers at the other end, with gradations between. It would seem that the fast-twitch fibers should produce quick saccadic type movements and the slow fibers should produce slower pursuit movements and provide muscle tone. However, all fibers apparently are active at all times and share some level of involvement in all ocular movements.^{11,13,15,16} Extraocular muscles are among the fastest and most fatigue resistant of striated muscle.¹⁷

Muscle spindles and Golgi tendon organs have been identified in human extraocular muscle, although it is unclear whether these structures provide any useful proprioceptive information relative to the extraocular muscles.¹⁸ Afferent information regarding extraocular muscle proprioception is thought to be mediated by a receptor that is unique to extraocular muscle, the *myotendinous cylinder (palisade ending)*.¹⁵

EYE MOVEMENTS

FICK'S AXES

Before a discussion of the individual muscles and the resultant eye movements caused by their contraction, it is necessary to define certain terms. All eye movement can be described as rotations around one or more axes. According to Fick, these axes divide the globe into quadrants and intersect at the center of rotation, a fixed nonmoving point¹⁹ and the approximate geometric center of the eye. For convenience, it is assumed that the eye rotates around this fixed point, located 13.5 mm behind the cornea; this point varies in ametropia, is slightly more posterior in myopia, and is slightly more anterior in hyperopia.⁵ The **X-axis** is the **horizontal** or **transverse** axis and runs from nasal to temporal. The **Y-axis** is the **sagittal** axis running from the anterior pole to the posterior pole. The **Z-axis** is the **vertical** axis and runs from superior to inferior (Figure 10-4). The anterior pole of the globe is the reference point used in the description of any eye movement.

DUCTIONS

Movements involving just one eye are called **ductions** (Figure 10-5). Rotations around the vertical axis move

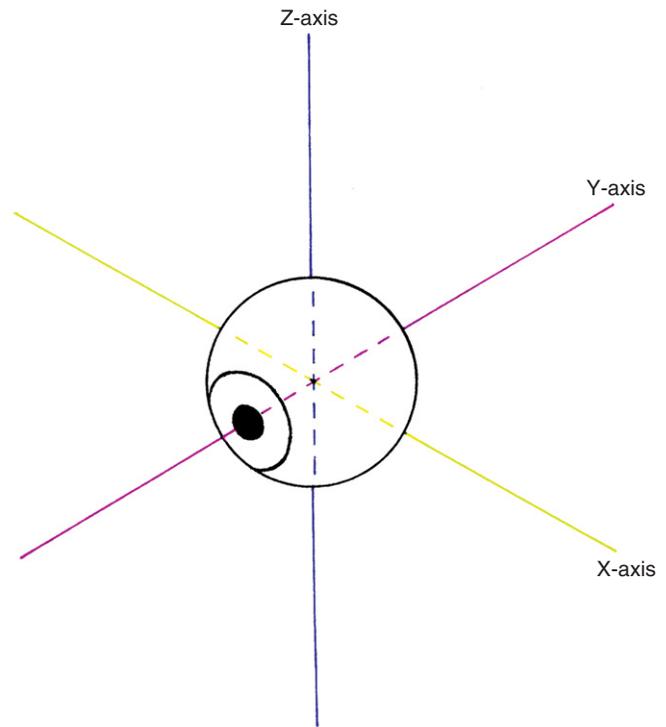


FIGURE 10-4

Fick's axes: X-axis is horizontal; Y-axis is sagittal; and Z-axis is vertical.

the anterior pole of the globe medially—**adduction**—or laterally—**abduction**. Rotations around the horizontal axis move the anterior pole of the globe up—**elevation (supraduction)**—or down—**depression (infraduction)**.

Torsions or cyclorotations are rotations around the sagittal axis and are described in relation to a point at the 12-o'clock position on the superior limbus. **Intorsion (incyclorotation)** is the rotation of that point nasally, and **extorsion (excyclorotation)** is the rotation of that point temporally. Torsional movements may occur in an attempt to keep the horizontal retinal raphe parallel to the horizon.²⁰ With a head tilt of 30 degrees, the ipsilateral eye is intorted approximately 7 degrees, and the contralateral eye is extorted approximately 8 degrees.²¹

Torsional movements have been questioned by some investigators who believe that true torsion occurs only in pathologic conditions.²² Others have documented torsion in normal eye movements and with head tilt.²³⁻²⁶

VERGENCES AND VERSIONS

Movements involving both eyes are either vergences or versions, depending on the relative directions of

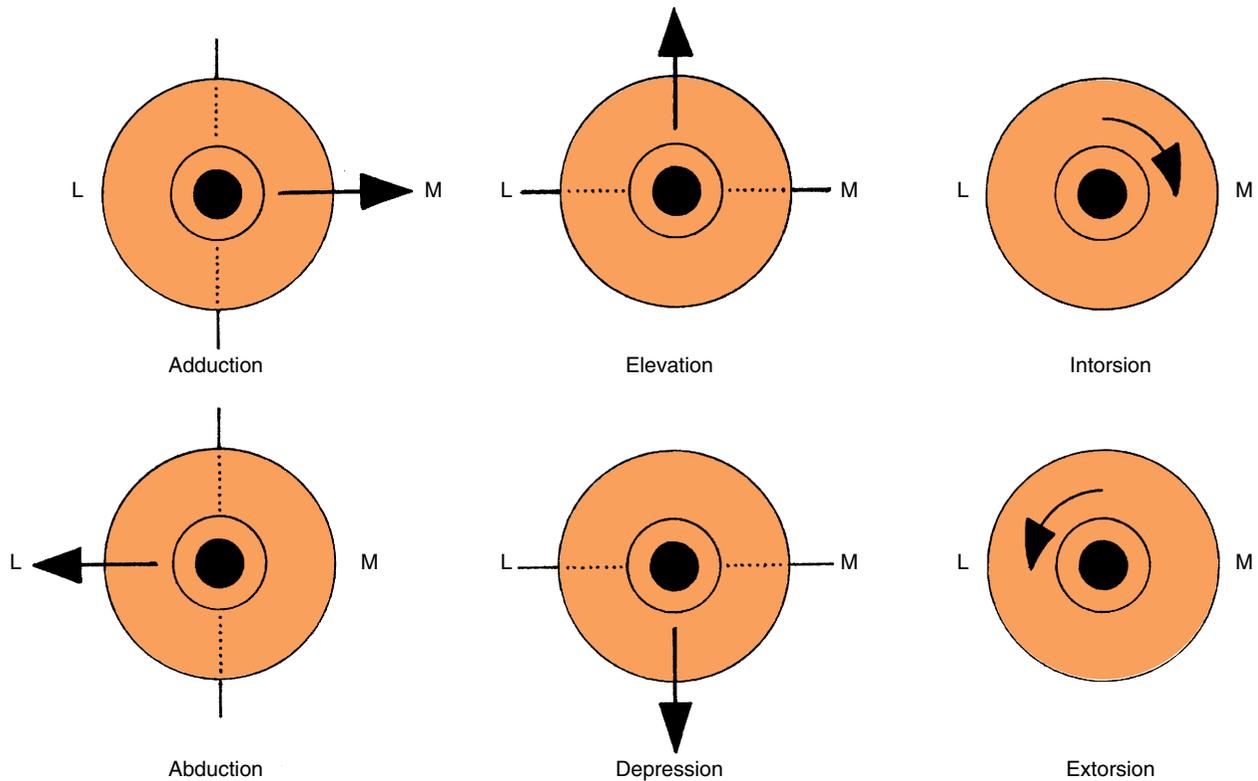


FIGURE 10-5

Movements of the eye in duction. Anterior pole is point of reference. *L*, Lateral; *M*, medial.

movement. In vergence movements the eyes move in opposite left-right directions; these are disjunctive movements. In **convergence** each eye is adducted, and in **divergence** each eye is abducted. Version movements are conjugate movements and occur when the eyes move in the same direction. **Dextroversion** is right gaze, and **levoversion** is left gaze. In **supraversion** both eyes are elevated, and in **infraversion** both eyes are depressed. Table 10-1 lists terms for monocular and binocular eye movements and some combination movements.

POSITIONS OF GAZE

The **primary position of gaze** is defined as the position of the eye with the head erect, the eye located at the intersection of the sagittal plane of the head and the horizontal plane passing through the centers of rotation of both eyes, and the eye focused for infinity.¹⁶ Secondary positions of gaze are rotations around either the vertical axis or the horizontal axis; tertiary positions are rotations around both the vertical and the horizontal axes.

MACROSCOPIC ANATOMY OF THE EXTRAOCULAR MUSCLES

The six extraocular muscles are medial rectus, lateral rectus, superior rectus, inferior rectus, superior oblique, and inferior oblique (Figure 10-6). From longest to shortest, the rectus muscles are the superior, the medial, the lateral, and the inferior.²⁷

ORIGIN OF THE RECTUS MUSCLES

The four rectus muscles have their origin on the **common tendinous ring (annulus of Zinn)**. This oval band of connective tissue is continuous with the periorbita and is located at the apex of the orbit anterior to the optic foramen and the medial part of the superior orbital fissure. The upper and lower areas are thickened bands and sometimes are referred to as the **upper and lower tendons or limbs**. The medial and lateral rectus muscles take their origin from both parts of the tendinous ring. The superior rectus is attached to the upper limb, and the inferior rectus is joined to the

Table 10-1 Ocular Movement Terminology

Monocular		Binocular	
Eye Movement*	Term	Eye Movement	Term
Medial	Adduction	Right	Dextroversion
Lateral	Abduction	Left	Levoersion
Up	Elevation, supraduction, or sursumduction	Up	Supraversion or sursumversion
Down	Depression, infraduction, or deorsumduction	Down	Infraversion or deorsumversion
Rotation of 12-o'clock position medially	Intorsion, incyclorotation, or incycloduction	Up and right	Dextroelevation
Rotation of 12-o'clock position laterally	Extorsion, excyclorotation, or excycloduction	Up and left	Levoelevation
Anterior out of orbit	Protrusion or exophthalmos	Down and right	Dextrodepression
Posterior into orbit	Retraction or enophthalmos	Down and left	Levodepression
		Both eyes adduct	Convergence
		Both eyes abduct	Divergence
		Both eyes extort	Excyclovergence
		Both eyes intort	Incyclovergence
		Rotation of 12-o'clock position to right	Dextrocycloverision
		Rotation of 12-o'clock position to left	Levocycloverision

*For all movements the anterior pole of the globe is the reference point unless otherwise noted.

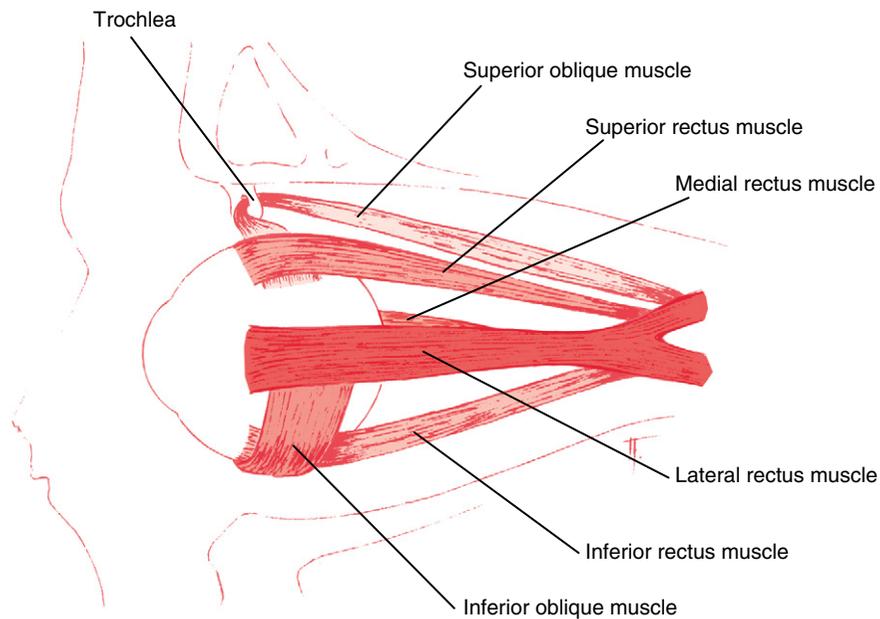


FIGURE 10-6
Globe in orbit as viewed from lateral side.

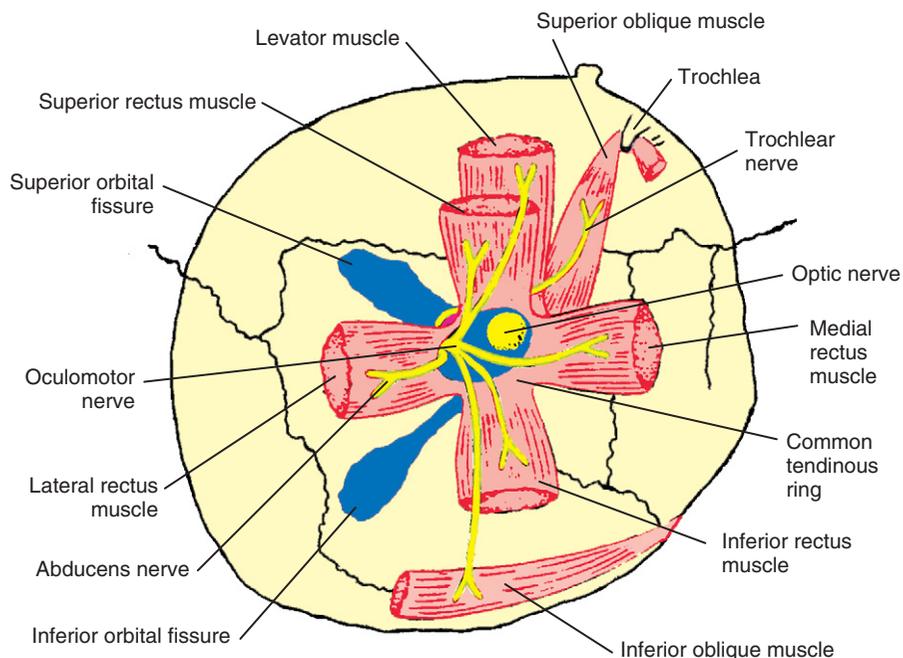


FIGURE 10-7
Annulus of Zinn. Orbital apex with globe removed. Relationship between superior orbital fissure and common tendinous ring is shown.

lower (Figure 10-7). The medial rectus and the superior rectus also attach to the dural sheath of the optic nerve.²⁷

CLINICAL COMMENT: RETROBULBAR OPTIC NEURITIS

Retrobulbar optic neuritis is an inflammation affecting the sheaths of the optic nerve. Generally, there are no observable fundus changes in this condition, but pain with extreme eye movement can be one of the early presenting signs.^{1,27} The optic nerve sheath is supplied with a dense sensory nerve network and, because of the close association of muscle and optic nerve sheath, eye movement can cause stretching of the optic nerve sheath, resulting in a sensation of pain.²⁸

The area enclosed by the tendinous ring is called the **oculomotor foramen**, and several blood vessels and nerves pass through the foramen, having entered the orbit either through the optic canal or the superior orbital fissure (see Figure 10-7). The optic nerve and ophthalmic artery enter the oculomotor foramen from the optic canal; the superior and inferior divisions of the oculomotor nerve, the abducens nerve, and the nasociliary nerve enter the oculomotor foramen from the superior orbital fissure (see Figure 10-7). These structures lie within the muscle cone, the area enclosed by the four rectus muscles and the connective tissue

joining them. Thus, the motor nerve to each rectus muscle can enter the surface of the muscle that lies within the muscle cone.

In 1887, Motais described a common muscle sheath between the rectus muscles enclosing the space within the muscle cone.⁵ More recently, dissections by Koorneef²⁹ revealed no definitive, continuous muscle sheath between the rectus muscles in the retrobulbar region.

The lacrimal and frontal nerves and the superior ophthalmic vein lie above the ring tendon, and the inferior ophthalmic vein lies below. They are outside the muscle cone.

INSERTIONS OF THE RECTUS MUSCLES: SPIRAL OF TILLAUX

The four rectus muscles insert into the globe anterior to the equator. A line connecting the rectus muscle insertions forms a spiral, as described by Tillaux. This spiral starts at the medial rectus, the insertion that is closest to the limbus, and proceeds to the inferior rectus, the lateral rectus, and finally the superior rectus, the insertion farthest from the limbus⁵ (Figure 10-8). In a recent study, variations were found from person to person in specific measurements, but the **spiral of Tillaux** was always observed.³⁰ The tendons of insertion pierce Tenon's capsule and merge with scleral fibers. A sleeve

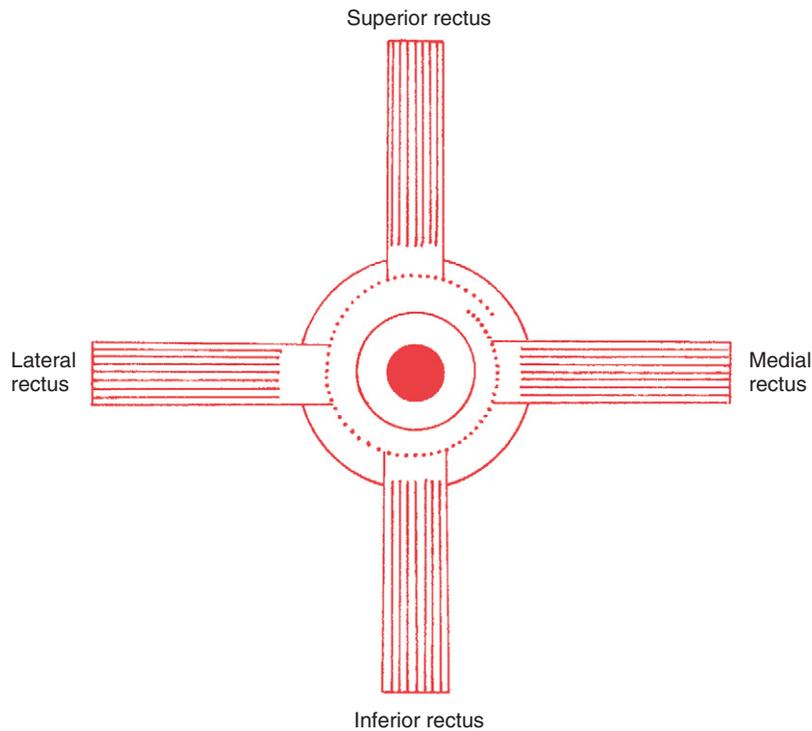


FIGURE 10-8
Insertions of rectus muscles forming spiral of Tillaux.

Table 10-2 Rectus Muscle Tendon of Insertion Measurements*

Muscle	Tendon Length	Distance from Limbus	Tendon Width
Medial rectus	3.7	5.5	10.3
Lateral rectus	8.8	6.9	9.2
Superior rectus	5.8	7.7	10.8
Inferior rectus	5.5	6.5	9.8

*All measurements in millimeters (mm).

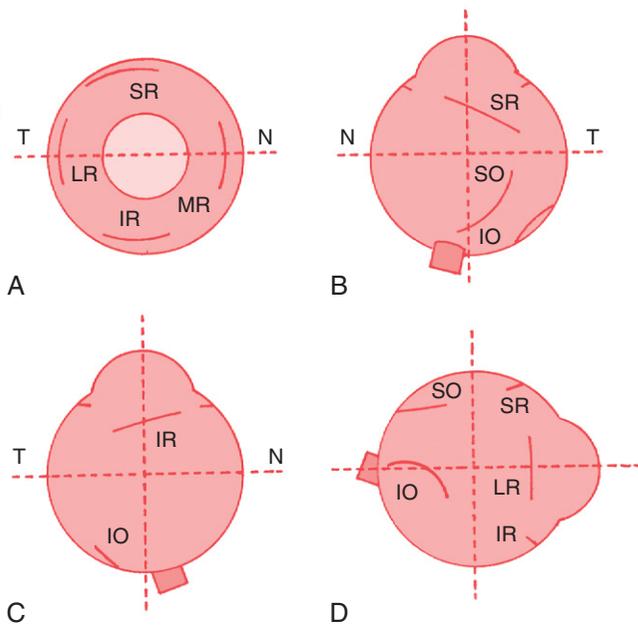
Modified from Eggers HM: In Tasman W, Jaeger EA, editors: *Duane's foundations of clinical ophthalmology*, Philadelphia, 1994, Lippincott.

of the capsule covers the tendon for a short distance, and the muscle can slide freely within this sleeve.^{5,12} Connective tissue extends from the insertions joining them to each other.

MEDIAL RECTUS MUSCLE

The **medial rectus muscle** is the largest of the extraocular muscles, with its size probably resulting from the frequency of its use in convergence.²⁷ Its **origin** is from both the upper and the lower parts of the common ring tendon *and* from the sheath of the optic nerve. The medial rectus muscle parallels the medial orbital wall until it passes through a connective tissue pulley just

posterior to the equator of the globe; at this point it follows the curve of the globe to its insertion.³¹ The **insertion** of the medial rectus is about 5.5 mm from the limbus, and the tendon is approximately 3.7 mm long⁵ (Table 10-2). The insertion line lies vertically such that the horizontal plane of the eye approximately bisects it (Figure 10-9, A). The superior oblique muscle, ophthalmic artery, and nasociliary nerve lie above the medial rectus. Fascial expansions from the sheath of the muscle run to the medial wall of the orbit and form the well-developed medial check ligament (see Figure 8-18). The medial rectus is innervated by the inferior division of cranial nerve III, the oculomotor nerve, which enters the muscle on its lateral surface.

**FIGURE 10-9**

Insertions of extraocular muscles. Globe viewed from **A**, in front; **B**, above; **C**, below; and **D**, lateral side. *LR*, Lateral rectus; *MR*, medial rectus; *SR*, superior rectus; *IR*, inferior rectus; *SO*, superior oblique; *IO*, inferior oblique; *N*, nasal; *T*, temporal.

LATERAL RECTUS MUSCLE

The **lateral rectus muscle** has its **origin** on both limbs of the common tendinous ring *and* the spina recti lateralis, a prominence on the greater wing of the sphenoid bone. The lateral rectus muscle parallels the lateral orbital wall until it passes through a connective tissue pulley just posterior to the equator of the globe; at this point it follows the curve of the globe to its insertion.³¹ The **insertion** parallels that of the medial rectus and is approximately 6.9 mm from the limbus, and the length of the tendon is approximately 8.8 mm.⁵

The lacrimal artery and nerve run along the superior border of the lateral rectus muscle. The ciliary ganglion, the abducens nerve, and the ophthalmic artery lie medial to the lateral rectus between it and the optic nerve. Fascial expansions from the muscle sheath attach to the lateral wall of the orbit and form the lateral check ligament (see Figure 8-18). The lateral rectus is innervated by cranial nerve VI, the abducens nerve, which enters on the medial side of the muscle.

SUPERIOR RECTUS MUSCLE

The **superior rectus muscle** has its **origin** on the superior part of the common tendinous ring *and* the sheath of the optic nerve.²⁷ The muscle passes forward beneath

the levator muscle; the sheaths enclosing these two muscles are connected to each other, allowing coordination of eye movement with eyelid position and resulting in elevation of the eyelid with upward gaze. An additional band of this tissue connects to the superior conjunctival fornix. The superior rectus muscle parallels the roof of the orbit until it passes through a connective tissue pulley just posterior to the equator of the globe; at this point it follows the curve of the globe to its insertion.³¹

The **insertion** of the superior rectus is approximately 7.7 mm from the limbus⁵ and is curved slightly, with the convex side forward. The line of the insertion is oblique, with the nasal side closer to the limbus than the temporal side (see Figure 10-9, *B*). The tendon length is approximately 5.8 mm.⁵ A line drawn from the origin to the insertion along the muscle will form an angle of approximately 23 degrees with the sagittal axis.

The frontal nerve runs above the superior rectus and levator muscles, and the nasociliary nerve and the ophthalmic artery lie below. The tendon of insertion for the superior oblique muscle runs below the anterior part of the superior rectus muscle (see Figure 10-6).

The superior rectus is innervated by the superior division of the oculomotor nerve, which enters the muscle on its inferior face. Branches pass either through the muscle or around it to innervate the levator.

INFERIOR RECTUS MUSCLE

The **inferior rectus muscle** has its **origin** on the lower limb of the tendinous ring; its **insertion** is about 6.5 mm from the limbus in an arc, convex side forward, with the nasal side nearer the limbus; the tendon length is approximately 5.5 mm.⁵ The inferior rectus approximately parallels the superior rectus, making an angle of 23 degrees with the sagittal axis. The inferior rectus muscle parallels the orbital floor until it passes through a connective tissue pulley just posterior to the equator of the globe; at this point it follows the curve of the globe to its insertion, which is parallel to the insertions of the superior rectus (see Figure 10-9, *C*).³¹

Below the inferior rectus lies the floor of the orbit and above it is the inferior division of the oculomotor nerve. Anteriorly, the inferior oblique muscle comes between the inferior rectus and the orbital floor (see Figure 10-6). The sheaths of these two inferior muscles unite to contribute to the suspensory ligament of Lockwood (see Figure 8-17). The *capsulopalpebral fascia*, an anterior extension from the sheath of the inferior rectus muscle and the suspensory ligament, inserts into the inferior edge of the tarsal plate, allowing coordination of eye movements with eyelid position and ensuring lowering of the lid on downward gaze.³² The inferior rectus is innervated by the inferior division of cranial

nerve III, the oculomotor nerve, which enters the muscle on its superior surface.

SUPERIOR OBLIQUE MUSCLE

The **superior oblique muscle** has its **origin** on the lesser wing of the sphenoid bone, medial to the optic canal near the frontoethmoid suture.¹⁶ The muscle courses forward and passes through the **trochlea**, a U-shaped piece of cartilage attached to the orbital plate of the frontal bone (see Figure 10-6). The tendon of insertion actually begins approximately 1 cm *posterior* to the trochlea. Normally, no connective adhesions exist between these two structures, allowing the tendon to slide easily through the trochlea.¹

The superior oblique muscle is the longest and thinnest of the extraocular muscles because of its long (2.5 cm) tendon of insertion.²⁷ The tendon of insertion changes direction as it passes through the trochlea to run in a posterior direction and lies inferior to the superior rectus muscle. The **insertion** of the superior oblique muscle attaches in the superoposterior lateral quadrant of the globe³³ and is fan shaped, concave forward, and oblique (see Figure 10-9, B).

The trochlea is considered the *physiologic* or effective origin of the superior oblique muscle in determining muscle action because it acts as a pulley and changes the direction of muscle pull. In considering the action of the superior oblique, a line is drawn from the trochlea to the insertion rather than from the anatomic origin to the insertion. A line drawn from the physiologic origin to the insertion makes an angle of approximately 55 degrees with the visual axis.³³ The superior oblique muscle lies above the medial rectus, with the nasociliary nerve and the ophthalmic artery lying between them. Innervation is by the trochlear nerve, cranial nerve IV, which enters the posterior area of the muscle.

INFERIOR OBLIQUE MUSCLE

The **inferior oblique muscle** has its **origin** on the maxillary bone just posterior to the inferior medial orbital rim and lateral to the nasolacrimal canal.³⁴ The inferior oblique is the only extraocular muscle to have its anatomic origin in the anterior orbit. The muscle runs from the medial corner of the orbit to the lateral aspect of the globe, its length approximately paralleling the tendon of insertion of the superior oblique muscle.

The **insertion** of the inferior oblique is on the posterior portion of the globe on the lateral side, mostly inferior, lying just outer to the macular area (see Figure 10-9, D).^{1,27} The insertion is curved concave downward. The muscle makes an angle of approximately 51 degrees with the visual axis.³³ Above the inferior oblique are the inferior rectus and globe, and below it lies the floor of

Table 10-3 Extraocular Muscle Innervation

Muscle	Nerve
Medial rectus	Inferior division of oculomotor (CN III)
Lateral rectus	Abducens (CN VI)
Superior rectus	Superior division of oculomotor (CN III)
Inferior rectus	Inferior division of oculomotor (CN III)
Superior oblique	Trochlear (CN IV)
Inferior oblique	Inferior division of oculomotor (CN III)

CN, Cranial nerve.

the orbit. The inferior oblique is innervated by the inferior division of the oculomotor nerve, which enters the muscle on its upper surface.

Table 10-3 lists the motor innervation of the extraocular muscles.

MACROSCOPIC EXTRAOCULAR MUSCLE AND ORBITAL CONNECTIVE TISSUE STRUCTURE

The extraocular muscles have a layered organization. The *global layer* is adjacent to the globe and consists of fibers of various diameters.³⁵ This group of fibers extends the full length of the muscle and is attached at the origin and insertion through well-defined tendons.¹⁷ The global layer inserts into the sclera and causes movement of the globe.³⁶ The outer *orbital layer* is adjacent to orbital bone, consists of smaller-diameter fibers, and is more vascularized than the global layer.³⁷ These fibers end before the muscle tendon. The orbital layer of the oblique muscles may encircle the global layer.^{17,35} The orbital layer inserts into connective tissue muscle pulleys that can influence the rotational axis of the muscle.^{17,36}

The high quality of current magnetic resonance imaging (MRI) has been instrumental in identification of connective tissue sleeves or pulleys that couple the rectus muscles to the orbital walls and Tenon's capsule.^{31,38-41} Although not as prominent as the pulley of the superior oblique muscle, these pulleys can affect the mechanisms of muscle positioning. Smooth muscle-connective tissue struts attach the pulleys to the periorbita of the orbital wall and may help to refine coordination of binocular eye movements.^{36,39,41,42} The smooth muscle of the pulley is richly innervated by sympathetic and parasympathetic nerves, suggesting both excitatory and inhibitory capabilities.^{17,42} The smooth muscle either regulates the stiffness of the connective tissue or moves the pulleys to alter the pulling direction.³⁶ The pulleys reduce sideslip of the extraocular muscles during globe rotation and help to determine the effective direction of pull.³⁸ Pulley displacement can clinically mimic muscle dysfunction,

and orbital imaging may be needed to distinguish it accurately from a palsy. The pulley for the medial rectus is the best developed.⁴³

Dense connective tissue septa between the extraocular muscle sheaths and between the sheaths and the orbital bones form a highly organized network that contributes to the framework supporting the globe within the orbit. The horizontal rectus muscles are anchored to the periorbita at the anterior orbital walls through the medial and lateral check ligaments. The **medial check ligament** is attached to the bones of the medial orbital wall, and the **lateral check ligament** is attached to the lateral tubercle on the zygomatic bone of the lateral wall; both ligaments are posterior to the orbital septum. The medial check ligament is better developed than the lateral.²⁹ Traditionally, these ligaments were described as “brakes” that limit the extent of movement of the globe; that is, in abduction the medial check ligament stops lateral movement of the globe when extension of the medial rectus muscle starts to exert pull on the relatively inelastic ligament.

The connective tissue septa that connect muscle to muscle and periodically connect individual muscles to

the orbital walls along a significant portion of the muscle length have been identified in dissection studies.^{40,44,45} These intermuscular septa include those joining (1) lateral rectus, inferior rectus, and medial rectus; (2) medial rectus and superior rectus; (3) lateral rectus and superior rectus; (4) medial rectus to superior oblique and to orbital roof and floor; (5) medial rectus to periorbita of ethmoid; (6) superior oblique to frontoethmoid angle; (7) inferior rectus to orbital floor; (8) lateral rectus to lateral wall; (9) levator to adjacent periorbita;²⁹ and (10) superior oblique to orbital roof⁴⁰ (Figure 10-10).

The presence and orientation of these septa vary from front to back. Figure 10-11 shows a representation of the septa at mid-orbit. The considerable amount of attachment between muscle and bone helps to stabilize the muscle path and can limit eye movement.^{17,40}

ISOLATED AGONIST MODEL

One of the earliest models developed to explain eye movement is the isolated agonist model described by

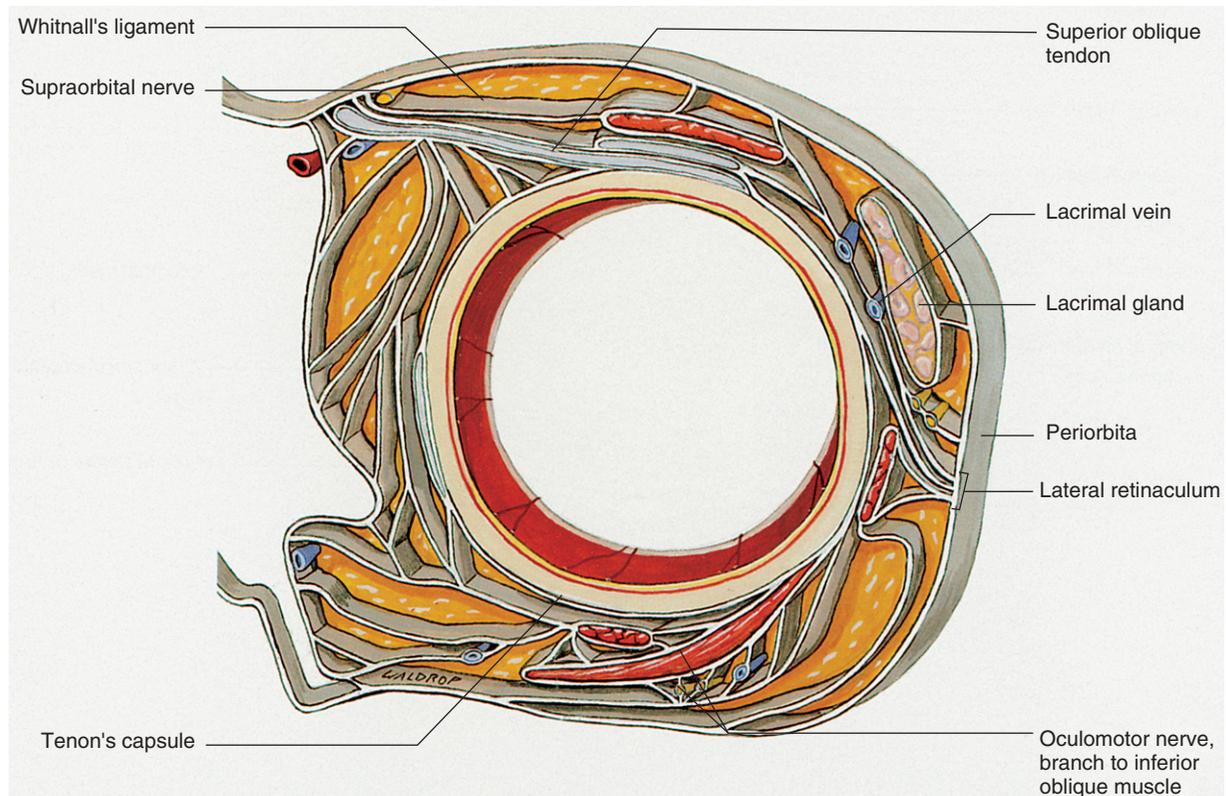


FIGURE 10-10

Connective tissue system in cross section through anterior orbit at level of Whitnall's ligament. (From Dutton JJ: *Atlas of clinical and surgical orbital anatomy*, Philadelphia, 1994, Saunders.)



FIGURE 10-11
Connective tissue system in cross section at mid-orbit. (From Dutton JJ: *Atlas of clinical and surgical orbital anatomy*, Philadelphia, 1994, Saunders.)

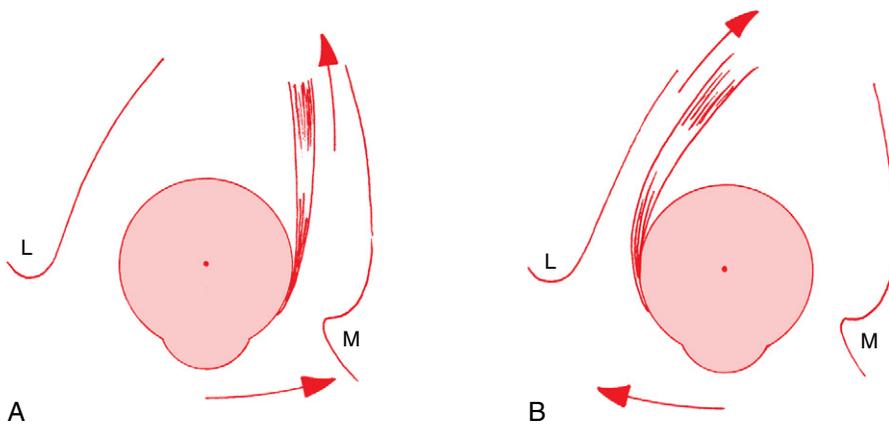


FIGURE 10-12
A, Adduction on contraction of medial rectus muscle with eye in primary position. **B**, Abduction on contraction of lateral rectus muscle with eye in primary position. *L*, Lateral; *M*, medial.

Duane.⁴⁶ This straightforward model has been used widely in the clinical evaluation of extraocular muscles and can be used to describe the movement around the axes that occurs with contraction of each muscle. However, it is important to remember that during eye movements, *all six extraocular muscles are in some state of contraction or relaxation*, and it is strictly hypothetical to discuss the movement of the eye as if only one muscle contracts. In each of these descriptions the eye begins in primary position.

MOVEMENTS FROM PRIMARY POSITION

Horizontal Rectus Muscles

The medial rectus lies parallel to the sagittal axis and perpendicular to the vertical axis; therefore it has only one action, which is rotation around the vertical axis in a nasal direction—adduction. The lateral rectus also lies parallel to the sagittal axis and perpendicular to the vertical axis; contraction causes rotation in a temporal direction—abduction (Figure 10-12).

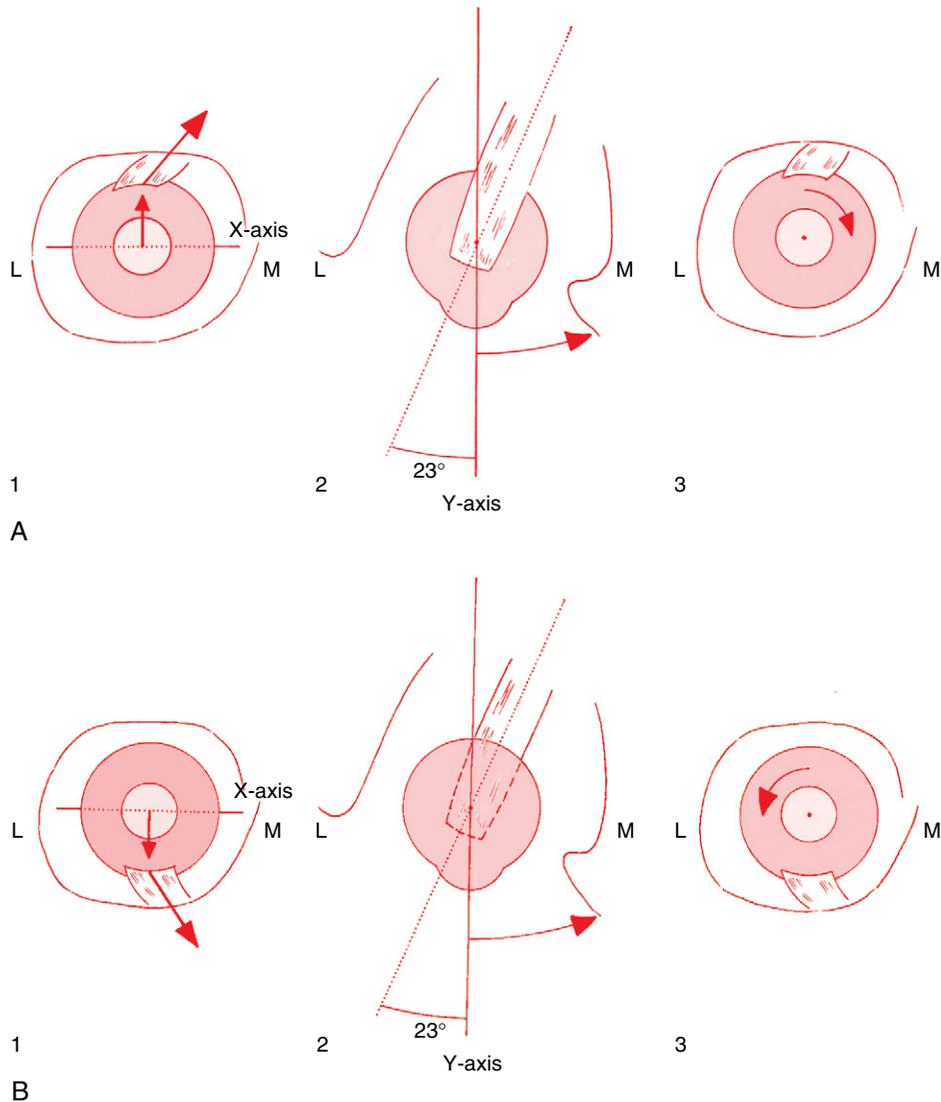


FIGURE 10-13

A, Globe movement around each of Fick's axes on contraction of superior rectus muscle, with eye in primary position. 1, Elevation, movement around the X-axis; 2, adduction, movement around Z-axis; 3, intorsion, movement around Y-axis. **B**, Globe movement around each of Fick's axes on contraction of inferior rectus muscle, with eye in primary position. 1, Depression, movement around X-axis; 2, adduction, movement around Z-axis; 3, extorsion, movement around Y-axis. *L*, Lateral; *M*, medial.

Vertical Rectus Muscles

The action of the superior rectus is more complex than that of the medial and lateral rectus muscles because it lies at an angle to each of the axes; with the insertion above the origin and on the anterior globe, movement around the horizontal axis causes elevation. The muscle insertion is lateral to the origin, so movement around the vertical axis causes adduction; the oblique insertion on the superior surface of the globe causes intorsion on

contraction (Figure 10-13, A). The primary action of the superior rectus is said to be elevation; adduction and intorsion are secondary actions.

The primary action of the inferior rectus is depression, because the insertion is below the origin and on the anterior of the globe. Secondary actions are adduction, because the insertion is lateral to the origin, and extorsion, which results from the oblique insertion on the inferior surface of the globe (Figure 10-13, B).

Table 10-4 Origin, Insertion, and Action of the Extraocular Muscles

Muscle	Origin	Insertion	Primary Action	Secondary Action
Medial rectus	Common ring tendon and optic nerve sheath	Anterior globe	Adduction	None
Lateral rectus	Common ring tendon and greater wing of sphenoid	Anterior globe	Abduction	None
Superior rectus	Common ring tendon and optic nerve sheath	Superior, anterior globe	Elevation	Adduction, intorsion
Inferior rectus	Common ring tendon	Inferior, anterior globe	Depression	Adduction, extorsion
Superior oblique	Anatomic: lesser wing of sphenoid Physiologic: trochlea	Superior, posterior, lateral globe	Intorsion	Depression, abduction
Inferior oblique	Medial maxillary bone	Inferior, posterior, lateral globe	Extorsion	Elevation, abduction

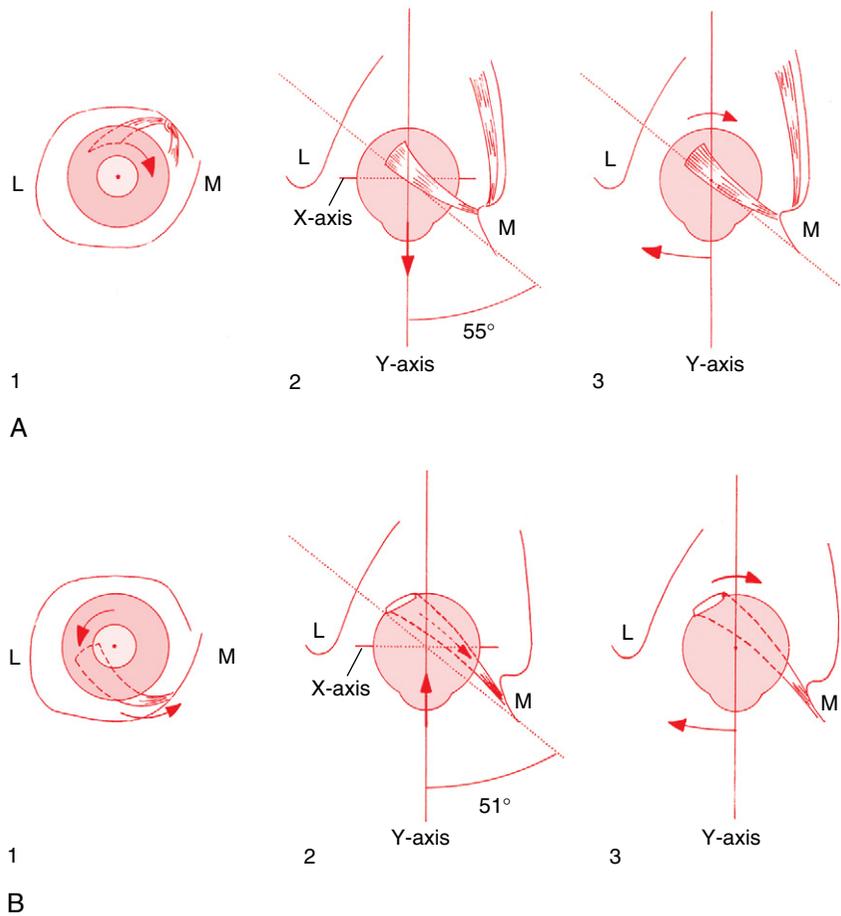


FIGURE 10-14

A, Globe movement around each of Fick's axes on contraction of superior oblique muscle, with eye in primary position. 1, Intorsion, movement around Y-axis; 2, depression, movement around X-axis; 3, abduction, movement around Z-axis. **B**, Globe movement around each of Fick's axes on contraction of inferior oblique muscle, with eye in primary position. 1, Extorsion, movement around Y-axis; 2, elevation, movement around X-axis; 3, abduction, movement around Z-axis. L, Lateral; M, medial.

Oblique Muscles

The primary action of the superior oblique muscle is intorsion.^{5,16,47-49} This action results from the oblique insertion on the posterosuperior lateral quadrant (Table 10-4); contraction rotates the eye around the sagittal axis, causing intorsion. The secondary actions are depression

and abduction.^{5,16,47-49} Depression occurs because the insertion is posterior and inferior to the physiologic origin; contraction of the muscle pulls the back of the eye up, and the anterior pole moves down. Because the insertion is lateral to the trochlea, contraction of the superior oblique pulls the back of the globe medially, thus moving the anterior pole laterally (Figure 10-14, A).

The primary action of the inferior oblique—extorsion—occurs because the muscle wraps around the lower portion of the globe and the insertion is lateral to the origin. Secondary actions are elevation and abduction.^{5,16,47-49} Because the insertion is on the posterior eye and above the origin, contraction pulls the back of the eye down, elevating the front. Abduction occurs because the insertion on the back of the eye is pulled toward the medial side; thus the anterior pole is moved laterally in abduction (Figure 10-14, B).

Some authors offer the contrasting view that the primary action of the superior oblique is depression, that of the inferior oblique is elevation, and the torsional actions are secondary.⁵⁰

MOVEMENTS FROM SECONDARY POSITIONS

As the position of the globe changes, the relationship between the muscle origin and insertion changes relative to the axes, and contraction of a muscle has a different effect than when the eye is in primary position. If the eye is elevated, contraction of the horizontal rectus muscles no longer causes strictly adduction or abduction, but also causes a slight elevation; if the eye is depressed, contraction causes further depression.⁵¹

Vertical Rectus Muscles

With the eye abducted approximately 23 degrees from primary position, the vertical rectus muscles parallel the sagittal axis, and lie perpendicular to the horizontal axis; thus only vertical movement will occur. In this position, contraction of the superior rectus will cause only elevation, and contraction of the inferior rectus will cause only depression⁴⁶ (Figure 10-15, B).

As the eye adducts, it approaches a position where the plane of the vertical rectus muscles is at a right angle to the sagittal axis; this occurs at approximately 67 degrees of adduction (which may be physically impossible because of the connective tissue constraints of the orbit). If the muscle plane of the vertical rectus muscles is at a right angle to the sagittal axis, and thus parallel to the horizontal axis, contraction of the superior or inferior rectus muscle will not cause vertical movement⁴⁶ (Figure 10-15, A).

Oblique Muscles

As the eye adducts 51 to 55 degrees, the plane of the oblique muscles becomes parallel to the sagittal axis and perpendicular to the horizontal axis. In this position the superior oblique will cause only depression, and the inferior oblique will cause only elevation. When the eye

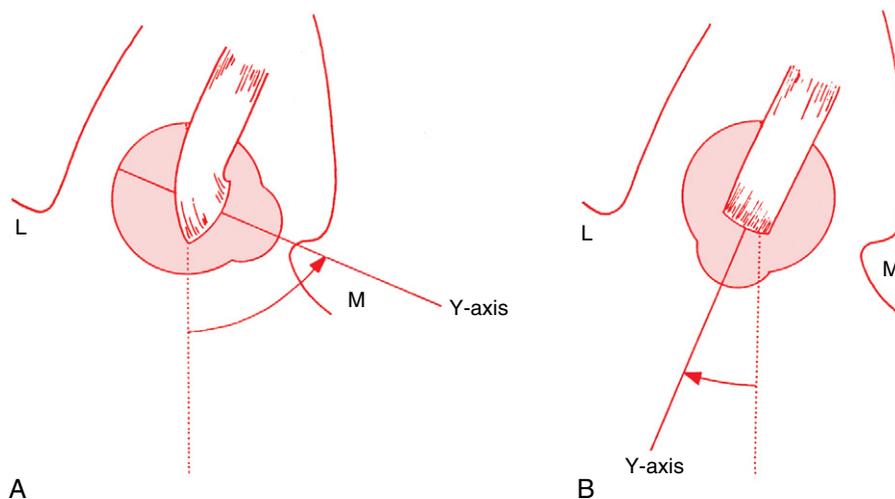
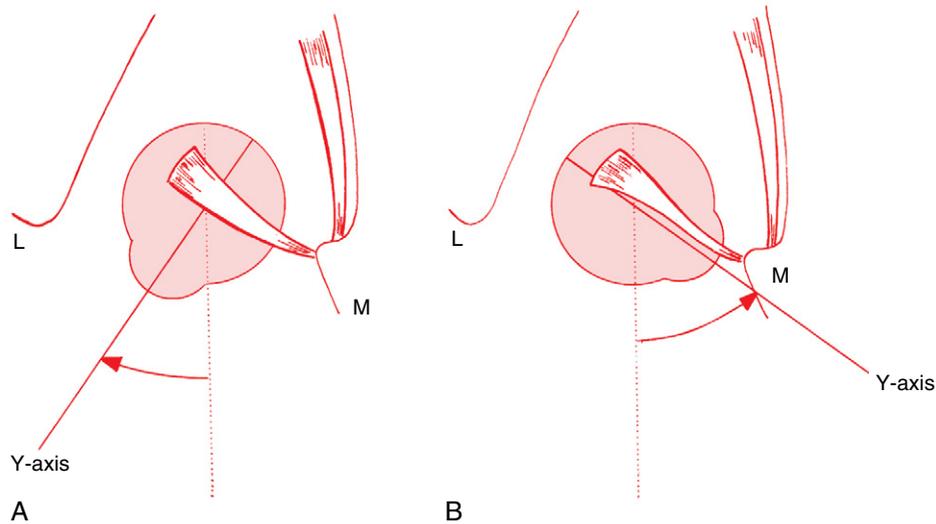


FIGURE 10-15

Relationship between line of muscle movement and Fick's axes when eye is in a secondary position. **A**, When eye is adducted 67 degrees (putting plane of muscle parallel to X-axis), contraction of superior rectus muscle cannot cause elevation. **B**, When eye is abducted 23 degrees (putting plane of muscle perpendicular to X-axis), contraction of superior rectus muscle causes only elevation. *L*, Lateral; *M*, medial.

**FIGURE 10-16**

Relationship between line of muscle movement and Fick's axes when eye is in a secondary position. **A**, When eye is abducted 35 degrees (putting plane of muscle parallel to X-axis), contraction of superior oblique muscle cannot cause depression. **B**, When eye is adducted 55 degrees (putting plane of muscle perpendicular to X-axis), contraction of superior oblique muscle almost exclusively causes depression. *L*, Lateral; *M*, medial.

is abducted 35 to 39 degrees, the plane of the oblique muscles makes a right angle with the sagittal axis and parallels the horizontal axis, and the obliques cannot cause vertical movement⁴⁶ (Figure 10-16).

This analysis is used in the clinical assessment of extraocular muscle function. As the eye increases in abduction, the elevating and depressing abilities of the *vertical rectus muscles* increase. As the eye increasingly moves into adduction, the elevating and depressing abilities of the *oblique muscles* increase.

AGONIST AND ANTAGONIST MUSCLES

In any position of gaze, innervation of all extraocular muscles is controlled carefully by the central nervous system, and each muscle is in some stage of contraction or relaxation. No single muscle acts alone; muscles work together as agonists, antagonists, or synergists. In all these movements, fine motor control should provide for smooth, continuous movements. According to **Sherrington's law of reciprocal innervation**, contraction of a muscle is accompanied by a simultaneous and proportional relaxation of the antagonist.⁵² In adduction the increased contraction of the medial rectus muscle is accompanied by the increased relaxation of the antagonist, the lateral rectus muscle.

When the superior rectus muscle and the inferior oblique muscle contract at the same time, the adduction action of the superior rectus and the abduction action of the inferior oblique, as well as the intorsion of the superior rectus and the extorsion of the inferior oblique, will counteract each other. The resultant eye movement is elevation; the muscles are synergists in elevation. Jampel⁵³ demonstrated this by stimulating the superior rectus and inferior oblique muscles simultaneously and noting that the eye moved directly up.

When the superior oblique and inferior rectus muscles were stimulated simultaneously, the eye moved directly downward.⁵³ The superior oblique and the inferior rectus are synergists in depression. The superior oblique is the antagonist for the inferior oblique in vertical movements and torsional movements but is synergistic for abduction.

In primary position the muscles are in a balanced state, each exerting contraction sufficient to keep the eye centered in the palpebral fissure. If one muscle is inactive, the eye will be deviated from primary position in the direction of the pull of the antagonist of the dysfunctional muscle. If the medial rectus muscle is paralyzed, the eye, in primary position, will be positioned temporally because of the *unopposed* action of the lateral rectus muscle.

CLINICAL COMMENT: EXTRAOCULAR MUSCLE ASSESSMENT

Assessment of eye position and movements can be an important tool in determining the integrity of the extraocular muscles and associated nerves. The practitioner first notes the position of each eye while directing the patient to fixate on a target straight ahead. An eye that is deviated toward the nose would indicate an underactive lateral rectus muscle; the medial rectus is unopposed by the lateral rectus. Figure 10-17, A, shows the direction of pull of each muscle when the eye is in primary position.

Ocular motility testing provides further information on the contractile abilities of the muscles. Evaluation of horizontal eye movement is straightforward. If the eye cannot adduct, the problem lies with the medial rectus; if the eye cannot move into the abducted position, the problem lies with the lateral rectus muscle.

With the more complex movements of the other muscles, the most reliable way to determine a dysfunctional muscle is to put the eye into a position in which one muscle is the primary actor. In the adducted position the oblique muscles are the primary elevator and depressor; in the abducted position the vertical rectus muscles are the primary elevator and depressor. This arrangement can be

represented by the "H" diagrams in Figure 10-17, B. Thus, when doing ocular motility testing it is important to move the eyes to such a position as to isolate the vertical abilities of these muscles. The usual manner of performing ocular motility testing follows:

1. Using a small target, usually a bead, the patient is instructed to follow the target.
2. The horizontal ability is determined first by moving the bead to the far right and to the far left, noting any inability of either eye to follow.
3. In left gaze the bead is elevated to determine the ability of the left superior rectus (left eye is abducted) and the right inferior oblique (right eye is adducted). The bead is depressed to determine the ability of the left inferior rectus and the right superior oblique muscles.
4. In right gaze the bead is elevated to determine the ability of the right superior rectus (right eye is abducted) and the left inferior oblique (left eye is adducted). The bead is depressed to determine the ability of the right inferior rectus and the left superior oblique muscles.

The extensive network of connective tissue septa and fibroelastic pulley system associated with the extraocular muscle may affect eye movement, and MRI may be an additional tool to determine the involved muscle once a strabismic condition is diagnosed.

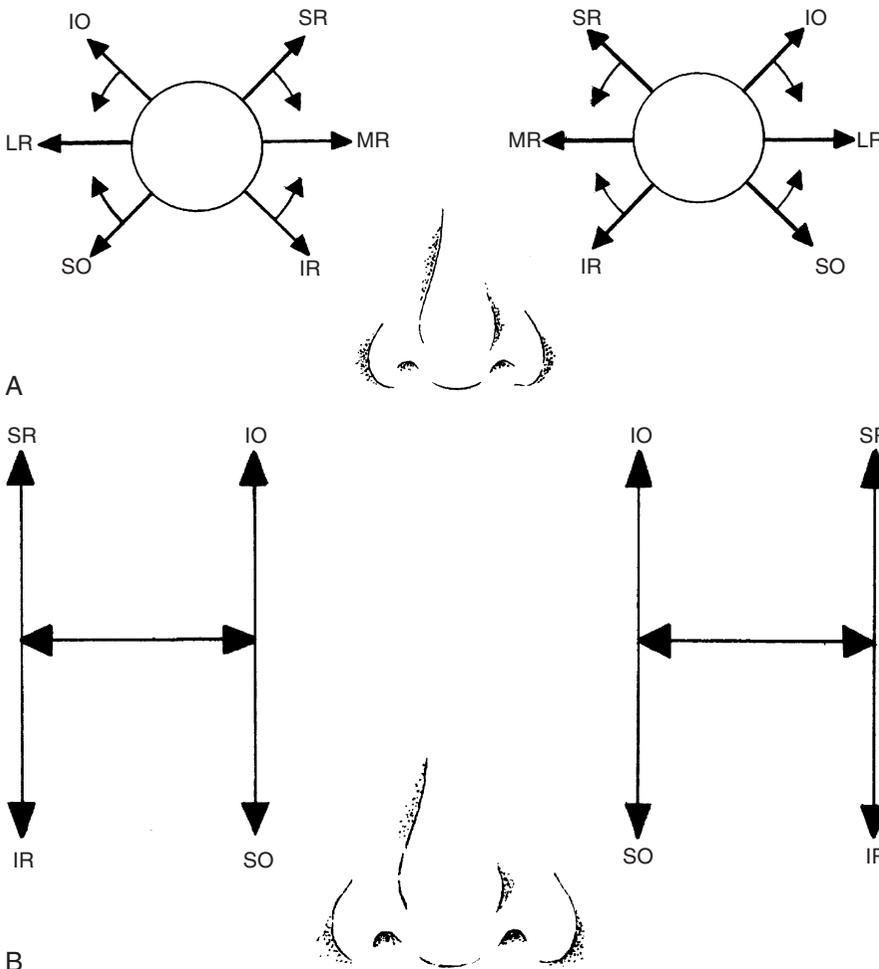


FIGURE 10-17

A, Direction of eye movement on contraction of each muscle, with eye in primary position. For example, if superior rectus muscle contracts, eye will move up and in and intort. Curved arrows represent torsional movements. **B**, Muscles that cause vertical movement when eye is either adducted or abducted. In adduction, for example, muscle that causes elevation is inferior oblique muscle. IO, Inferior oblique; IR, inferior rectus; LR, lateral rectus; MR, medial rectus; SO, superior oblique; SR, superior rectus.

CLINICAL COMMENT: STRABISMUS

When movement is not coordinated between the two eyes and the visual axes are not straight when the patient is asked to look in primary position, the patient is diagnosed with **strabismus**. This condition can be congenital or acquired. In congenital forms of strabismus, suppression is often used as an adaptation response to prevent diplopia. Suppression must be overcome to retrain the muscle to achieve binocular vision even if the treatment includes surgery. In acquired dysfunction the causative factor must be determined.

CLINICAL COMMENT: BROWN'S SUPERIOR OBLIQUE SHEATH SYNDROME

Inability to elevate the eye in the adducted position is usually caused by a dysfunctional inferior oblique muscle. However, such a limitation could also be caused by an immobile superior oblique muscle (Figure 10-18). Using electromyography, Brown⁵⁴ determined that a patient with inability to elevate the eye in adduction had a functional inferior oblique muscle, but that the movement of the superior oblique through the trochlea was restricted. The superior oblique could not lengthen when the inferior oblique contracted.⁵⁴ In congenital Brown's syndrome the cause could be a short or anchored tendon; in acquired Brown's syndrome the cause could be an accumulation of fluid or tissue between the trochlea and the tendon.^{47,55}

CLINICAL COMMENT: LONG-STANDING IMMOBILITY

In assessing ocular motility and determining the damaged muscle, it may be difficult to determine the dysfunctional muscle, especially if the injury is long term. As a muscle becomes inactive, it can become immobile and can neither contract nor stretch, in effect influencing the abilities of the other extraocular muscles to move the eye.

CLINICAL COMMENT: HYPERTHYROIDISM (GRAVES' DISEASE)

Enlargement of the extraocular muscles produced by Graves' disease is caused by chronic inflammatory infiltration of the muscles with glycoprotein and mucopolysaccharide deposition, resulting in proptosis.¹ In addition, restricted ocular motility is evident. However, evaluation of the restricted movement may not depict the correct dysfunctional muscle because fibrosis of the muscles can occur, limiting muscle activity. For example, if the medial rectus is fibrotic, eye movement may be restricted in the lateral direction because the medial rectus is unable to elongate and acts as a check on lateral movement. Restriction may appear to be impairment of the lateral rectus but may actually be caused by the fibrotic medial rectus muscle.



A



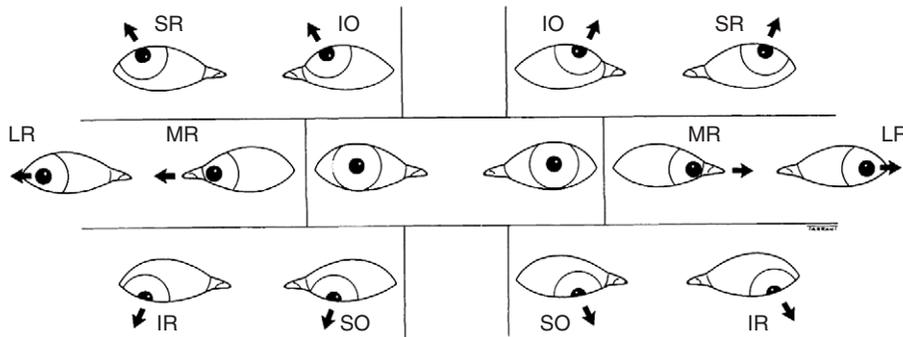
B



C

FIGURE 10-18

Brown's syndrome of left eye. **A**, Eyes straight in primary position. **B**, Limited elevation in adduction. **C**, Normal elevation in abduction. Positive forced duction test on elevating globe in adduction (not shown). (From Kanski JJ, Nischal KK: *Ophthalmology: clinical signs and differential diagnosis*, St Louis, 1999, Mosby.)

**FIGURE 10-19**

Six cardinal positions of gaze and yoke muscles. *IO*, Inferior oblique; *IR*, inferior rectus; *LR*, lateral rectus; *MR*, medial rectus; *SO*, superior oblique; *SR*, superior rectus. (From Kanski JJ: *Clinical ophthalmology*, ed 3, Oxford, England, 1995, Butterworth-Heinemann, p 429.)

CLINICAL COMMENT: FORCED DUCION TEST

If a fibrotic muscle is suspected, a forced duction test can be performed. With the patient under topical anesthesia, the practitioner grasps the conjunctiva near the limbus and attempts to move the eye in a direction opposite from the suspected restriction. Resistance will be met if the cause is fibrosis, but if the muscle is paralyzed, the eye can be moved. For instance, if the lateral rectus is suspect, the practitioner would attempt to move the eye medially. If the lateral rectus is fibrotic, resistance to movement occurs; if it is paralyzed, the eye can be moved with the forceps.⁴⁸

YOKE MUSCLES

Yoke muscles are those muscles of the two eyes acting together to cause binocular movements (Figure 10-19). **Hering's law of equal innervation** states that the innervation to the muscles of the two eyes is equal and simultaneous. Thus, the movements of the two eyes are normally symmetric.⁵⁶ In dextroversion, equal and simultaneous innervation is supplied to the yoke muscles—the right lateral rectus and left medial rectus; in convergence, equal and simultaneous innervation is supplied to the yoke muscles—the right medial rectus and left lateral rectus.

PAIRED ANTAGONIST MODEL

A model by Boeder⁵¹ analyzes the actions of the extraocular muscles as antagonist pairs. Figure 10-20 shows the path that the anterior pole of the eye traces with contraction of these pairs. The vertical pair of muscles have primary actions of elevation and depression and secondary actions of adduction and torsion. Adduction increases with medial movement, as do the torsional effects. In abduction, both muscles must relax.⁵¹

The primary actions of the paired obliques are intorsion and extorsion. The oblique muscle tendons

insert obliquely into the globe, and the torsional effects do not diminish with horizontal movement because the insertion does not act as a unit. In adduction the medial fibers of the superior oblique tendon exert greater contractile force, and in abduction the lateral fibers are shortened.⁵⁶ In adduction the lateral fibers of the inferior oblique tendon are shortened, and in abduction the medial fibers contract.⁵³

The contraction of one muscle is associated with lengthening of its antagonist. This state of relaxation or extension is considered an activity equivalent to contraction. In all positions of gaze, all muscles are in some state of activity. An analysis of the change of length of each muscle during a simple horizontal excursion shows that as the medial rectus contracts, the lateral rectus lengthens, and vice versa. The vertical rectus muscles behave as one, both contracting in adduction and lengthening in abduction. The obliques co-contract in abduction, but in adduction the superior oblique lengthens and the inferior oblique shortens⁵¹ (Figure 10-21).

COMPLEXITY OF THE OBLIQUE MUSCLES

Some controversy exists over the horizontal abilities of the inferior oblique muscle. The relationship of the muscle plane of the inferior oblique with the vertical axis determines whether the inferior oblique is an adductor or an abductor. If the muscle plane lies in front of the vertical axis, the inferior oblique will aid in adduction. With increasing lateral movement of the eye, however, a point will be reached at which the inferior oblique plane is put behind the vertical axis, causing the inferior oblique then to aid in abduction.³³ Animal studies in which the muscles are stimulated directly either singularly or collectively seem to support this view.^{53,57} When the superior oblique and inferior oblique were stimulated simultaneously, no ocular movement occurred; in some positions, these two muscles appeared to be complete antagonists, and

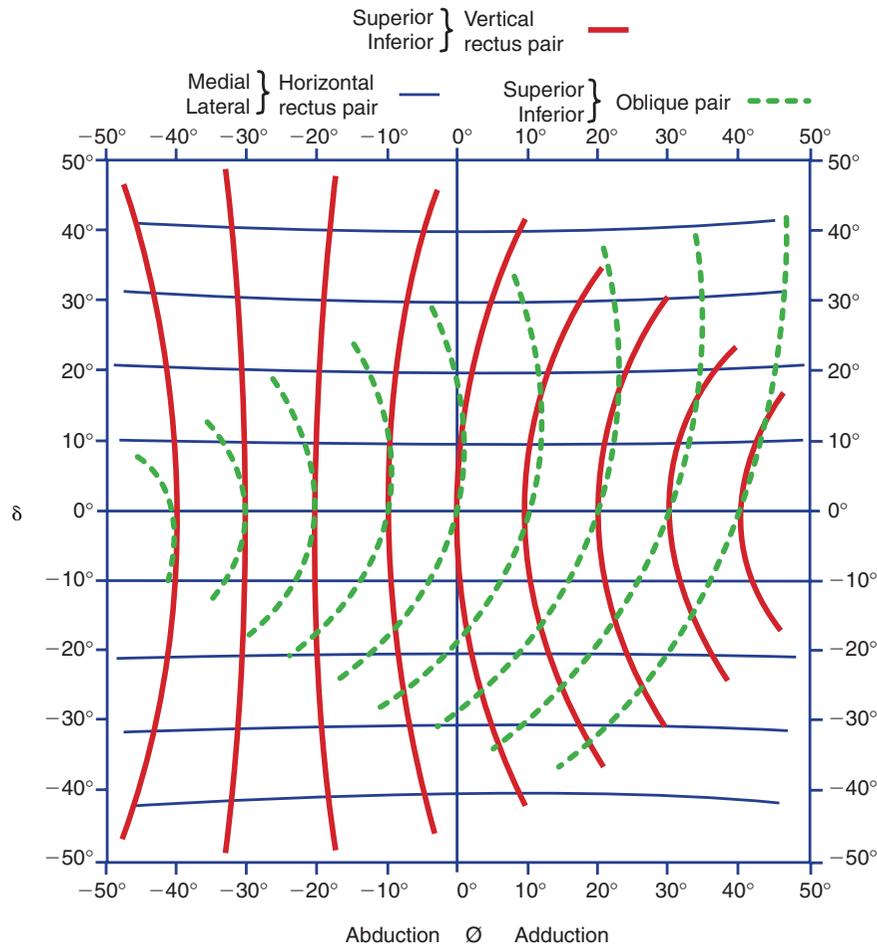


FIGURE 10-20
Traces of line of fixation with activity of each of three muscle pairs in various positions of gaze.
(From Boeder P: *Am J Ophthalmol* 51:469, 1961.)

abduction did not occur. These observations do not change the model used clinically. In adduction the obliques are responsible for elevation and depression, and in abduction the vertical recti are responsible for elevation and depression.

INNERVATION AND BLOOD SUPPLY

INNERVATION

The medial rectus, inferior rectus, and inferior oblique muscles are innervated by the inferior division of the oculomotor nerve. The superior rectus muscle is innervated by the superior division of the oculomotor nerve. The lateral rectus muscle is supplied by the

abducens nerve. The superior oblique muscle is innervated by the trochlear nerve. (See Table 10-3 and Figure 10-7.)

BLOOD SUPPLY

The extraocular muscles are supplied by two muscular branches from the ophthalmic artery: The superior (lateral) branch supplies the superior and lateral rectus and the superior oblique muscles, and the inferior (medial) branch supplies the inferior and medial rectus and the inferior oblique muscles.^{1,58} Other arteries make various contributions to the extraocular muscle blood supply, including the lacrimal, supraorbital, and infraorbital arteries. These vessels and the muscles they supply are described in Chapter 11.

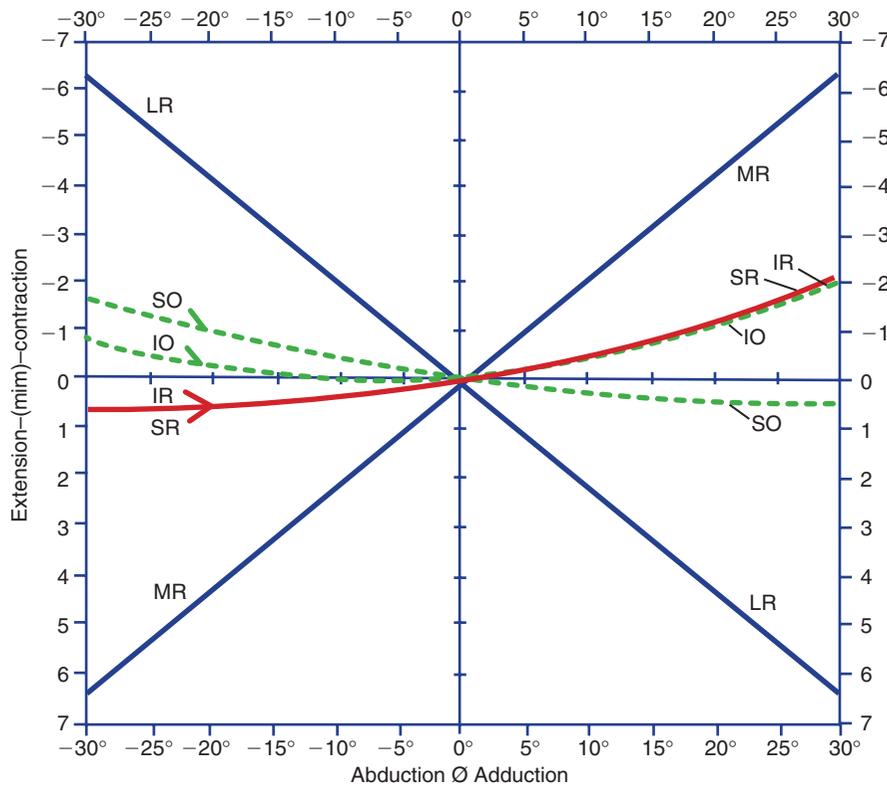


FIGURE 10-21

Changes in muscle length of all extraocular muscles occurring in a horizontal rotation. IO, Inferior oblique; IR, inferior rectus; LR, lateral rectus; MR, medial rectus; SO, superior oblique; SR, superior rectus. (From Boeder P: *Am J Ophthalmol* 51:469, 1961.)

AGING CHANGES IN THE EXTRAOCULAR MUSCLES

Both horizontal rectus muscles are displaced inferiorly with age, with the medial rectus displaced more than the lateral rectus. This may be the cause of a constant partial depression and may contribute to the impaired ability to elevate the eyes often observed in elderly persons, predisposing them to an incomitant (nonconcomitant) strabismus.⁴³ The superior rectus and inferior rectus muscles do not change locations.⁴³

Other age-related changes in extraocular muscles include a greater variety in fiber sizes, increased connective tissue in the muscle, increased adipose tissue in the bundles, deposits of lipofuscin, and degenerative changes.⁵⁹

REFERENCES

1. Doxanas MT, Anderson RL: *Clinical orbital anatomy*, Baltimore, 1984, Williams & Wilkins, p 116.
2. Honda H, Asakura S: Calcium-triggered movement of regulated actin in vitro: a fluorescence microscopy study, *J Mol Biol* 205(4):677, 1989.
3. Bagni MA, Cecchi G, Colomo F et al: Tension and stiffness of frog muscle fibres at full filament overlap, *J Muscle Res Cell Motil* 11:371, 1990.
4. Smith DA: The theory for sliding filament models for muscle contraction, *J Theor Biol* 146(4):433, 1990.
5. Eggers HM: Functional anatomy of the extraocular muscles. In Tasman W, Jaeger EA, editors: *Duane's foundations of clinical ophthalmology*, vol 1, Philadelphia, 1994, Lippincott.
6. Guyton AC: *Textbook of medical physiology*, ed 8, Philadelphia, 1991, Saunders, p 76.
7. Wirtschafter JD: Neuroanatomy of the ocular muscles. In Reeh MJ, Wobig JL, Wirtschafter JD, editors: *Ophthalmic anatomy*, San Francisco, 1981, American Academy of Ophthalmology, p 267.
8. Namba T, Nakamura T, Grob D: Motor nerve endings in human extraocular muscle, *Neurology* 18:403, 1968.
9. Hess A: Further morphological observations of "en plaque" and "en grappe" nerve endings on mammalian extrafusal muscle fibers with the cholinesterase technique, *Rev Can Biol* 21:241, 1962.
10. Brandt DE, Leeson CR: Structural differences of fast and slow fibers in human extraocular muscle, *Am J Ophthalmol* 62:478, 1966.
11. Brenin GM: The structure and function of extraocular muscle: an appraisal of the duality concept, *Am J Ophthalmol* 71:1, 1971.
12. Peachy L: The structure of the extraocular muscle fibers of mammals. In Bach-y-Rita P, Collins CC, Hyde JE, editors: *The control of eye movements*, New York, 1971, Academic Press, p 47.
13. Scott AB, Collins CC: Division of labor in human extraocular muscle, *Arch Ophthalmol* 90:319, 1973.

14. Montagnani S, De Rosa P: Morphofunctional features of human extrinsic ocular muscles, *Doc Ophthalmol* 72(2):119, 1989.
15. Porter JD: Extraocular muscle: cellular adaptations for a diverse functional repertoire, *Ann NY Acad Sci* 956:7, 2002.
16. Burde RM, Feldon SE: The extraocular muscles. In Hart WM Jr, editor: *Adler's physiology of the eye*, ed 9, St Louis, 1992, Mosby, p 101.
17. Porter JD, Andrade FH, Baker RS: The extraocular muscles. In Kaufman PL, Alm A, editors: *Adler's physiology of the eye*, ed 10, St Louis, 2003, Elsevier, p 787.
18. Ruskell GL: Extraocular muscle proprioceptors and proprioception, *Prog Ret Eye Res* 18(3):269, 1999.
19. Alpern M: Movements of the eyes. In Dawson H, editor: *The eye*, New York, 1962, Academic Press.
20. Walls GL: The evolutionary history of eye movements, *Vision Res* 2:69, 1962.
21. Linwong M, Herman SJ: Cycloduction of the eyes with head tilt, *Arch Ophthalmol* 85:570, 1971.
22. Jampel RS: Ocular torsion and the function of the vertical extraocular muscles, *Am J Ophthalmol* 77:292, 1975.
23. Duke-Elder S: *Textbook of ophthalmology*, vol 4, St Louis, 1949, Mosby.
24. Diamond SG, Markham CH: Ocular counterrolling as an indicator of vestibular otolith function, *Neurology* 33:1460, 1983.
25. Collewijn H, Van der Steer J, Ferman L et al: Human ocular counterroll: assessment of static and dynamic properties from electromagnetic scleral coil recordings, *Exp Brain Res* 59:185, 1985.
26. Ott D, Eckmiller R: Ocular torsion measured by TV and scanning laser ophthalmoscopy during horizontal pursuit in humans and monkeys, *Invest Ophthalmol Vis Sci* 30(12):2512, 1989.
27. Warwick R: *Eugene Wolff's anatomy of the eye and orbit*, ed 7, Philadelphia, 1976, Saunders, p 248.
28. Burton H: Somatic sensations from the eye. In Hart WM Jr, editor: *Adler's physiology of the eye*, ed 9, St Louis, 1992, Mosby, p 185.
29. Koorneef L: Orbital connective tissue. In Jakobiec FA, editor: *Ocular anatomy, embryology, and teratology*, Philadelphia, 1982, Harper & Row, p 835.
30. DeGottreau P, Gajisin S: Anatomic, histologic, and morphometric studies of the ocular rectus muscles and their relation to the eye globe and Tenon's capsule, *Klin Monatsbl Augenheilkd* 200(5):515, 1992 (abstract).
31. Porter JD, Poukens V, Baker RS et al: Structure-function correlations in the human medial rectus extraocular muscle pulleys, *Invest Ophthalmol Vis Sci* 37:468, 1996.
32. Wobig JL: The eyelids. In Reeh MJ, Wobig JL, Wirtschafter JD, editors: *Ophthalmic anatomy*, San Francisco, 1981, American Academy of Ophthalmology, p 38.
33. Krewson WE: Comparison of the oblique extraocular muscles, *Arch Ophthalmol* 32:204, 1944.
34. Wobig JL: The extrinsic ocular muscles. In Reeh MJ, Wobig JL, Wirtschafter JD, editors: *Ophthalmic anatomy*, San Francisco, 1981, American Academy of Ophthalmology, p 33.
35. Wasicky R, Ziya-Ghazvini F, Blumer R et al: Muscle fiber types of human extraocular muscles: a histochemical and immunohistochemical study, *Invest Ophthalmol Vis Sci* 41(5):980, 2000.
36. Demer JL, Oh SY, Poukens V: Evidence for active control of rectus extraocular muscle pulleys, *Invest Ophthalmol Vis Sci* 41:1280, 2000.
37. Oh SY, Poukens V, Cohen MS et al: Structure-function correlation of laminar vascularity in human rectus extraocular muscles, *Invest Ophthalmol Vis Sci* 42:17, 2001.
38. Clark RA, Miller JM, Demer JL: Three-dimensional location of human rectus pulleys by path inflections in secondary gaze positions, *Invest Ophthalmol Vis Sci* 41:3787, 2000.
39. Clark RA, Miller JM, Demer JL: Location and stability of rectus muscle pulleys, *Invest Ophthalmol Vis Sci* 38:227, 1997.
40. Ettl A, Kramer J, Daxer A et al: High-resolution magnetic resonance imaging of the normal extraocular musculature, *Eye* 11:793, 1997.
41. Demer JL, Miller JM, Poukens V: Surgical implications of the rectus extraocular muscle pulleys, *J Pediatr Ophthalmol Strabismus* 33(4):208, 1996.
42. Demer JL, Poukens V, Miller JM et al: Innervation of extraocular pulley smooth muscle in monkeys and humans, *Invest Ophthalmol Vis Sci* 38(9):1774, 1997.
43. Clark RA, Demer JL: Effect of aging on human rectus extraocular muscle paths demonstrated by magnetic resonance imaging, *Am J Ophthalmol* 134:872, 2002.
44. Miller JM: Functional anatomy of normal human rectus muscles, *Vision Res* 29(2):223, 1989.
45. Miller JM, Demer JL, Rosenbaum AL: Effects of transposition surgery on rectus muscle paths by magnetic resonance imaging, *Ophthalmology* 100(4):475, 1993.
46. Duane A: The monocular movements, *Arch Ophthalmol* 8:531, 1936.
47. Leigh RJ, Zee DS: *The neurology of eye movements*, Philadelphia 1983, Davis, pp 145, 170.
48. Von Noorden GK, Maumenee AE: *Atlas of strabismus*, ed 2, St Louis, 1973, Mosby, pp 6, 112.
49. Kanski JJ: *Clinical ophthalmology*, ed 3, Oxford, England, 1994, Butterworth-Heinemann, p 428.
50. Bron AJ, Tripathi RC, Tripathi BJ: *Wolff's anatomy of the eye and orbit*, ed 8, London, 1997, Chapman & Hall.
51. Boeder P: The cooperation of extraocular muscles, *Am J Ophthalmol* 51:469, 1969.
52. Sherrington CS: Experimental note on two movements of the eyes, *J Physiol (Lond)* 17:27, 1984.
53. Jampel RS: The fundamental principle of the action on the oblique ocular muscles, *Am J Ophthalmol* 69:623, 1970.
54. Brown HW: Congenital structural muscle anomalies. In Allen ED, editor: *Strabismus ophthalmic symposium*, St Louis, 1950, Mosby, p 250.
55. Helveston EM, Merriam WW, Ellis FD et al: The trochlea, a study of the anatomy and physiology, *Ophthalmology* 89:124, 1982.
56. Hering E: *Theory of binocular vision*, New York, 1977, Plenum.
57. Jampel RS: The action of the superior oblique muscle, *Arch Ophthalmol* 75:535, 1966.
58. Hayreh SS: The ophthalmic artery. III. Branches, *Br J Ophthalmol* 46:212, 1962.
59. McKelvie P, Friling R, Davey K et al: Changes as the result of ageing in extraocular muscles: a post-mortem study, *Aust NZ J Ophthalmol* 27:420, 1999.

Circulation to the head and neck is supplied by the common carotid artery, which divides into two vessels, the internal carotid and the external carotid. The internal carotid artery supplies the structures within the cranium, including the eye and related structures. The external carotid artery supplies the superficial areas of the head and neck and provides a small portion of the circulation to the ocular adnexa.

INTERNAL CAROTID ARTERY

The **internal carotid artery** runs upward through the neck and enters the skull through the carotid canal, located in the petrous portion of the temporal bone just superior to the jugular fossa. Within the anterior portion of the canal, only thin bone separates the artery from the cochlea and the trigeminal ganglion. The internal carotid artery leaves the canal and immediately enters the cavernous sinus, where it runs forward along the medial wall beside the sphenoid bone; it then exits through the roof of the sinus. Within the sinus the abducens nerve is closely adherent to the lateral border of the internal carotid.¹ Throughout its pathway—up the neck, into the skull, and through the cavernous sinus—the internal carotid is surrounded by a plexus of sympathetic nerves from the superior cervical ganglion. The second and third cranial nerves accompany the vessel as it leaves the sinus; the optic nerve lies medial and the oculomotor nerve lies lateral to the internal carotid. The ophthalmic artery branches from the internal carotid artery just as it emerges from the cavernous sinus medial to the anterior clinoid process of the sphenoid bone. It is usually the first major branch from the internal carotid artery.²

CLINICAL COMMENT: SCLEROSIS OF THE INTERNAL CAROTID ARTERY

In some postmortem studies, compression of the optic nerve caused by sclerosis of the internal carotid artery was found, with pathologic changes such as atrophy, evident in the optic nerve. Visual field defects may be caused by this compression and should be one of the differential diagnoses when optic nerve head atrophy accompanies a field defect.³

OPHTHALMIC ARTERY

The **ophthalmic artery** enters the orbit within the dural sheath of the optic nerve and passes through the optic canal, below and lateral to the nerve² (Figure 11-1). Once in the orbit the ophthalmic artery emerges from the meningeal sheath, runs inferolateral to the optic nerve for a short distance, and then crosses either above or below the nerve. Together with the nasociliary nerve, the ophthalmic artery runs toward the medial wall of the orbit.⁴ The artery continues forward between the medial rectus and superior oblique muscles, giving off branches to various areas. Just posterior to the superior medial orbital margin, it divides into its terminal branches, the supratrochlear and dorsonasal arteries. In general, the intraorbital arteries are located in the adipose compartments and perforate the connective tissue septa as they pass between sections.⁵ The ophthalmic artery is the main blood supply to the globe and adnexa but is supplemented by a few branches from the external carotid supply.

Throughout its rather tortuous course, many branches from the ophthalmic artery emerge: (1) central retinal artery, (2) lacrimal artery, (3) ciliary arteries (usually two), (4) ethmoid arteries (usually two), (5) supraorbital artery, (6) muscular arteries (usually two), (7) medial palpebral arteries (superior and inferior), (8) supratrochlear artery, and (9) dorsonasal artery.

Marked variability is evident in the order of the origin of the branches of the ophthalmic artery, and the sequence appears to correlate with whether the artery crosses above or below the optic nerve. The most common patterns of distribution are shown in Table 11-1.⁶ Many anatomic variations can occur in the branches and their courses; those most often reported are included here.

CENTRAL RETINAL ARTERY

One of the first branches of the ophthalmic artery, the **central retinal artery**, is among the smallest branches. The central retinal artery leaves the ophthalmic artery as it lies below the optic nerve (see Figure 11-1). The artery runs forward a short distance before entering the meningeal sheath of the nerve about 10 to 12 mm behind the globe (Figure 11-2). While within the optic nerve, the central retinal artery provides branches to the

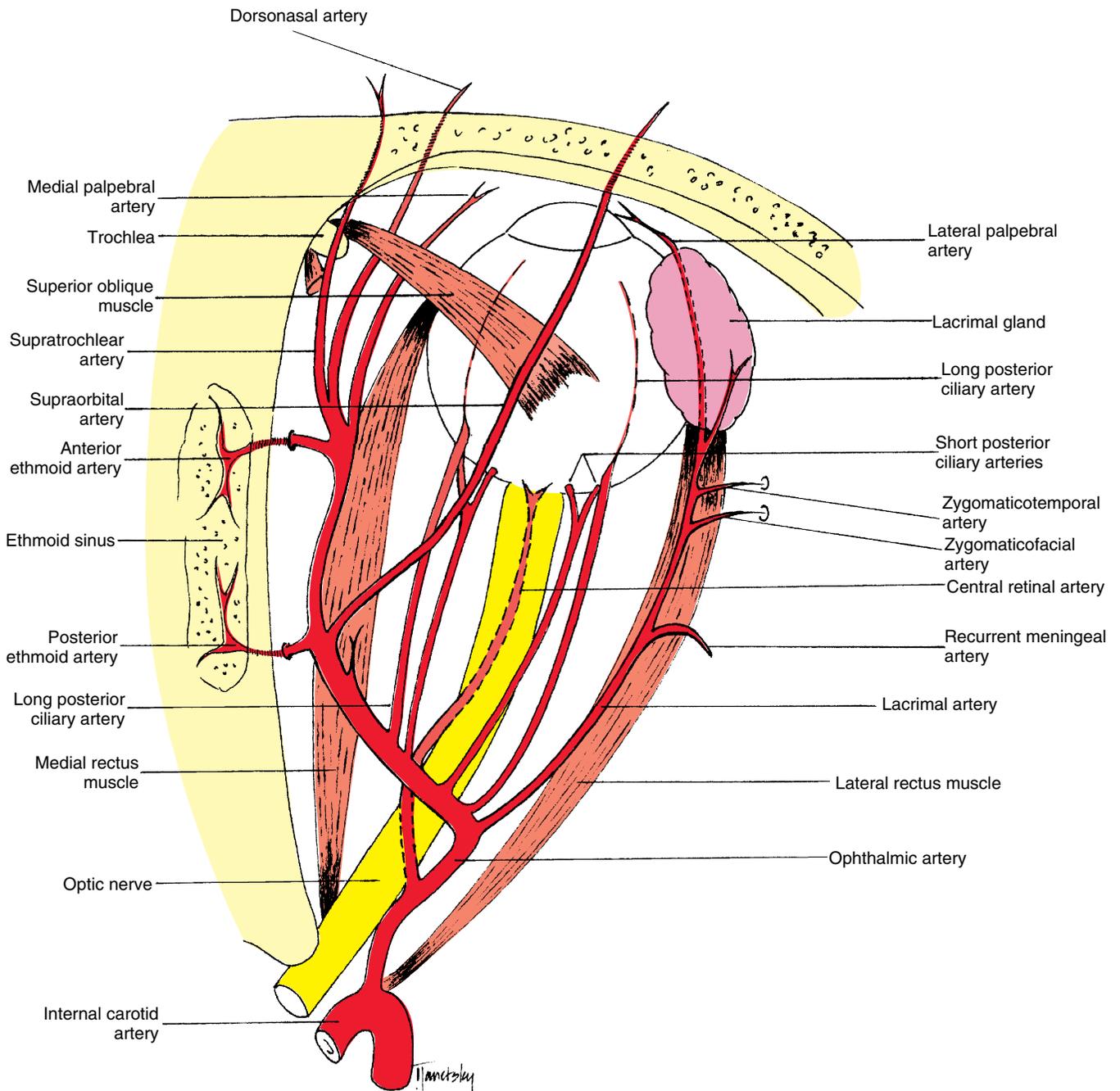


FIGURE 11-1
Orbit viewed from above, illustrating branches of ophthalmic artery.

Table 11-1 Order of Origin of Branches of Ophthalmic Artery

Order of Origin	Sequence of Branches when Ophthalmic Artery:	
	Crosses Above Optic Nerve	Crosses Below Optic Nerve
1	Central retinal and medial posterior ciliary	Lateral posterior ciliary
2	Lateral posterior ciliary	Central retinal
3	Lacrimal	Medial muscular
4	Muscular to superior rectus and levator	Medial posterior ciliary
5	Posterior ethmoid and supraorbital, jointly or separately	Lacrimal
6	Medial posterior ciliary	Muscular to superior rectus and levator
7	Medial muscular	Posterior ethmoid and supraorbital, jointly or separately
8	Muscular to superior oblique and medial rectus, jointly or separately	Muscular to superior oblique and medial rectus, jointly or separately
9	To areolar tissue	Anterior ethmoid
10	Anterior ethmoid	To areolar tissue
11	Medial palpebral or inferior medial palpebral	Medial palpebral or inferior medial palpebral
12	Superior medial palpebral	Superior medial palpebral
Terminal	Dorsonasal and supratrochlear	Dorsonasal and supratrochlear

Modified from Hayreh SS: *Br J Ophthalmol* 46:212, 1962.

nerve and pia mater.⁶ (Often, these branches are called collateral branches.) As the central retinal artery runs forward within the optic nerve, a sympathetic nerve plexus (the nerve of Tiedemann) surrounds the artery.⁷ The central retinal artery passes through the lamina cribrosa and enters the optic disc just nasal to center, branching superiorly and inferiorly. These branches divide into nasal and temporal branches, then continue to branch dichotomously within the retinal nerve fiber layer. The retinal blood vessels are discussed in Chapter 4.

CLINICAL COMMENT: RETINAL VENOUS BRANCH OCCLUSION

The branches of the central retinal artery and vein are joined in a common connective tissue sheath at the point where the vessels cross each other. Generally, the artery crosses over the vein and, in such disease processes as arteriosclerosis, may compress the vein at the crossing, causing at first a deflection of the vessel, which in time may progress to a venous occlusion. Restriction of flow in the vein results in retinal edema and hemorrhage in the area surrounding the occlusion.

LACRIMAL ARTERY

One of the largest branches, the **lacrimal artery**, leaves the ophthalmic artery just after it enters the orbit (see Figure 11-1); rarely, it branches before the ophthalmic artery enters the optic canal.⁸ The lacrimal artery and the lacrimal nerve run forward along the upper border

of the lateral rectus muscle. Within the orbit the lacrimal artery may supply branches to the lateral rectus muscle.

A **recurrent meningeal artery** (see Figure 11-1) might branch from the lacrimal artery and course back, leaving the orbit through the lateral aspect of the superior orbital fissure and then forming an anastomosis with the middle meningeal artery, a branch from the external carotid artery circulation.⁹ Other branches, the **zygomaticotemporal artery** and the **zygomaticofacial artery**, exit the orbit through foramina of the same name within the zygomatic bone (see Figure 11-1) and anastomose with branches from the external carotid in the temporal fossa and on the face.⁶

The lacrimal artery continues forward to supply the lacrimal gland. Terminal branches pass through the gland, pierce the orbital septum, and enter the lateral side of the upper and lower eyelids to form the **lateral palpebral arteries** (Figure 11-3). These anastomose with branches from the medial palpebral arteries and form vessel arches called the **palpebral arcades**. Other terminal branches from the lacrimal artery enter the conjunctiva and form a capillary network.

POSTERIOR CILIARY ARTERIES

The **posterior ciliary arteries** are branches of the ophthalmic artery, and much variation can occur in their distribution.¹⁰ The **short posterior ciliary arteries** arise as one or two branches that then form 10 to 20 branches.

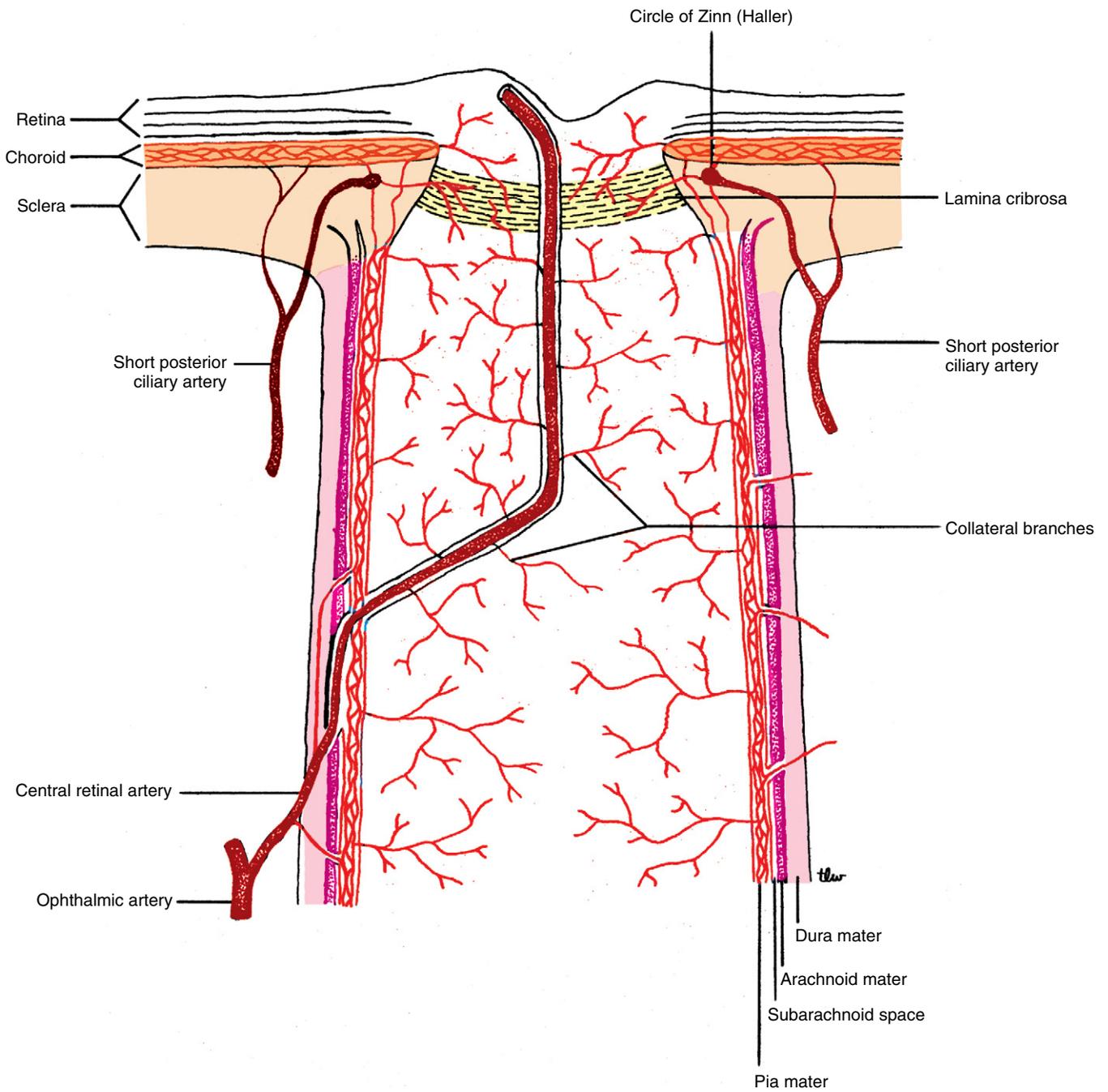


FIGURE 11-2
Longitudinal section of the optic nerve.

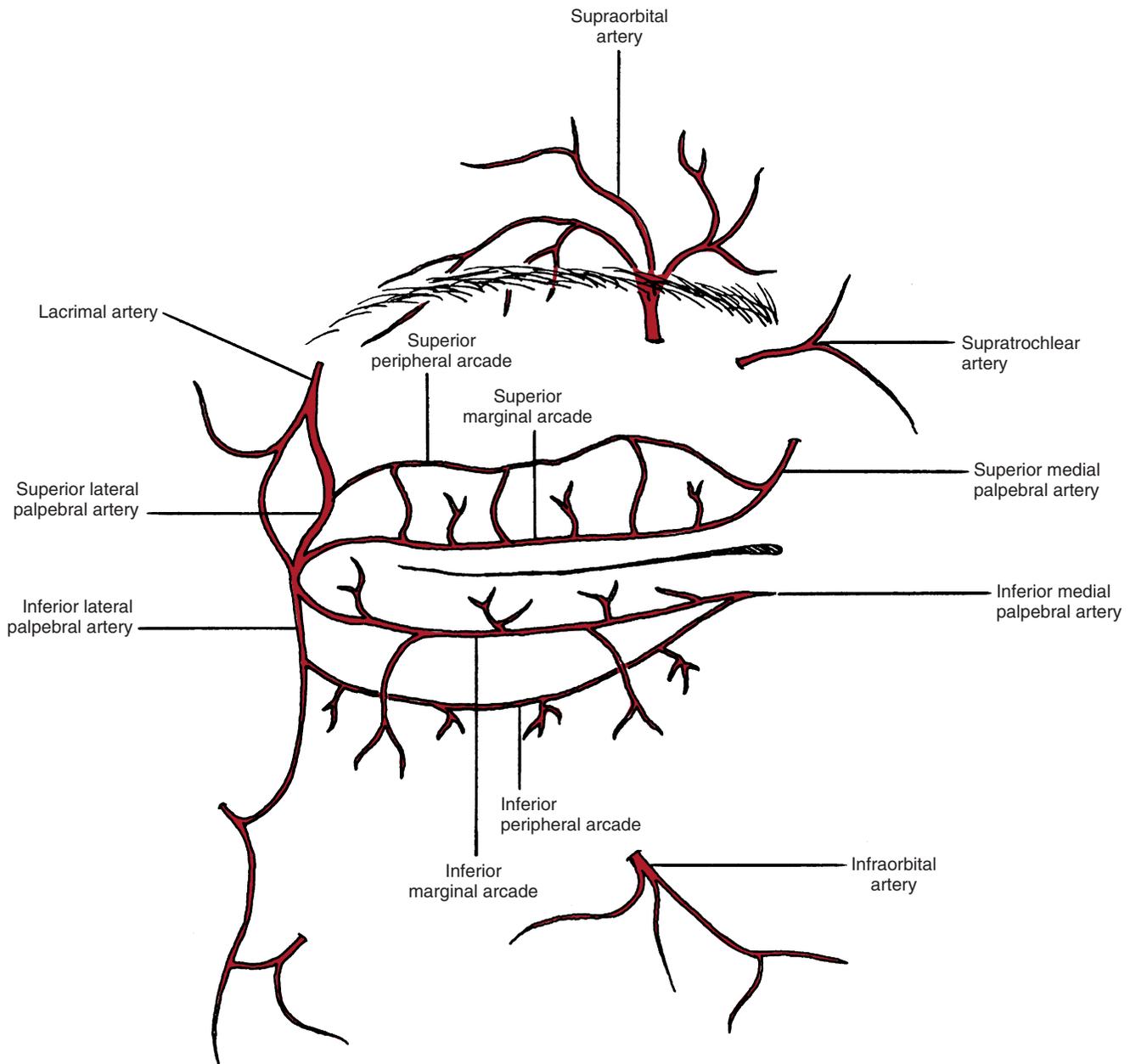
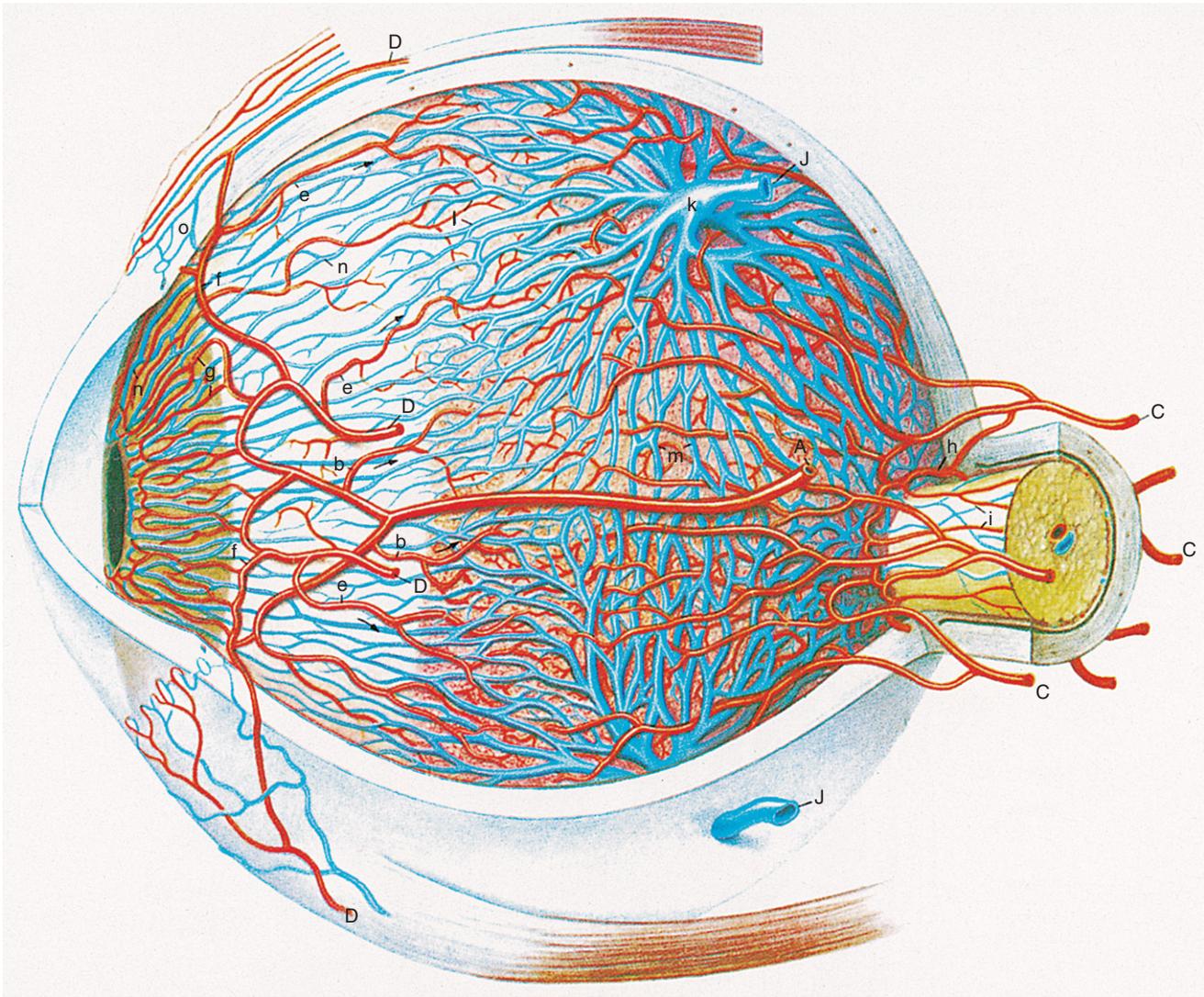


FIGURE 11-3
Lateral and medial palpebral arteries.

They enter the sclera in a ring around the optic nerve and form the arterial network within the choroidal stroma (Figure 11-4). Other branches from the short posterior ciliary arteries anastomose to form the **circle of Zinn (Zinn-Haller)** (see Figure 11-2), which encircles the optic nerve at the level of the choroid.^{11,12} The most superficial nerve fibers that occupy the surface of the optic disc are supplied by capillaries from the

retinal vasculature.^{12,13} The peripapillary choroidal network, formed by branches from the short posterior ciliary arteries, supplies the remaining prelaminar region of the optic nerve.¹³⁻¹⁵ These vessels do not anastomose with the peripapillary choriocapillaris.¹³ The laminar region is supplied by the short posterior ciliary arteries either directly or as branches from the circle of Zinn.¹³⁻¹⁶

**FIGURE 11-4**

Uveal blood vessels. Blood supply of the eye is derived from ophthalmic artery. Except for central retinal artery, which supplies inner retina, almost the entire blood supply of the eye comes from the uveal vessels. There are two long posterior ciliary arteries; one enters uvea nasally and one enters temporally along horizontal meridian of eye near optic nerve (A). These two arteries give off three to five branches (b) at the ora serrata, which pass directly back to form anterior choriocapillaris. These capillaries nourish retina from equator forward. Short posterior ciliary arteries enter choroid around optic nerve (C). They divide rather rapidly to form posterior choriocapillaris, which nourishes retina as far anteriorly as equator (choriocapillaris not shown). This system of capillaries is continuous with those derived from long posterior ciliary arteries. Anterior ciliary arteries (D) pass forward with rectus muscles, then pierce sclera to enter ciliary body. Before joining major circle of iris, these arteries give off 8 to 12 branches (e) that pass back through ciliary muscle to join anterior choriocapillaris. Major circle of iris (f) lies in pars plicata and sends branches posteriorly into ciliary body as well as forward into iris (g). Circle of Zinn (h) is formed by pial branches (i) as well as branches from short posterior ciliary arteries. Circle of Zinn lies in sclera and furnishes part of blood supply to optic nerve and disc. Vortex veins exit from eye through posterior sclera (j) after forming an ampulla (k) near internal sclera. Venous branches that join anterior and posterior part of vortex system are meridionally oriented and are fairly straight (l), whereas those joining vortices on medial and lateral sides are oriented circularly about the eye (m). Venous return from iris and ciliary body (n) is mainly posterior into vortex system, but some veins cross anterior sclera and limbus (o) to enter episcleral system of veins. (From Hogan MJ, Alvarado JA, Weddell JE: *Histology of the human eye*, Philadelphia, 1971, Saunders.)



FIGURE 11-5

Fundus photograph of the right eye. A cilioretinal artery can be seen looping up into retina at temporal edge of optic disc. (Courtesy Family Vision Center, Pacific University, Forest Grove, Oregon.)

CLINICAL COMMENT: ANTERIOR ISCHEMIC OPTIC NEUROPATHY

Anterior ischemic optic neuropathy (AION) results from nonperfusion or hypoperfusion of the ciliary blood supply to the optic nerve head.¹³ The oval that forms the circle of Zinn can be divided into superior and inferior portions by the entry points of the medial and lateral short ciliary arteries forming it. This may be the anatomic basis for the altitudinal visual field loss that characterizes nonarteritic AION. The inferior field is more often affected, but there is no adequate explanation for the preferential involvement of the superior part of the ring of vessels.¹⁷

CLINICAL COMMENT: CILIORETINAL ARTERY

A **cilioretinal artery** may arise either from the vessels entering the choroid or from the circle of Zinn; thus this vessel, located within the retina, arises from the ciliary circulation and not from the retinal supply. Various studies report a cilioretinal artery occurring in 15% to 50% of the population and usually entering the retina from the temporal side of the optic disc to supply the macular area^{18,19} (Figure 11-5). If occlusion of the central retinal artery occurs, the direct blood supply to the macular area will be maintained in those individuals with such a cilioretinal artery.

Two long branches of the posterior ciliary arteries enter the sclera, one lateral and one medial to the ring of short ciliary arteries. These are the **long posterior ciliary arteries**, which run between the sclera and the

choroid to the anterior globe (Figure 11-6). Here the arteries enter the ciliary body and branch superiorly and inferiorly.¹³ These branches anastomose with each other and with the anterior ciliary arteries to form a circular blood vessel, the **major arterial circle of the iris** (Figure 11-7). This circular artery is located in the ciliary stroma near the iris root and is the source of the radial vessels found in the iris. Before forming the major circle, branches from the long posterior ciliary arteries supply the ciliary body and the anterior choroid, where they form a network that anastomoses with the choroidal vessels from the short posterior ciliary arteries (see Figure 11-4).

ETHMOID ARTERIES

As the ophthalmic artery courses near the medial wall, two branches arise and enter the ethmoid bone (see Figure 11-1). The **posterior ethmoid artery** passes through the posterior ethmoid canal to supply the posterior ethmoid sinus and the sphenoid sinus; it sends branches into the nasal cavity to supply the upper part of the nasal mucosa. The **anterior ethmoid artery** generally is larger and passes through the anterior ethmoid canal and supplies the anterior and middle ethmoid sinuses, the sphenoid sinus, the frontal sinus, the nasal cavity, and the skin of the nose.

SUPRAORBITAL ARTERY

The **supraorbital artery** arises from the ophthalmic artery as it lies medial to the optic nerve (see Figure 11-1). The supraorbital artery runs upward to a position above the superior extraocular muscles, turns anteriorly, and runs with the supraorbital nerve between the periorbita of the orbital roof and the levator muscle. It passes through the supraorbital notch or foramen, often dividing into two branches to supply the skin and the muscles of the forehead and scalp (see Figure 11-3). Terminal branches anastomose with the artery from the opposite side, with the supratrochlear artery, and with the anterior temporal artery from the external carotid. While the supraorbital artery is in the orbit, it sends branches to the superior rectus, superior oblique, and levator muscles and to the periorbita.

MUSCULAR ARTERIES

Much variation occurs in the vessels supplying the muscles, and in any individual, any combination of the vessels named here might be present. In one common presentation, the muscular arteries come off the ophthalmic artery as two branches, the **lateral** (or **superior**) and the **medial** (or **inferior**). The lateral (superior) branch supplies the lateral rectus, superior

Rights were not granted to include this figure in electronic media.
Please refer to the printed publication.

FIGURE 11-6

Horizontal section of the eye showing ciliary circulation. (From Vaughan D, Asbury T: *General ophthalmology*, East Norwalk, Conn, 1980, Appleton & Lange.)

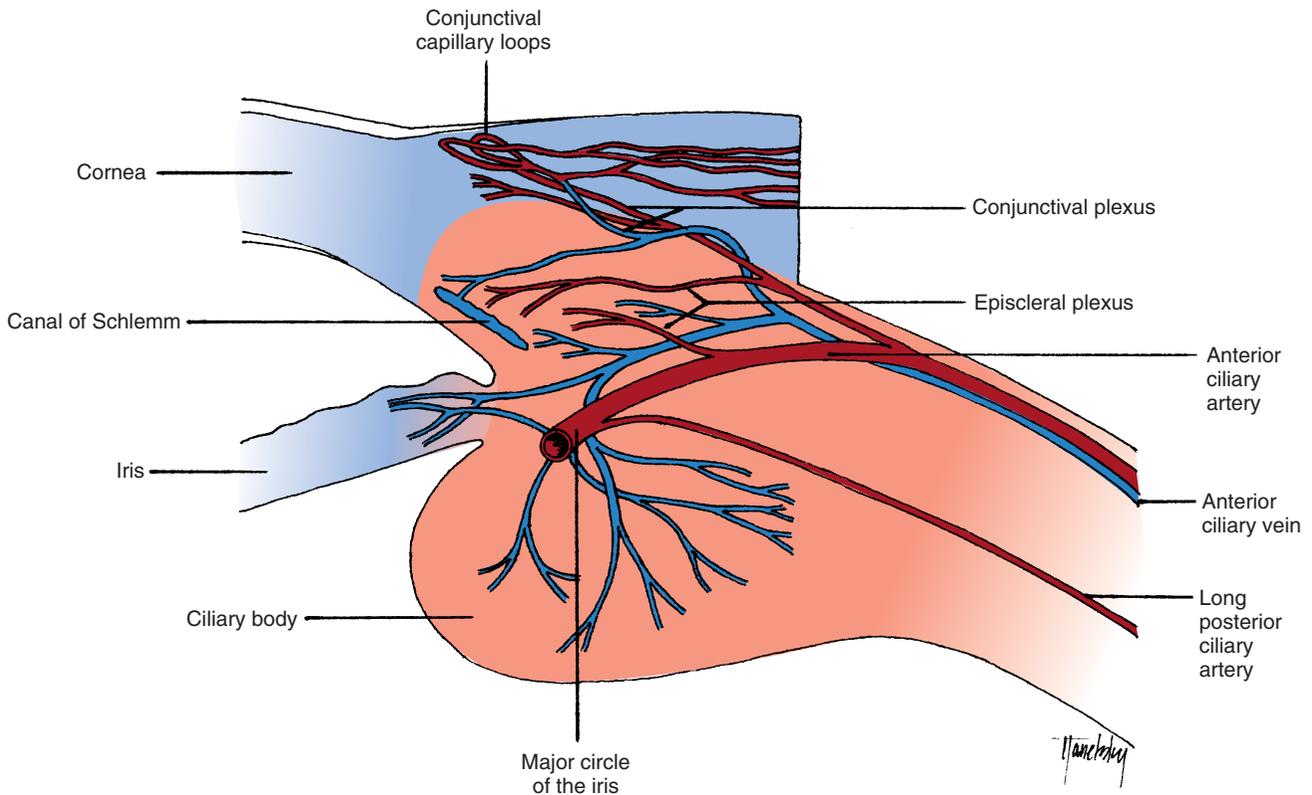


FIGURE 11-7

Section through ciliary body and limbal area, showing branches of anterior ciliary artery.

rectus, superior oblique, and levator muscles.⁶⁻⁸ The medial (inferior) branch supplies the medial rectus, inferior rectus, and inferior oblique muscles.⁶⁻⁸ Additional branches supplying the muscles may come from other sources. The lacrimal artery supplies the lateral and superior rectus muscles. The supraorbital artery supplies the superior rectus, superior oblique, and levator muscles. The infraorbital artery supplies the inferior rectus and inferior oblique muscles (Table 11-2).

ANTERIOR CILIARY ARTERIES

The **anterior ciliary arteries** branch from the vessels supplying the rectus muscles. These arteries exit the muscles near the muscle insertions, run forward along the tendons a short distance, then loop inward to pierce the sclera just outer to the limbus (see Figure 11-4). An accumulation of pigment may be evident at the point at which the artery enters the sclera. Before entering the sclera, the anterior ciliary arteries send branches into the conjunctiva, forming a network of vessels in the limbal conjunctiva (see Figure 11-7). Other branches enter the episclera to form a network of vessels before entering the uvea. The anterior ciliary arteries then enter the

Table 11-2 Extraocular Muscle Blood Supply

Muscle	Arterial Supply
Medial rectus	Medial (inferior) muscular
Lateral rectus	Lateral (superior) muscular Lacrimal
Superior rectus	Lateral (superior) muscular Lacrimal Supraorbital
Inferior rectus	Medial (inferior) muscular Infraorbital
Superior oblique	Lateral (superior) muscular Supraorbital
Inferior oblique	Medial (inferior) muscular Infraorbital

ciliary body and anastomose with the branches of the long posterior ciliary arteries, forming the major circle of the iris (see Figure 11-4). Generally, two anterior ciliary arteries emanate from each of the rectus muscles, with the exception of the lateral rectus, which provides only one such artery.

CLINICAL COMMENT: “RED EYE”

Inflammations generate an increase of the blood supply to the affected area, causing hyperemia. In cases of a “red eye,” an understanding of the organization of the blood supply in the limbal area can help in differentiating a less serious presentation, such as conjunctivitis, from a more serious situation, such as uveitis. In **conjunctivitis** and mild corneal involvement, the superficial blood vessels are injected, giving the conjunctiva a bright-red color that often increases toward the fornix. The vessels move with conjunctival movement and can be blanched with a topical vasoconstrictor. In **uveitis** the deeper scleral and episcleral vessels are injected, giving the circumlimbal area a purplish or rose-pink color.²⁰ These vessels do not move with the conjunctiva and are not blanched with a topical vasoconstrictor.

MEDIAL PALPEBRAL ARTERIES

Two **medial palpebral arteries** branch either directly from the ophthalmic artery or from the dorsonasal artery near the trochlea of the superior oblique muscle. The medial palpebral arteries pierce the orbital septum on either side of the medial palpebral ligament and enter the superior and inferior eyelids (see Figure 11-3). These branches run through the eyelid and form arches between the orbicularis muscle and the tarsal plate. They anastomose with branches from the lacrimal artery and form the vessels known as the **palpebral arcades**. Usually, two arcades occur in each lid: the *marginal* arcade, which runs near the marginal edge of the tarsal plate, and the *peripheral* arcade, which runs near the peripheral edge of the tarsal plate. These provide the blood supply for the eyelid structures. Additional branches from the medial palpebral arteries supply the structures in the medial canthus.

SUPRATROCHLEAR ARTERY

One of the terminal branches of the ophthalmic artery, the **supratrochlear artery**, pierces the orbital septum at the superior, medial corner of the orbit⁴ (see Figure 11-3). It passes with the supratrochlear nerve upward to supply the skin of the forehead and scalp and the muscles of the forehead. The supratrochlear artery forms anastomoses with the supraorbital artery, the opposite supratrochlear artery, and the anterior temporal artery of the external carotid supply.

DORSONASAL ARTERY

The other terminal branch of the ophthalmic artery, the **dorsonasal artery (dorsal nasal artery)**, also leaves the orbit by piercing the orbital septum below the trochlea above the medial palpebral ligament.⁴ It sends vessels to

supply the lacrimal sac, then runs alongside the nose to anastomose with the angular artery from the external carotid supply.

EXTERNAL CAROTID ARTERY

The other branch of the common carotid, the **external carotid artery**, passes upward through the tissue of the neck. Only those few branches of this artery that supply the globe and orbit are discussed. The branches from the internal and external carotid arteries that supply the ocular structures, as well as their most common anastomoses, are shown in the flow chart in Figure 11-8.

FACIAL ARTERY

The **facial artery** arises from the external carotid near the angle of the mandible, runs along the posterior edge of the lower jaw, and curves upward over the outside of the jaw and across the cheek to the angle of the mouth. It ascends along the side of the nose and sends a terminal branch, the **angular artery**, to the medial canthus (Figure 11-9). The angular artery supplies the lacrimal sac, the medial part of the lower lid, and the skin of the cheek. Some branches pass beneath the medial canthal ligament to anastomose with the infraorbital artery, and some anastomose with the dorsonasal artery.

SUPERFICIAL TEMPORAL ARTERY

The **superficial temporal artery** is a terminal branch of the external carotid artery (see Figure 11-9). Branches of the superficial temporal artery that supply areas near the orbit are the anterior temporal, zygomatic, and transverse facial arteries.²¹ The **anterior temporal artery** supplies the skin and muscles of the forehead and anastomoses with the supraorbital and supratrochlear arteries. The **zygomatic artery** extends above the zygomatic arch and supplies the orbicularis muscle. The **transverse facial artery** supplies the skin of the cheek and anastomoses with the infraorbital artery.

CLINICAL COMMENT: TEMPORAL ARTERITIS

Temporal arteritis (or giant cell arteritis) is an inflammatory condition that can affect large arteries but is found primarily in the arteries in the temporal or occipital region. The disease often is accompanied by swelling, redness, and tenderness in the temporal area. Ocular symptoms, including vision loss, may occur. Biopsy of the superficial temporal artery often is necessary to confirm the diagnosis before treatment begins.²² The biopsy is taken from the artery as it crosses the zygomatic process and travels superiorly anterior to the ear.²³

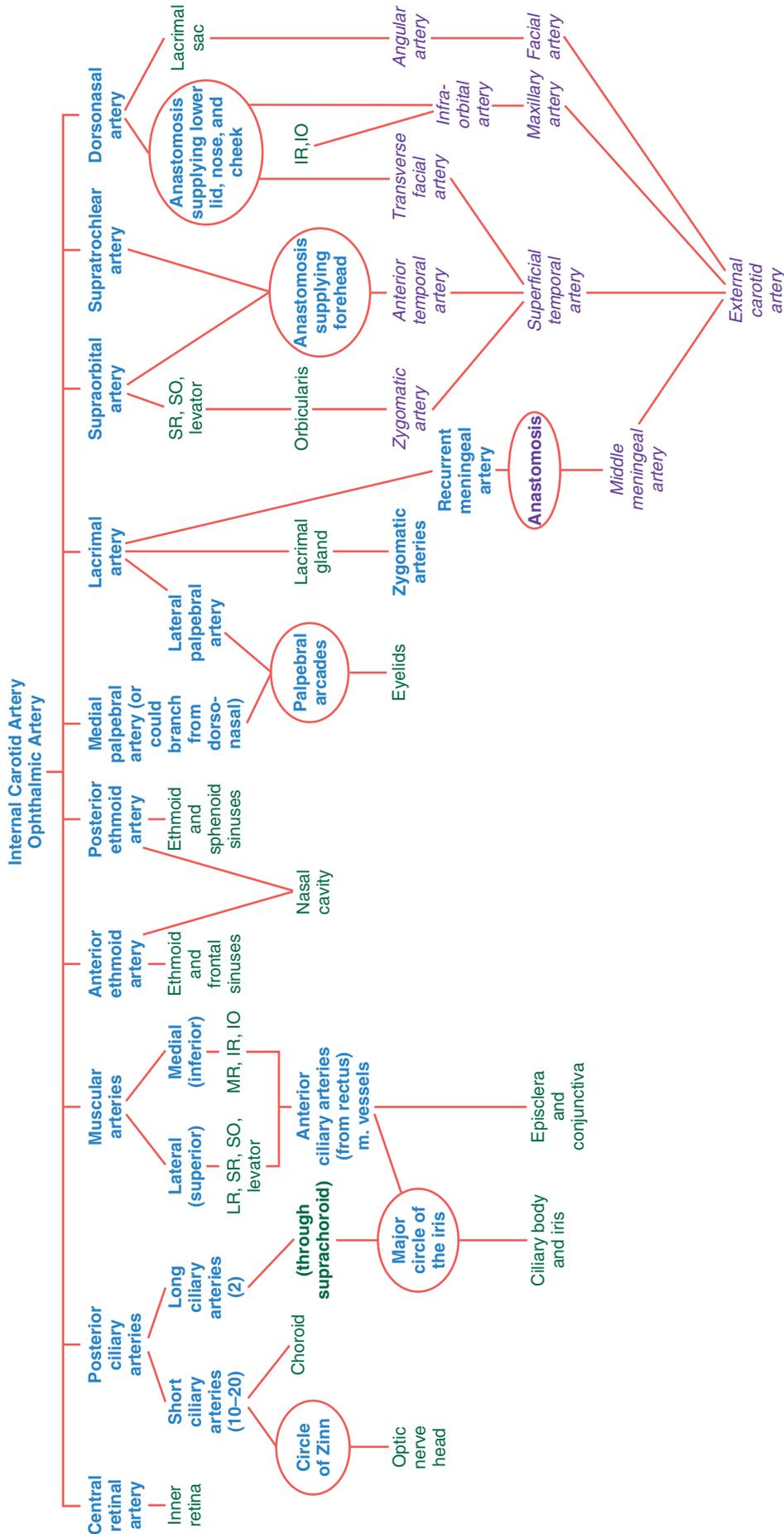
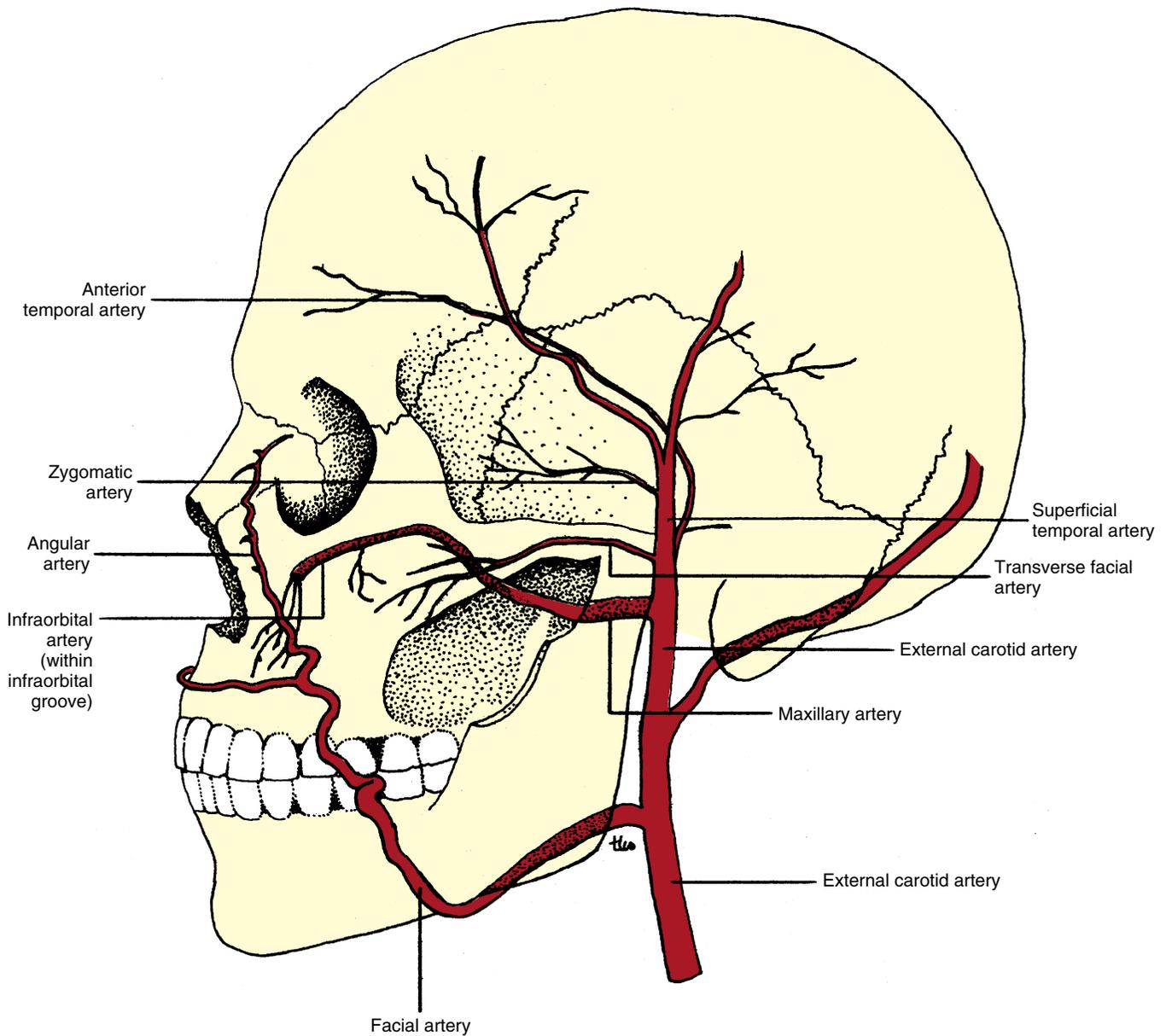


FIGURE 11-8

Flow chart of branches of internal and external carotid arteries that supply orbital structures. Blue indicates branches of internal carotid artery; purple indicates branches of external carotid artery; green indicates target structures. LR, Lateral rectus; SR, superior rectus; SO, superior oblique; MR, medial rectus; IR, inferior rectus; IO, inferior oblique.

**FIGURE 11-9**

Branches of external carotid artery that supply ocular adnexa. (Redrawn from Clemente CD: *Anatomy: a regional atlas of the human body*, Munich, 1987, Urban and Schwarzenberg. Copyright 1987, Lea & Febiger.)

MAXILLARY ARTERY

The other branch of the external carotid that supplies areas in proximity to the orbit is the **maxillary artery**. It passes through the infratemporal fossa and then upward, medial to the mandibular joint toward the maxillary bone (see Figure 11-9). Within the infratemporal fossa, the maxillary artery shows some variability in both its branching pattern and in its topographic relations with other structures.²⁴⁻²⁶ It runs along the pterygo-

palatine fossa and enters the orbit through the inferior orbital fissure as the **infraorbital artery**. The artery then runs forward along the infraorbital groove in the maxillary bone, passes through the infraorbital canal, and exits through the infraorbital foramen (see Figure 11-3). It supplies the lower eyelid and lacrimal sac, and it anastomoses with the angular artery and the dorso-nasal artery.²¹ While in the infraorbital canal, the infraorbital artery supplies the inferior rectus and inferior

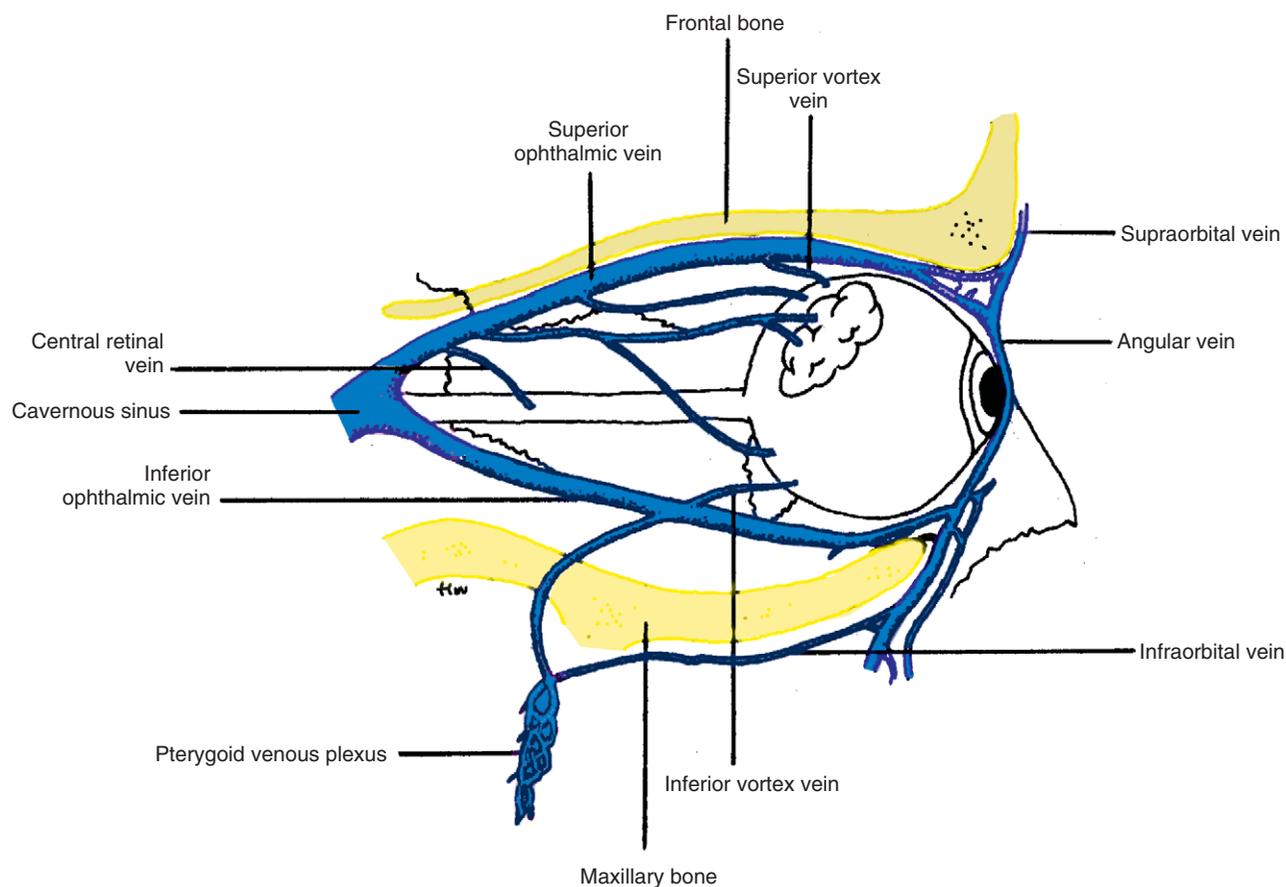


FIGURE 11-10

View from lateral side of orbit showing veins draining globe and orbit. (From Mathers LH, Chase RA, Dolph J et al: *Clinical anatomy principles*, St Louis, 1996, Mosby.)

oblique muscles and sends some branches to the maxillary sinus and to the teeth of the upper jaw.

VEINS OF THE ORBIT

The veins of the orbit have no valves; thus the direction of blood flow may change and is determined by pressure gradients.⁴ Over a large part of their path, the veins are embedded within the connective tissue septa that compartmentalize the orbit.⁵ Unlike the parallel routes of veins and arteries in most of the body, many orbital veins follow a course that differs from the corresponding arteries.^{8,27} The orbit has a single ophthalmic artery but two ophthalmic veins. The superior and inferior ophthalmic veins primarily drain into the cavernous sinus.

SUPERIOR OPHTHALMIC VEIN

The **superior ophthalmic vein** is formed by the joining of the angular and supraorbital veins within the orbit

(Figure 11-10). The **supraorbital vein** enters the orbit through the supraorbital notch, and the **angular vein** passes through the orbital septum above the medial palpebral ligament.²⁸

The superior ophthalmic vein, the larger of the two ophthalmic veins, runs with the ophthalmic artery and, as it passes posteriorly, receives blood from veins that drain the superior orbital structures. It passes below the superior rectus muscle and crosses the optic nerve to the upper part of the superior orbital fissure, where it leaves the orbit to empty into the cavernous sinus.

The veins that drain into the superior ophthalmic vein are the anterior and posterior ethmoid veins, the muscular veins draining the superior and medial muscles, the lacrimal vein, the central retinal vein, and the upper vortex veins.²⁸

CENTRAL RETINAL VEIN

The venous branches located in the retinal tissue come together and exit the eyeball as a single **central retinal**

vein. This vessel leaves the optic nerve approximately 10 to 12 mm behind the lamina cribrosa alongside the central retinal artery. It emerges from the meningeal sheath of the optic nerve and either joins the superior ophthalmic vein or exits the orbit and drains directly into the cavernous sinus.

CLINICAL COMMENT: PAPPILLEDEMA

*The sheaths that surround the optic nerve are continuous with the meningeal sheaths of the brain. The subarachnoid space, located within these layers, contains cerebrospinal fluid. Thus, the fluid that surrounds the optic nerve is continuous with the fluid found throughout the cranial cavity. With increased intracranial pressure the central retinal vein can be compressed as it crosses the subarachnoid space on its exit from the optic nerve. The central retinal artery is not affected, because it has a thicker sheath and is not compressed as easily as is the vein.²⁹ The resultant blockage causes congestion of the retinal veins and edema of the retina. Edema of the optic nerve head (**papilledema**) will be evident as blurred disc margins, with hemorrhages sometimes evident as well.*

VORTEX VEINS

The **vortex veins** drain the choroid, and usually one of the four or five vortex veins is located in each quadrant (see Figure 11-4). These veins exit the globe 6 mm posterior to the equator.⁷ The vortex veins can be seen with an indirect ophthalmoscope and a dilated pupil.

INFERIOR OPHTHALMIC VEIN

The **inferior ophthalmic vein** begins as a plexus near the anterior floor of the orbit. It drains blood from the lower and lateral muscles, the inferior conjunctiva, the lacrimal sac, and the lower vortex veins.²⁸ It may form two branches, one that empties into either the superior ophthalmic vein^{27,30} or the cavernous sinus and one that empties into the **pterygoid venous plexus** (see Figure 11-10). The latter branch exits the orbit through the inferior orbital fissure, and the other branch passes through the superior orbital fissure either to join the superior ophthalmic vein or to empty directly into the cavernous sinus.

ANTERIOR CILIARY VEINS

The **anterior ciliary veins** receive branches from the conjunctival capillary network and then accompany the anterior ciliary arteries, pierce the sclera, and join with the muscular veins.

INFRAORBITAL VEIN

The **infraorbital vein** is formed by several veins that drain the face. It enters the infraorbital foramen and, along with the infraorbital artery and nerve, passes posteriorly through the infraorbital canal and groove. It receives branches from some structures in the inferior part of the orbit and may communicate with the inferior ophthalmic vein. The infraorbital vein drains into the pterygoid venous plexus (see Figure 11-10).

CAVERNOUS SINUS

The **cavernous sinus** is a relatively large venous channel formed by a splitting of the dura mater on each side of the body of the sphenoid bone. The cavernous sinus extends from the medial end of the superior orbital fissure to the petrous portion of the temporal bone. The internal carotid artery and the abducens nerve are located medially within the sinus, covered by the endothelial lining of the sinus. The oculomotor, ophthalmic, and maxillary nerves are found in the lateral wall of the cavernous sinus (Figure 11-11). The cavernous sinus drains into the **superior petrosal sinus**, located along the upper crest of the petrous portion of the temporal bone, and into the **inferior petrosal sinus**, located in the groove between the petrous portion and the occipital bone. Both drain either directly or indirectly into the **internal jugular vein** (Figure 11-12).

CLINICAL COMMENT: CAVERNOUS SINUS THROMBOSIS

Infections of the face or orbit can be dangerous. An infected embolus that forms in a facial or orbital vein can readily pass into the cavernous sinus via an ophthalmic vein because these veins do not have valves. A cavernous sinus thrombosis can be fatal and must be treated aggressively with antibiotics.

CLINICAL COMMENT: CAROTID–CAVERNOUS SINUS FISTULA

*A **carotid–cavernous sinus fistula** is an abnormal communication between the internal carotid artery and the cavernous sinus caused by a tear in the artery wall, either traumatic or spontaneous. The sinus communicates directly with the veins of the orbit, so arterial pressure can be transmitted to the ophthalmic veins, which may become pulsatile. If arterial pressure is reduced, because of this leak a decrease in perfusion to ocular tissue will occur.^{31,32}*

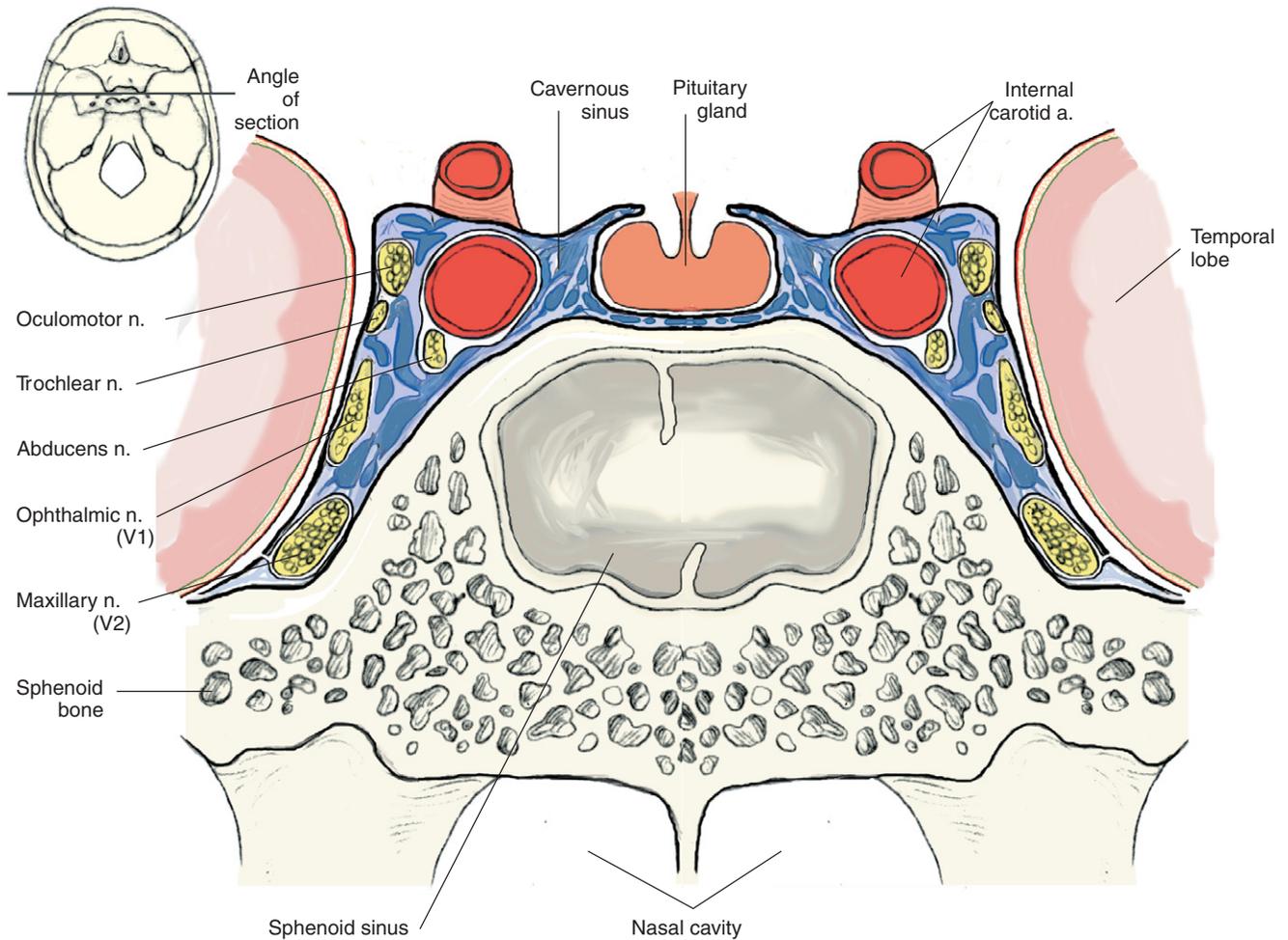


FIGURE 11-11

Coronal section through sphenoid bone and cavernous sinus showing location of internal carotid as it passes through sinus. (From Mathers LH, Chase RA, Dolph J et al: *Clinical anatomy principles*, St Louis, 1996, Mosby.)

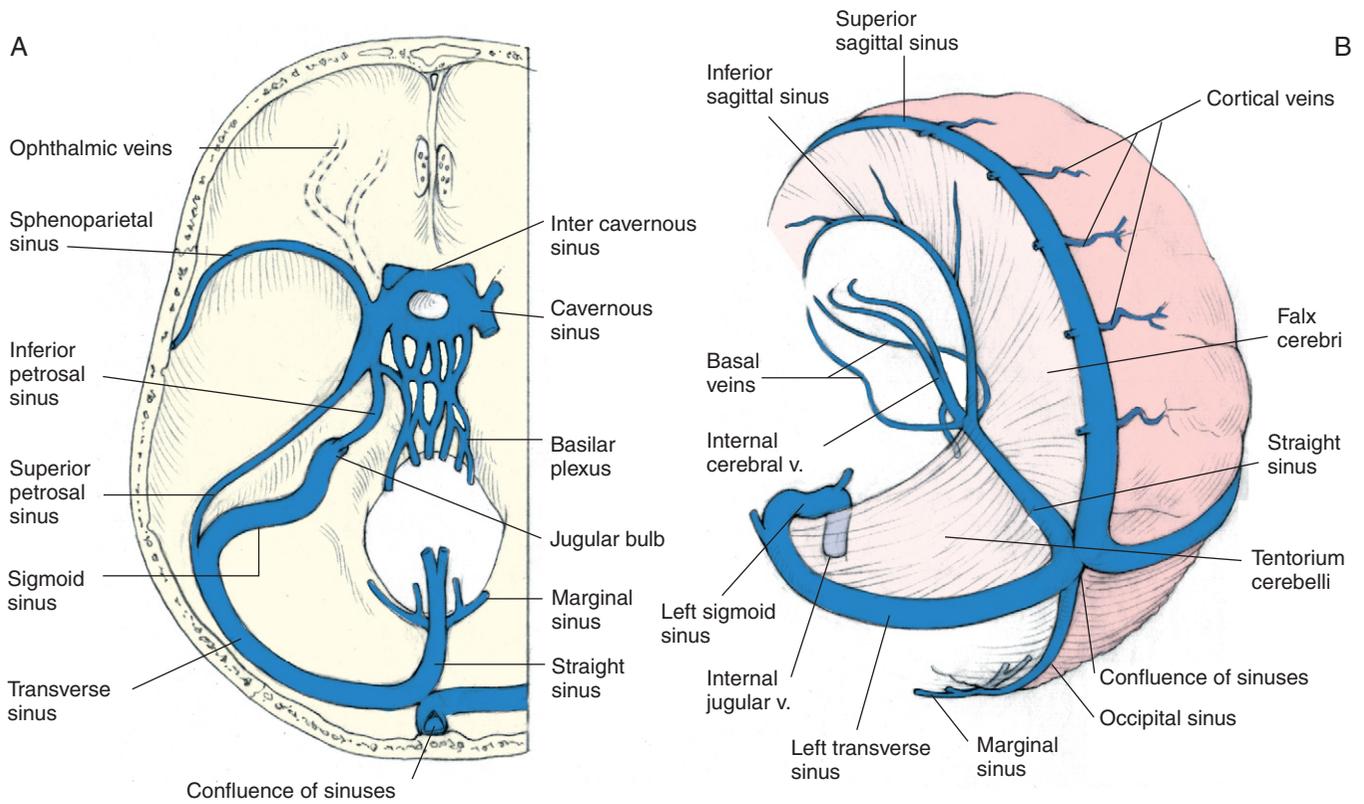


FIGURE 11-12

Superior view of venous sinus drainage of cranium. (From Mathers LH, Chase RA, Dolph J et al: *Clinical anatomy principles*, St Louis, 1996, Mosby.)

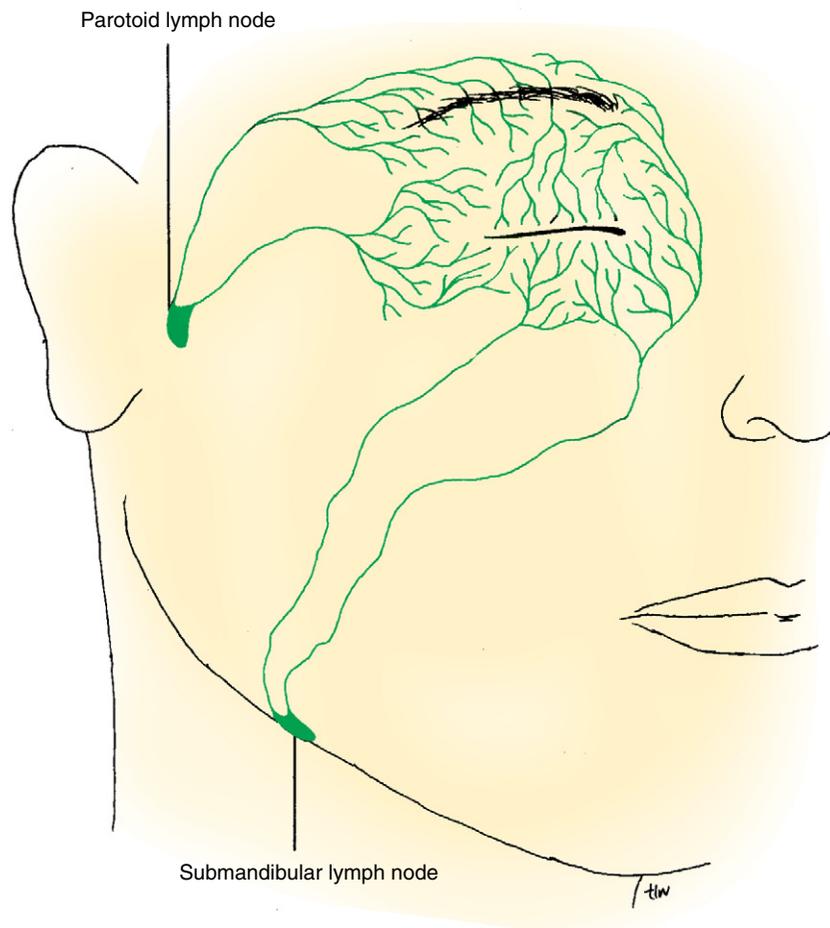


FIGURE 11-13
Lymphatic drainage of the ocular adnexa.

LYMPHATIC DRAINAGE

No lymphatic vessels occur in the globe proper; lymphatics are found in the conjunctiva and the eyelids. The lymphatics that drain the medial aspects of the lids and the medial canthal structures (including the lacrimal sac) empty into the **submandibular lymph nodes**. Those that drain the lateral eyelids and the lacrimal gland empty into the **parotid lymph nodes** in the preauricular area^{8,30} (Figure 11-13).

EFFECT OF AGING ON OCULAR CIRCULATION

The density and diameter of the choriocapillaris decrease with age. Because there is a coincident decrease in retinal cells, this decrease in blood flow may be a response to decreased metabolic need.^{33,34}

REFERENCES

1. Nuza AB, Taner D: Anatomical variations of the intracavernous branches of the internal carotid artery with reference to the relationship of the internal carotid artery and sixth cranial nerve, *Acta Anat (Basel)* 138(3):238, 1990.
2. Hayreh SS, Dass R: The ophthalmic artery. I. Origin and intracranial and intra-canalicular course, *Br J Ophthalmol* 46:65, 1962.
3. Liu XJ: Pathological changes of the optic nerve from compression by the internal carotid artery, *Chung Hua Yen Ko Tsa Chih* 26(6):364, 1990 (abstract).
4. Hayreh SS: The ophthalmic artery. II. Intraorbital course, *Br J Ophthalmol* 46:165, 1962.
5. Koorneef L: Orbital connective tissue. In Jakobiec FA, editor: *Ocular anatomy, embryology, and teratology*, Philadelphia, 1982, Harper & Row, p 835.
6. Hayreh SS: The ophthalmic artery. III. Branches, *Br J Ophthalmol* 46:212, 1962.
7. Warwick R: *Eugene Wolff's anatomy of the eye and orbit*, ed 7, Philadelphia, 1976, Saunders, pp 92, 146, 406.
8. Doxanas MT, Anderson RL: *Clinical orbital anatomy*, Baltimore, 1984, Williams & Wilkins, p 153.

9. Diamond MK: Homologies of the meningeal-orbital arteries of humans: a reappraisal, *J Anat* 178:223, 1991.
10. Yoshii I, Ikeda A: A new look at the blood supply of the retro-ocular space, *Anat Rec* 233:321, 1992.
11. Olver JM: Functional anatomy of the choroidal circulation: methyl methacrylate casting of human choroid, *Eye* 4:262, 1990.
12. Onda E, Cioffi GA, Bacon DR et al: Microvasculature of the human optic nerve, *Am J Ophthalmol* 120:92, 1995.
13. Hayreh SS: The blood supply of the optic nerve head and the evaluation of it: myth and reality, *Prog Retin Eye Res* 20(5):563, 2001.
14. Hayreh SS: Blood supply of the optic nerve head and its role in optic atrophy, glaucoma, and oedema of the optic disc, *Br J Ophthalmol* 53:721, 1969.
15. Hayreh SS: Pathogenesis of cupping of the optic disc, *Br J Ophthalmol* 58:863, 1974.
16. Borchert MS: Vascular anatomy of the visual system, *Ophthalmol Clin North Am* 9(3):327, 1996.
17. Olver JM, Spalton DJ, McCartney AC: Microvascular study of the retrolaminar optic nerve in man: the possible significance in anterior ischaemic optic neuropathy, *Eye* 4:7, 1990.
18. Hayreh SS: The central artery of the retina: its role in the blood supply of the optic nerve, *Br J Ophthalmol* 47:651, 1963.
19. Justice J Jr, Lehmann RP: Cilioretinal arteries: a study based on a review of stereo fundus photographs and fluorescein angiographic findings, *Arch Ophthalmol* 94:1355, 1976.
20. Catania LJ: *Primary care of the anterior segment*, East Norwalk, Conn, 1988, Appleton & Lange, p 194.
21. Tucker SM, Lindberg JV: Vascular anatomy of the eyelids, *Ophthalmology* 101:1118, 1994.
22. Berkow R, editor: *The Merck manual*, ed 14, Rahway, NJ, 1982, Merck, p 557.
23. Sires BS, Gausas R, Cook BE Jr et al: Orbit. In Kaufman PL, Alm A, editors: *Adler's physiology of the eye*, ed 10, St Louis, 2003, Elsevier.
24. Morton AL, Khan A: Internal maxillary artery variability in the pterygopalatine fossa, *Otolaryngol Head Neck Surg* 104(2):204, 1991.
25. Ortug G, Moriggl B: The topography of the maxillary artery within the infratemporal fossa, *Anat Anz* 172(3):197, 1991 (abstract).
26. Pretterklieber ML, Skopakoff C, Mayr R: The human maxillary artery reinvestigated: topographical relations in the infratemporal fossa, *Acta Anat (Basel)* 142(4):281, 1991.
27. Murakami K, Murakami G, Komatsu A et al: Gross anatomical study of veins in the orbit, *Nippon Ganka Gakkai Zasshi* 95(1):31, 1991 (abstract).
28. Cheung N, McNab AA: Venous anatomy of the orbit, *Invest Ophthalmol Vis Sci* 44(3):988, 2003.
29. Whiting AS, Johnson LN: Papilledema: clinical clues and differential diagnosis, *Am Fam Physician* 45(3):125, 1992.
30. Wobig JL: The blood vessels and lymphatics of the orbit and lid. In Wobig JL, Reeh MJ, Wirtschafter JD, editors: *Ophthalmic anatomy*, San Francisco, 1981, American Academy of Ophthalmology, p 77.
31. De Keizer R: Carotid-cavernous and orbital arteriovenous fistulas: ocular features, diagnostic and hemodynamic considerations in relation to visual impairment and morbidity, *Orbit* 22(2):121, 2003.
32. Bhatti MT, Peters KR: A red eye and then a really red eye, *Surv Ophthalmol* 48(2):224, 2003.
33. Grunwald JE, Hariprasad SM, DuPont J: Effect of aging on foveolar choroidal circulation, *Arch Ophthalmol* 116:150, 1998.
34. Lam AK, Chan S, Chan H et al: The effect of age on ocular blood supply determined by pulsatile ocular blood flow and color Doppler ultrasonography, *Optom Vis Sci* 89(4):305, 2003.



Cranial Nerve Innervation of Ocular Structures

The orbital structures are innervated by cranial nerves (CNs) II, III, IV, V, VI, and VII (Table 12-1). Motor functions of the striated muscles are controlled by CN III, the oculomotor nerve; CN IV, the trochlear nerve; CN VI, the abducens nerve; and CN VII, the facial nerve. CN V, the trigeminal nerve, carries the sensory supply from the orbital structures. CN II, the optic nerve, carries visual information and is discussed in Chapter 13. This chapter discusses sensory and motor innervation of the orbit, including pathways, functions, and presenting signs of dysfunction.

THE NERVOUS SYSTEM

Information comes into the central nervous system (CNS) via afferent fibers. Afferent sensory fibers usually have specialized nerve endings that respond to such sensations as touch, pressure, temperature, and pain.

Information processing occurs within the brain or spinal cord and involves communication between different areas of the CNS through fiber tracts. A fiber tract also may be called a **fasciculus**, a **peduncle**, or a **brachium**. The portion of the cranial nerve from the cell body in the nucleus to the exit from the brain stem is the *fascicular* part of the nerve.

Efferent fibers, either somatic or autonomic, carry information from the CNS to the target structures: muscles, organs, or glands. The efferent pathway in the somatic system generally consists of a fiber that runs the distance from the CNS to the target muscle. The autonomic pathway generally has a synapse within its pathway (see Chapter 14).

AFFERENT PATHWAY: ORBITAL SENSORY INNERVATION

The eye is richly supplied with sensory nerves that carry sensations of touch, pressure, warmth, cold, and pain. Sensations from the cornea, iris, conjunctiva, and sclera consist primarily of pain; even light touching of the cornea is registered as irritation or pain.¹

TRIGEMINAL NERVE

The fibers of the trigeminal nerve (CN V) serving ocular structures are sensory and originate in the innervated structures. The description of the pathways of these nerves as they join to become larger nerves, come together in the ganglion of the fifth cranial nerve, and then exit the ganglion and enter the pons. It is hoped that this presentation, although unconventional, will enable the reader to keep in mind the actual direction of the action potential, and thus the information flow, in these fibers. Figure 12-1 shows the branches and paths of the trigeminal nerve within the orbit.

Ophthalmic Division of Trigeminal Nerve

Nasociliary Nerve. Sensory fibers from the structures of the medial canthal area—caruncle, canaliculi, lacrimal sac, medial aspect of eyelids, and skin at the side of the nose—join to form the **infra-trochlear nerve**. This nerve penetrates the orbital septum, enters the orbit below the trochlea, and runs along the upper border of the medial rectus muscle, becoming the nasociliary nerve as other branches join it (see Figure 12-1).

Sensory fibers from the skin along the center of the nose, the nasal mucosa, and the ethmoid sinuses form the **anterior ethmoid nerve**; fibers from the ethmoid sinuses and the sphenoid sinus form the **posterior ethmoid nerve**. The ethmoid nerves enter the orbit with their companion arteries through foramina within the frontoethmoid suture.² Both nerves join the nasociliary nerve as it runs along the medial aspect of the orbit (see Figure 12-1).

Corneal sensory innervation is dense, estimated to be three to four times as dense as other epithelial tissue innervation.¹ Three networks of nerves are formed. One is located in the corneal epithelium, another (the sub-epithelial plexus) is in the anterior stroma, and the third is in the middle of the stroma³ (Figure 12-2). No nerves are found in posterior stroma, Descemet's membrane, or endothelium. The fibers from these plexus come together in peripheral stroma and radiate out into the limbus as 70 to 80 branches; they become myelinated in the last 2 mm of the cornea.⁴⁻⁶

Table 12-1 Orbital Cranial Nerves

Cranial Nerve	Origin	Destination	Function
II: Optic	Retinal ganglion cells	Lateral geniculate body	Sensory: sight
III: Oculomotor, inferior division	Midbrain	Medial rectus muscle Inferior rectus muscle Inferior oblique muscle Ciliary ganglion	Motor: adduction Depression, adduction, extorsion Elevation, abduction, extorsion Parasympathetic: motor to iris sphincter and ciliary muscle for miosis and accommodation
III: Oculomotor, superior division	Midbrain	Superior rectus muscle Superior palpebral levator muscle	Elevation, adduction, intorsion Motor: elevation of eyelid
IV: Trochlear	Midbrain	Superior oblique muscle	Motor: depression, abduction, intorsion
VI: Abducens	Pons	Lateral rectus muscle	Motor: abduction
VII: Facial	Pons	Frontalis, procerus, corrugator, and orbicularis muscles Sphenopalatine ganglion	Motor: facial expressions, closure of eyelids Parasympathetic: secretomotor to lacrimal gland for lacrimation

Some of these branches join with nerves from other anterior segment structures to form two **long ciliary nerves**. These long ciliary nerves, one on the lateral side and one on the medial side of the globe, course between the choroid and sclera to the back of the eye, where they leave the globe at points approximately 3 mm on each side of the optic nerve (Figure 12-3). (In addition to afferent fibers, the long ciliary nerves transmit sympathetic fibers to the dilator muscle of the iris.) The two long ciliary nerves then join the nasociliary nerve.

CLINICAL COMMENT: (SCLERAL) NERVE LOOPS (OF AXENFELD)

A slight variation can occur in the pathway of the long ciliary nerve in which the fibers loop into the sclera from the suprachoroidal space, forming a dome-shaped elevation about 2 mm from the limbus on either the nasal or the temporal side. Often this raised area is pigmented, usually blue or black, and should be differentiated from a melanoma.⁷ The nerve loop may be painful when touched, a characteristic that should aid in its diagnosis.⁴

The other branches radiating from the cornea into the limbus join other sensory nerves from the anterior segment; they enter the choroid, join with the choroidal nerves, then course to the back of the eye, where they leave as 6 to 10 **short ciliary nerves** (see Figure 12-3). The short ciliary nerves exit the sclera in a ring around the optic nerve in company with the short posterior ciliary arteries and enter the ciliary ganglion (see Figure 12-1). The sensory fibers do not synapse but pass through the ganglion, leaving as the **sensory root of the ciliary ganglion**, which then joins the nasociliary nerve. (The short ciliary nerves carry sympathetic and parasympathetic fibers in addition to sensory fibers.)

Thus, the **nasociliary nerve** is formed by the joining of the infratrochlear nerve, the anterior and posterior ethmoid nerves, the long ciliary nerves, and the sensory root of the ciliary ganglion (see Figure 12-1). The nasociliary nerve exits the orbit by passing through the common tendinous ring *and* the superior orbital fissure into the cranial cavity.

CLINICAL COMMENT: HERPES ZOSTER

***Herpes zoster** is an acute CNS infection caused by the varicella-zoster virus. Signs and symptoms include pain and rash in the distribution area supplied by the affected sensory nerves.⁸ It is believed that the virus lies dormant in a sensory ganglion and, on becoming activated, migrates down the sensory pathway to the skin.⁹ An eruption of herpes zoster is more common in elderly persons but may occur at any age and may be related to a delayed hypersensitivity reaction.¹⁰ Approximately 10% of all cases affect the ophthalmic division of the trigeminal nerve.¹¹ Involvement of the tip of the nose often indicates that the eye will also be involved, reflecting the distribution of the nasociliary branches. This association of ocular involvement with zoster affecting the tip of the nose is Hutchinson's sign.¹²*

Frontal Nerve. Sensory fibers from the skin and muscles of the forehead and upper eyelid come together and form the **supratrochlear nerve**. This nerve enters the orbit by piercing the superior medial corner of the orbital septum (Figure 12-4).

Sensory fibers from the skin and muscles of the forehead and upper eyelid form a second nerve, the **supraorbital nerve**, lateral to the supratrochlear nerve. The supraorbital nerve enters the orbit as one or two branches; one branch enters through the supraorbital notch, accompanying the supraorbital artery. The

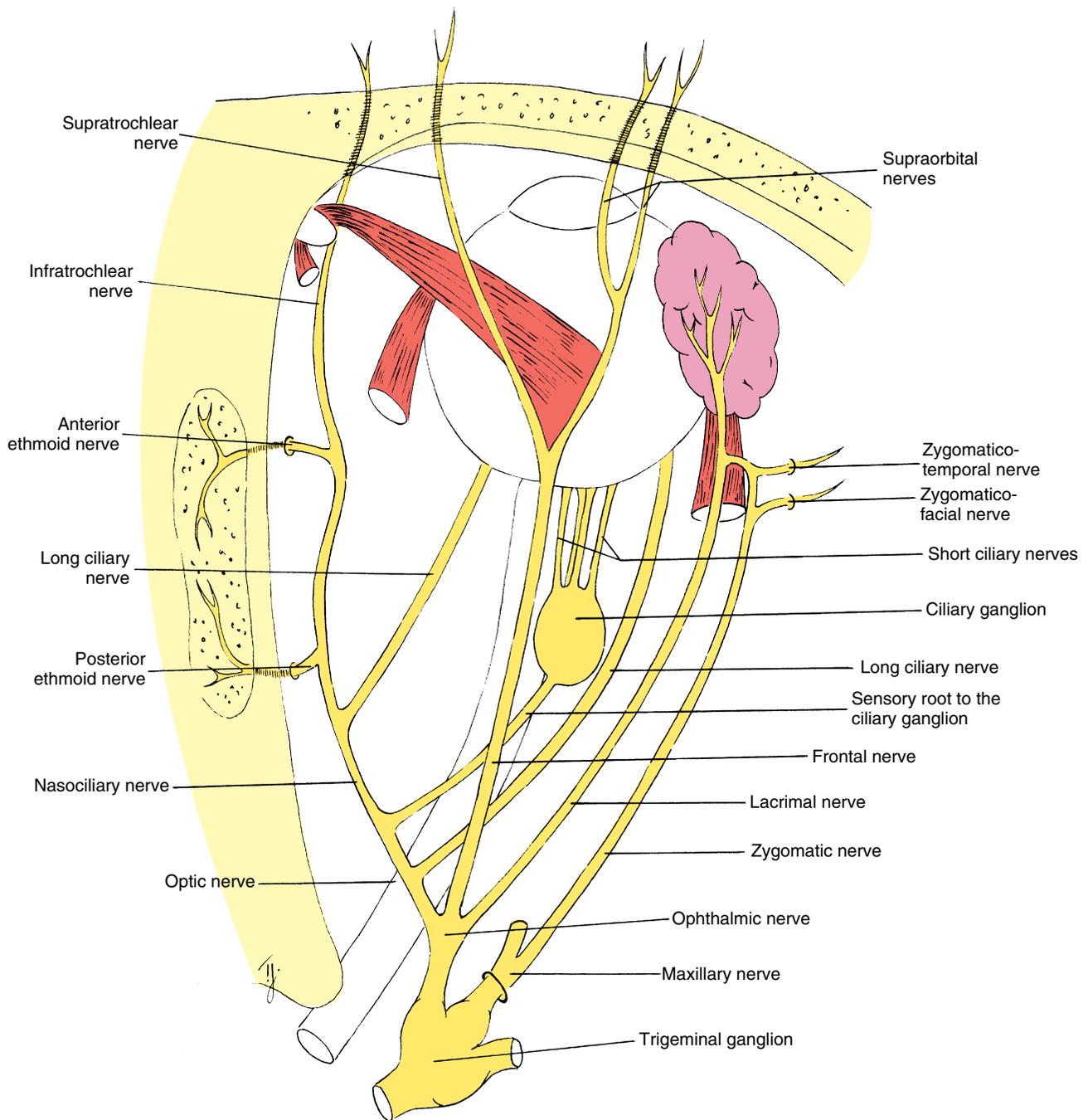


FIGURE 12-1
Orbit viewed from above showing branches of ophthalmic nerve.

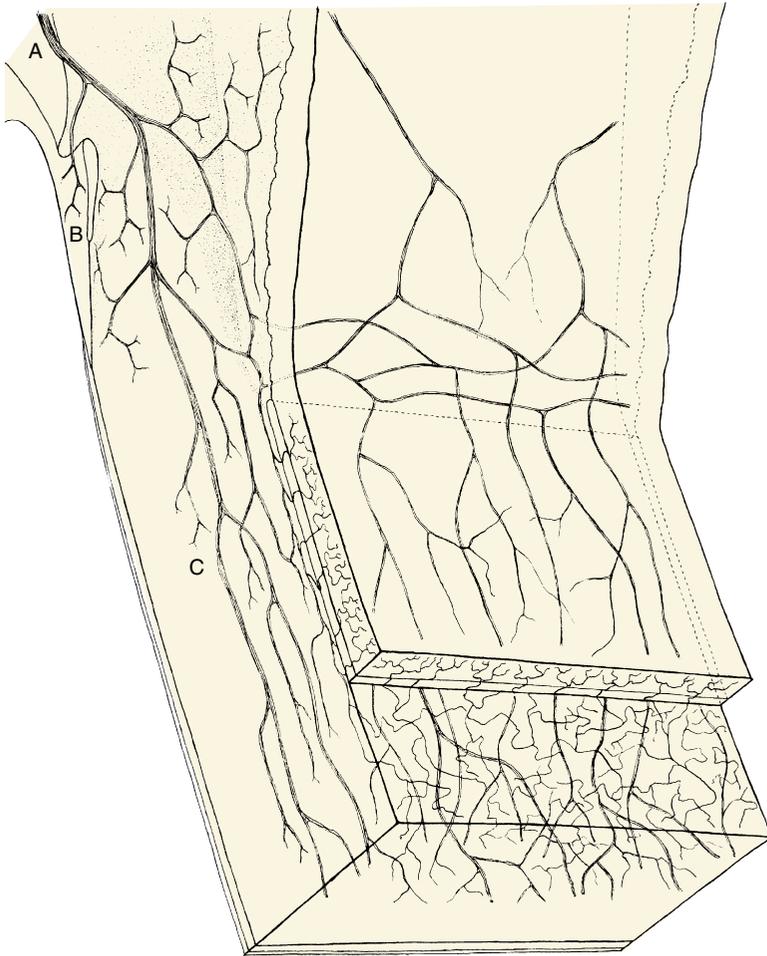


FIGURE 12-2

Innervation of limbus and cornea. Long ciliary nerve (A) supplies limbal region, then sends branches into cornea. Nerves also supply trabecular meshwork (B) and region of Schlemm's canal. Note paucity of nerves in deep cornea (C) and their absence in region of Descemet's membrane. (From Hogan MJ, Alvarado JA, Weddell JE, editors: *Histology of the human eye*, Philadelphia, 1971, Saunders.)

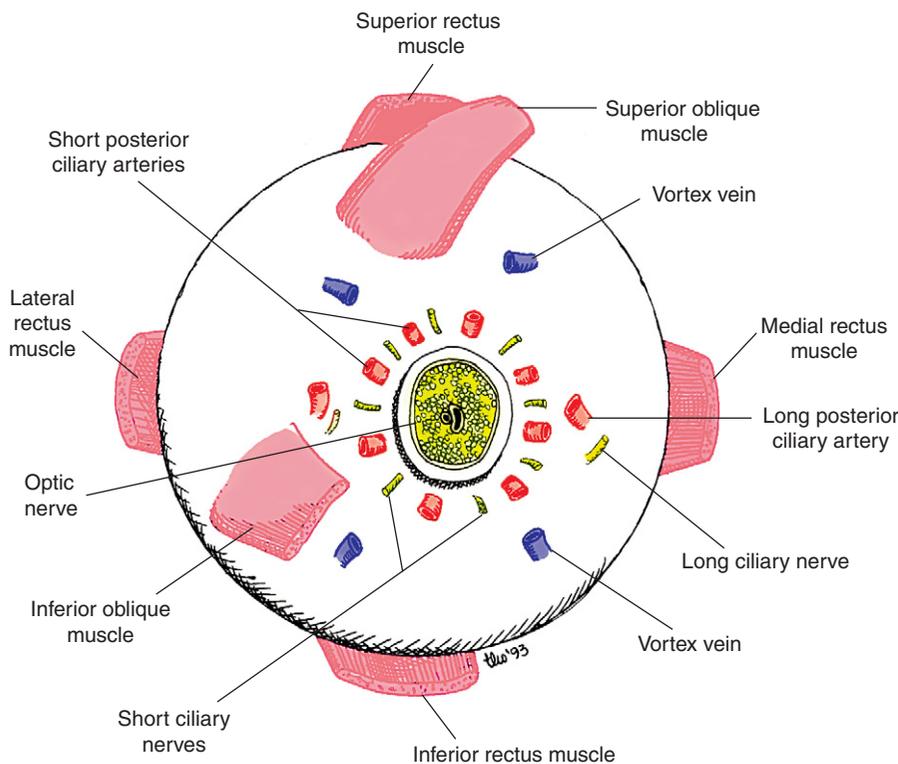


FIGURE 12-3

Posterior sclera. Posterior portion of globe showing optic nerve passing through posterior scleral foramen; long and short ciliary arteries and nerves passing through posterior apertures; and vortex veins passing through middle apertures.

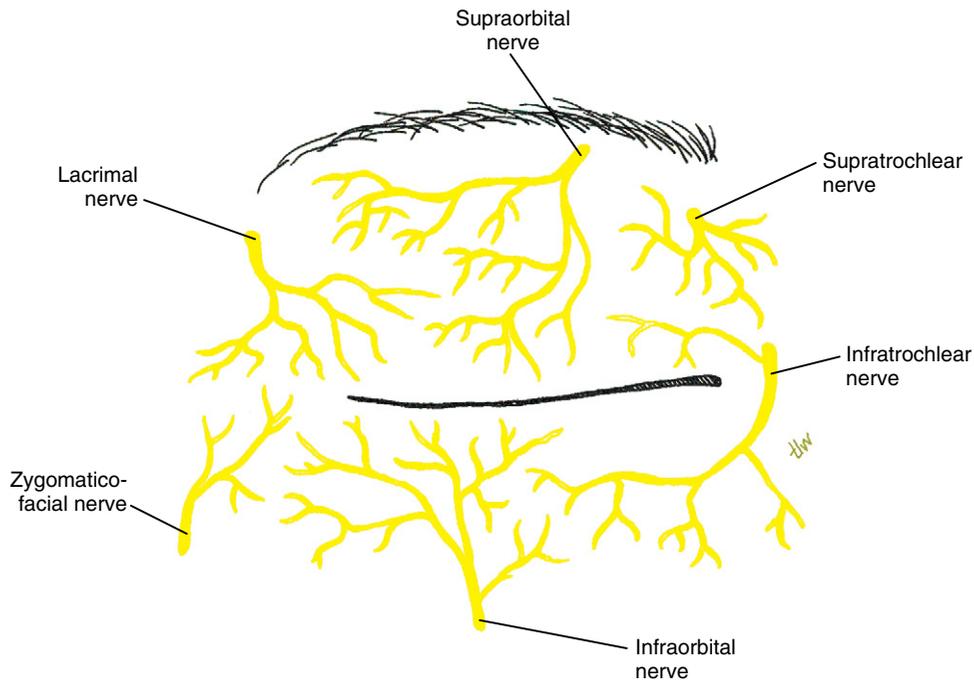


FIGURE 12-4
Sensory innervation to upper and lower eyelids.

supraorbital nerve joins the supratrochlear nerve midway in the orbit and forms the **frontal nerve** (see Figure 12-1). The frontal nerve courses back through the orbit between the levator muscle and the periorbita, exiting the orbit through the superior orbital fissure *above* the common tendinous ring.

Lacrimal Nerve. Sensory fibers from the lateral aspect of the upper eyelid and temple area come together and enter the lacrimal gland; they join the sensory fibers that serve the gland itself to form the **lacrimal nerve**. The lacrimal nerve leaves the gland and runs posteriorly along the upper border of the lateral rectus muscle (see Figure 12-1). It receives a branch from the zygomatic nerve containing the autonomic innervation of the lacrimal gland. The lacrimal nerve exits the orbit through the superior orbital fissure *above* the muscle cone.

Ophthalmic Nerve Formation

After exiting the orbit, the nasociliary nerve, the lacrimal nerve, and the frontal nerve join and form the ophthalmic division of the trigeminal nerve (see Figure 12-1). The **ophthalmic nerve** then enters the lateral wall of the cavernous sinus. While in the wall of the sinus the nerve receives sensory fibers from the oculomotor, trochlear, and abducens nerves. Some of

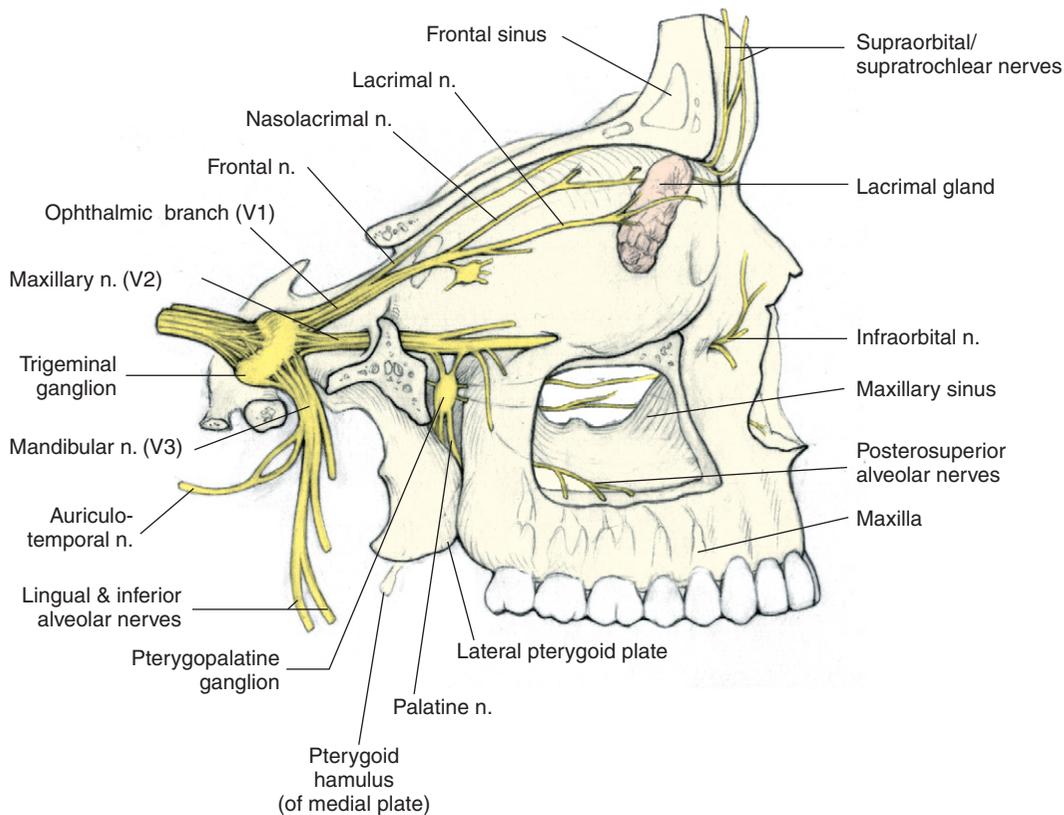
these fibers probably carry proprioceptive information from the extraocular muscles.¹³

Maxillary Division of Trigeminal Nerve

Infraorbital Nerve. The **infraorbital nerve**, formed by sensory fibers from the cheek, upper lip, and lower eyelid, enters the maxillary bone through the infraorbital foramen (Figure 12-5). It runs posteriorly through the infraorbital canal and groove; while it is in the maxillary bone, branches join from the upper teeth and maxillary sinus. As the nerve leaves the infraorbital groove it exits the orbit through the inferior orbital fissure and joins other fibers in forming the maxillary nerve.

CLINICAL COMMENT: REFERRED PAIN

Referred pain is pain felt in an area remote from the actual site of involvement; however, the two areas usually are connected by a sensory nerve network. Frequently, the pathways of the trigeminal nerve are involved in referred pain. A common example is a momentary severe bilateral frontal headache sometimes experienced when an individual eats ice cream.⁴ An abscessed tooth can cause pain described by a patient as ocular pain and should be suspected when no orbital cause for the pain can be found. These two situations likely occur because the overload of sensation carried by the infraorbital nerve is interpreted by the brain as coming from another area also served by the trigeminal nerve.

**FIGURE 12-5**

Three divisions of trigeminal nerve. (From Mathers LH, Chase RA, Dolph J et al: *Clinical anatomy principles*, St Louis, 1996, Mosby.)

Zygomatic Nerve. Sensory fibers from the lateral aspect of the forehead enter the orbit through a foramen in the zygomatic bone as the *zygomaticotemporal nerve*. Fibers from the lateral aspect of the cheek and lower eyelid enter the orbit through a foramen in the zygomatic bone as the *zygomaticofacial nerve*.¹² These two nerves join to become the **zygomatic nerve** and course along the lateral orbital wall, exiting the orbit through the inferior orbital fissure and joining with the maxillary nerve (see Figure 12-1).

Maxillary Nerve Formation

Having been formed by the joining of the infraorbital nerve, the zygomatic nerve, and nerves from the roof of the mouth, upper teeth and gums, and mucous membranes of the cheek, the **maxillary nerve** traverses the area between the maxilla and the sphenoid bone. As it passes near the pterygopalatine fossa, it receives some autonomic fibers from the pterygopalatine ganglion (see Figure 12-5). (These autonomic fibers are destined for the lacrimal gland and are discussed in Chapter 14.) The maxillary nerve enters the skull through the foramen rotundum.

Mandibular Division of Trigeminal Nerve

The mandibular nerve innervates the lower face and contains both sensory and motor fibers. It enters the skull via the foramen ovale.

TRIGEMINAL NERVE FORMATION

As these three divisions—the ophthalmic, maxillary, and mandibular—enter the skull, they run posteriorly within the lateral wall of the cavernous sinus^{14,15} (Figure 12-6) and enter the **trigeminal ganglion (gasserian ganglion, semilunar ganglion)**, where they synapse. The ganglion, flattened and semilunar in shape, is located lateral to the internal carotid artery and the posterior portion of the cavernous sinus. The motor fibers of the mandibular division, which innervate the muscles of mastication, pass along the lower edge of the ganglion.¹⁶ Only the sensory fibers synapse within the ganglion.

The fibers leave the trigeminal ganglion and enter the lateral aspect of the pons as either the sensory root or the motor root of the **trigeminal nerve**. The sensory root carries information from the structures of the face and head, including all orbital structures. After entering

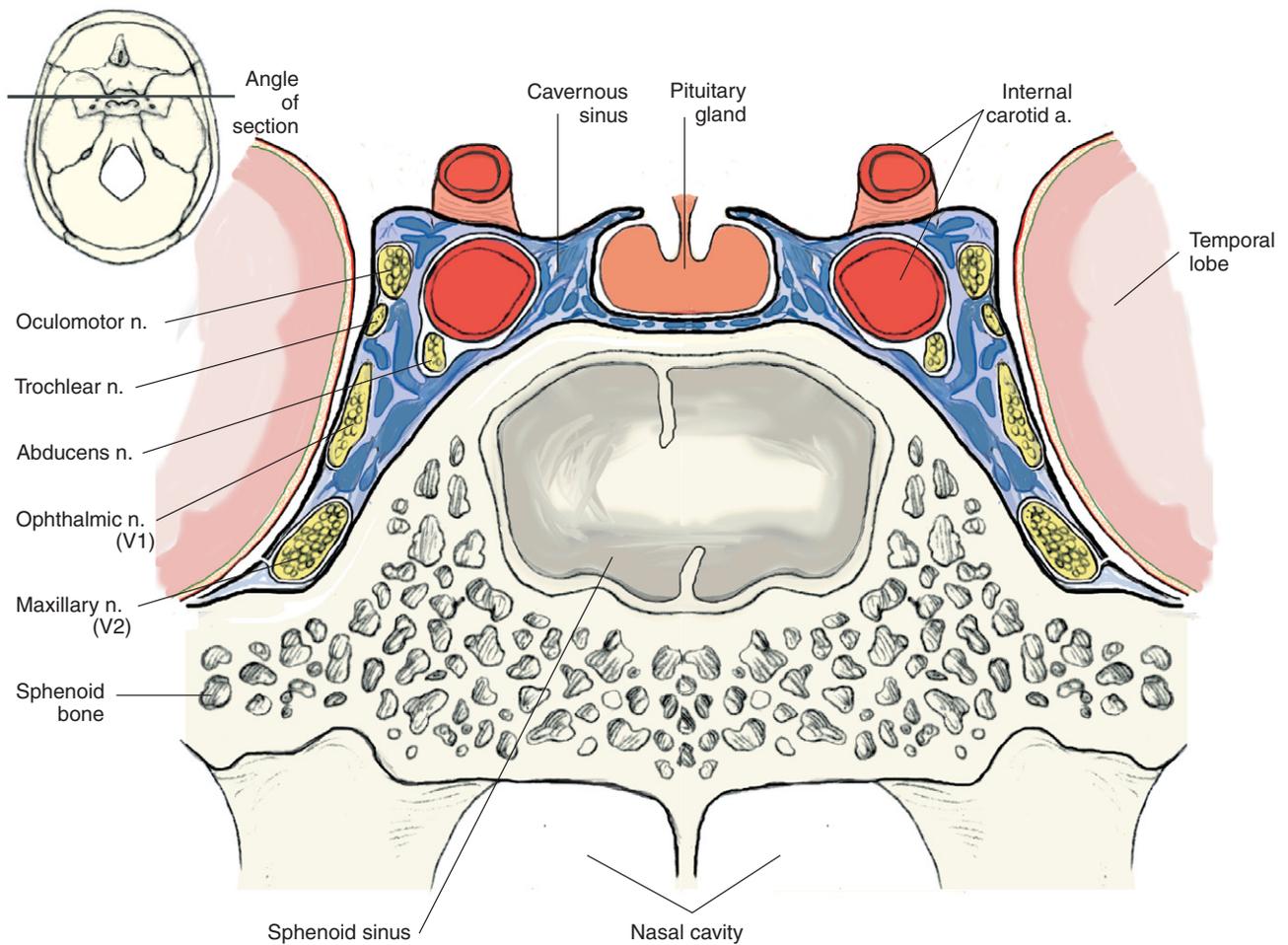
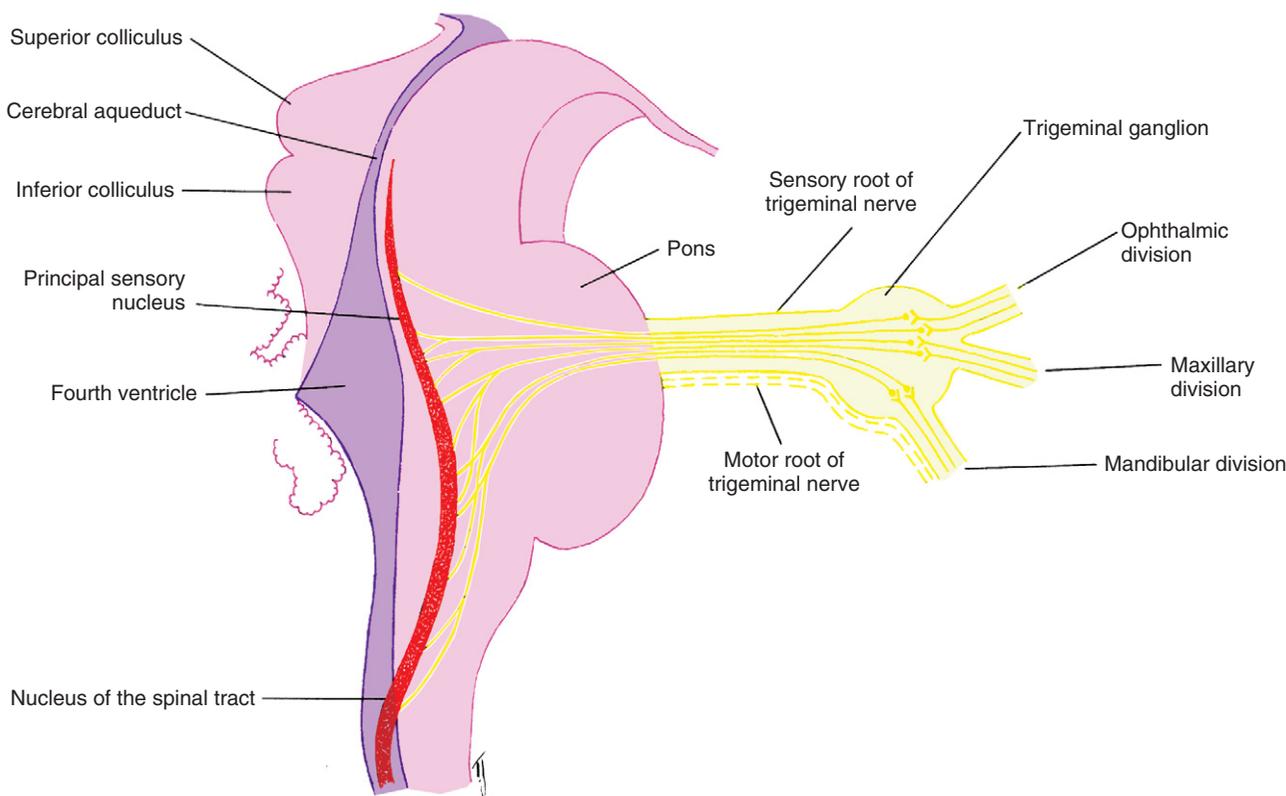


FIGURE 12-6
Detailed cross section of cavernous sinus. (From Mathers LH, Chase RA, Dolph J et al: *Clinical anatomy principles*, St Louis, 1996, Mosby.)

**FIGURE 12-7**

Sagittal section through brain stem showing divisions, ganglion, motor and sensory roots, and nuclei of cranial nerve V.

the brain stem these fibers form an ascending and a descending tract, both terminating in the sensory nuclei of the trigeminal nerve (Figure 12-7). The ascending tract terminates in the *principal sensory nucleus* in the pons; it registers the sensations of touch and pressure.¹ The descending tract, which carries pain and temperature sensations, courses through the pons and medulla to the elongated *nucleus of the spinal tract*.¹ The tract extends into the second cervical segment of the spinal cord.¹⁷ Information from the trigeminal nuclei is relayed to the thalamus.

CLINICAL COMMENT: OCULOCARDIAC REFLEX

The oculocardiac reflex consists of bradycardia (slowed heartbeat), nausea, and faintness and can be elicited by pressure on the globe or stretch on the extraocular muscles (e.g., during ocular surgery).¹⁸⁻²⁰ Fibers from the trigeminal spinal nucleus project into the reticular formation near the vagus nerve nuclei and can activate vagus synapses, precipitating this reflex. The motor aspect of the reflex can be blocked by retrobulbar anesthesia or intravenous or intramuscular atropine.^{1,12,21,22}

EFFERENT PATHWAY: MOTOR NERVES

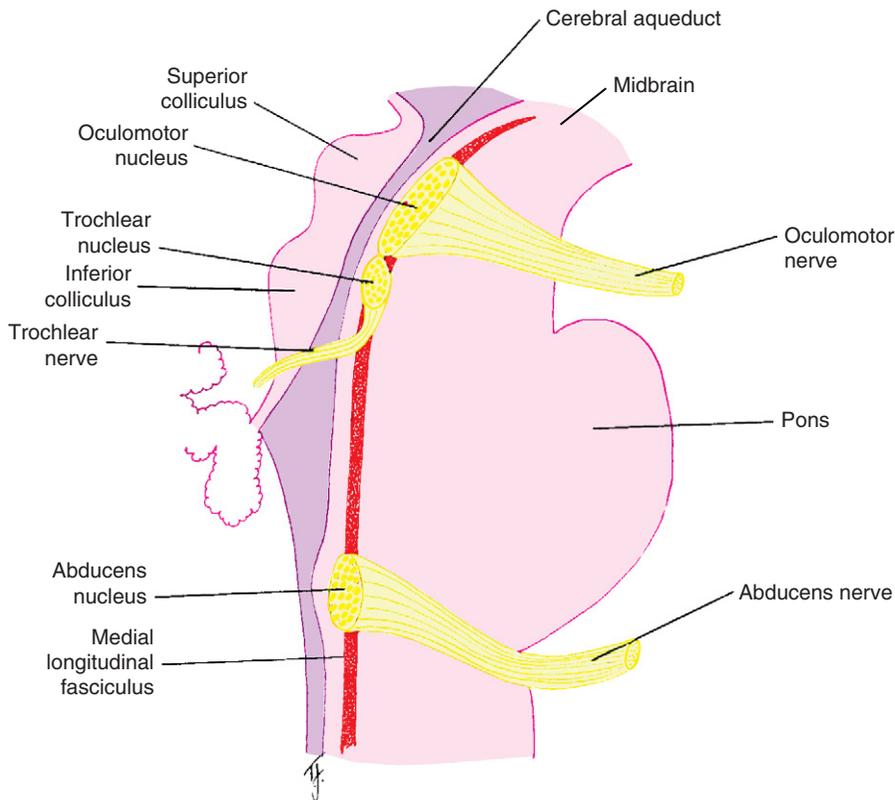
The cranial nerves that supply striated muscles of the orbit and adnexa are the oculomotor nerve, the trochlear nerve, the abducens nerve, and the facial nerve.

OCULOMOTOR NERVE: CRANIAL NERVE III

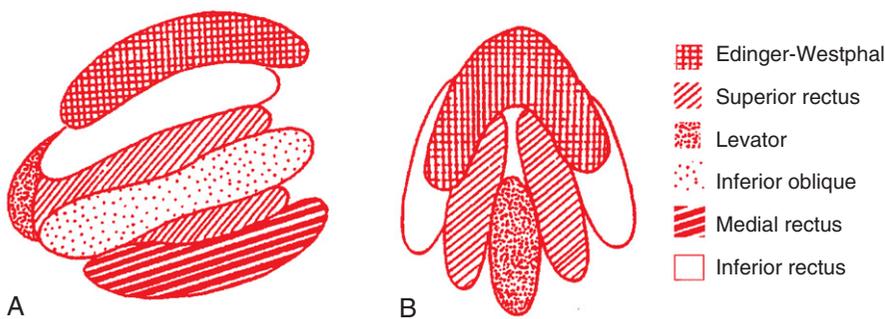
The **oculomotor nerve** innervates the superior rectus, medial rectus, inferior rectus, inferior oblique, and superior palpebral levator muscles. It also provides a route along which the autonomic fibers travel to innervate the iris sphincter muscle, the ciliary muscle, and the smooth muscles of the eyelid.

Oculomotor Nucleus

The **oculomotor nucleus** is located in the midbrain, ventral to the cerebral aqueduct, at the level of the superior colliculus (Figure 12-8). It extends in a column from the posterior edge of the floor of the third ventricle to the trochlear nucleus.^{2,12}

**FIGURE 12-8**

Sagittal section through brain stem showing trigeminal, oculomotor, trochlear, abducens, and facial nuclei.

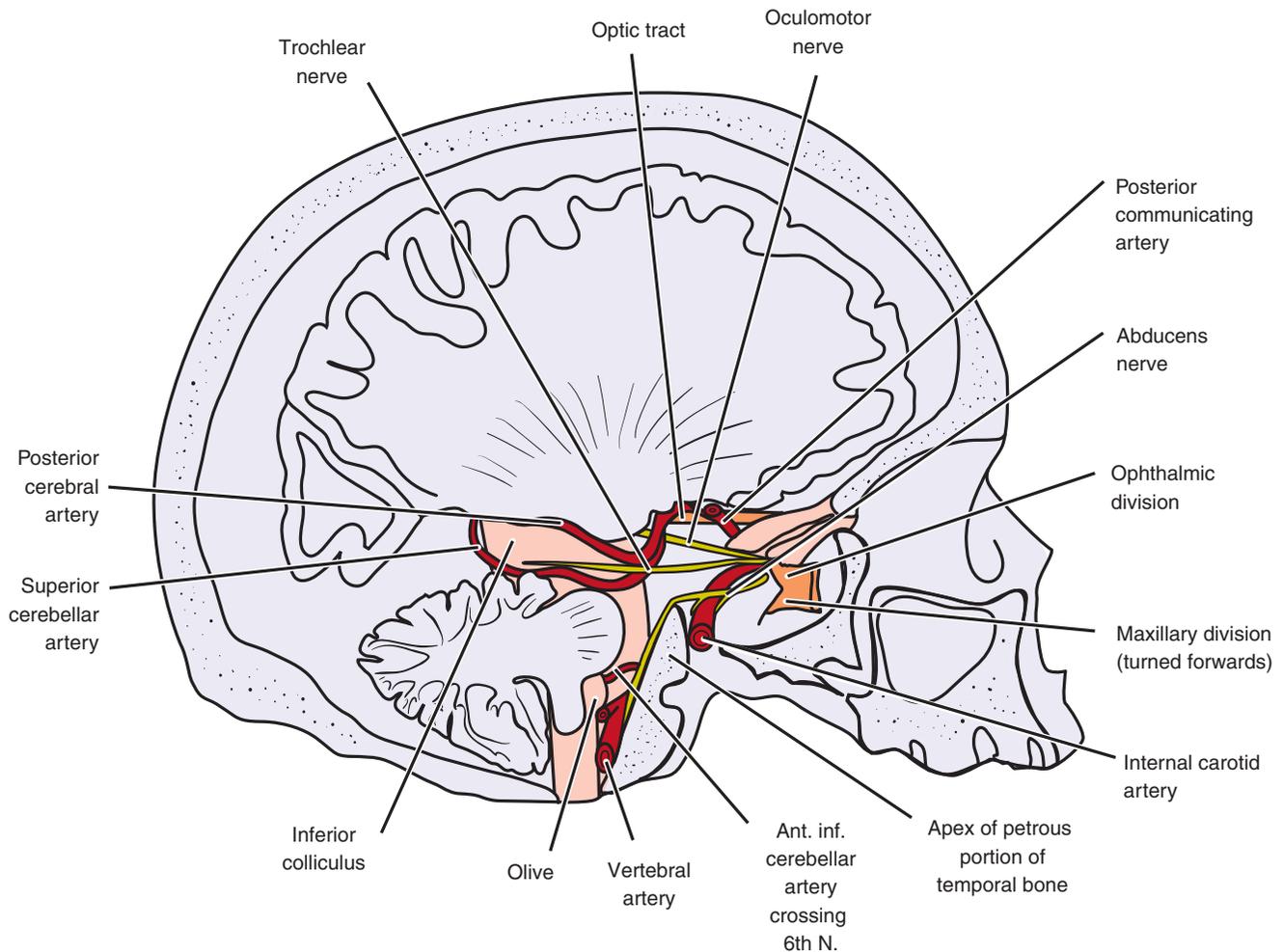
**FIGURE 12-9**

Oculomotor nerve nuclei. **A**, Lateral view. **B**, Dorsal view.

A definitive area or subnucleus within the oculomotor nucleus controls each muscle. The proposed arrangement of the subnuclei are postulated primarily on the basis of animal models.^{21,23-25} The nucleus for the medial rectus is located toward the lower border of the oculomotor nucleus; the inferior rectus nucleus lies toward the upper border, with the nucleus for the inferior oblique between. The nucleus of the superior rectus lies in the medial and caudal two thirds of the oculomotor nucleus. Each of these subnuclei are found in the right and left oculomotor nucleus. The nucleus

for the levator muscle is single and is located centrally in the caudal area (Figure 12-9).

Fibers to the inferior rectus, inferior oblique, and medial rectus muscles supply the ipsilateral eye; fibers innervating the superior rectus muscle decussate and supply the contralateral eye. The decussating fibers pass through the opposite superior rectus nucleus; thus, damage to the right oculomotor nucleus might have bilateral superior rectus muscle involvement.²⁵⁻²⁸ The centrally placed caudal nucleus provides innervation for both levator muscles.

**FIGURE 12-10**

Sagittal section through brain showing relationships among cranial nerves III, IV, and VI and neighboring blood vessels.

An autonomic nucleus, the *accessory third nerve nucleus (Edinger-Westphal nucleus)*, supplies parasympathetic innervation to the ciliary and iris sphincter muscles. It is located in the rostral, ventral portion of the oculomotor nucleus^{28,29} (see Figure 12-9).

Oculomotor Nerve Pathway

Fibers from each of the individual nuclei join, forming the fascicular part of the nerve that passes through the red nucleus and the cerebral peduncle. These fibers emerge from the interpeduncular fossa on the anterior aspect of the midbrain as the **oculomotor nerve**. The nerve passes between the superior cerebellar and posterior cerebral arteries as it runs forward, lateral to, and slightly inferior to the posterior communicating artery of the circle of Willis (Figure 12-10). The nerve

pierces the roof of the cavernous sinus and runs within its lateral wall above the trochlear nerve^{2,14} (see Figure 12-6). While in the cavernous sinus the oculomotor nerve sends small sensory branches to the ophthalmic nerve and receives sympathetic fibers from the plexus around the internal carotid artery.^{2,17}

The oculomotor nerve exits the sinus and enters the orbit through the superior orbital fissure, having divided into superior and inferior divisions; both divisions are located *within* the oculomotor foramen. The *superior branch* runs medially above the optic nerve and enters the superior rectus on its inferior surface; additional fibers either pierce the muscle or pass around its border to innervate the levator³⁰ (Figure 12-11).

The *inferior branch* runs below the optic nerve and divides into three branches. One branch enters the medial rectus on its lateral surface, and one enters the

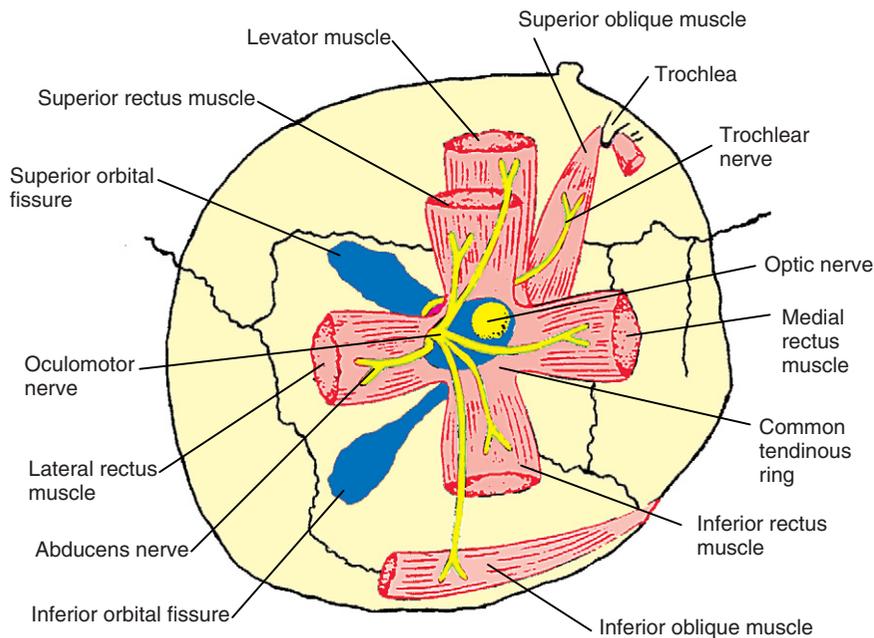


FIGURE 12-11

Orbital apex with the globe removed, showing relationship between superior orbital fissure and common tendinous ring.

inferior rectus on its upper surface. The third branch gives off parasympathetic fibers that form the parasympathetic root to the ciliary ganglion; then it runs along the lateral border of the inferior rectus, crossing it to enter the inferior oblique muscle near its midpoint^{4,31,32} (see Figure 12-11).

TROCHLEAR NERVE: CRANIAL NERVE IV

The **trochlear nerve** innervates the superior oblique muscle.

Trochlear Nucleus

The **trochlear nucleus** is located in the midbrain, anterior to the cerebral aqueduct and below the oculomotor nucleus, at the level of the inferior colliculus (see Figure 12-8). The fibers travel dorsally and decussate. CN IV is the only cranial nerve to cross; thus the trochlear nucleus innervates the contralateral superior oblique muscle.

Trochlear Nerve Pathway

Of the cranial nerves, the trochlear nerve is the only one that leaves the dorsal aspect of the CNS. It is the most slender of the cranial nerves, and its attachment is very delicate. (The small diameter of the nerve probably reflects the fact that it supplies only one muscle, the most slender of the extraocular muscles.) As the **trochlear nerve** emerges from the dorsal midbrain below the inferior colliculus, it decussates and curves around the cerebral peduncle at the upper border of the

pons, approximately paralleling the superior cerebellar and posterior cerebral arteries. It passes between these two vessels and runs forward lateral to the oculomotor nerve (see Figure 12-10).

The trochlear nerve enters the wall of the cavernous sinus and lies between the oculomotor nerve and the ophthalmic division of the trigeminal nerve (see Figure 12-6).^{4,14} While in the sinus the trochlear nerve sends sensory fibers to the ophthalmic nerve. It enters the orbit through the superior orbital fissure *above* the common tendinous ring, outside the muscle cone (see Figure 12-11). The trochlear nerve runs with the frontal nerve to the medial side of the orbit above the levator and superior rectus muscles and enters the upper surface of the superior oblique muscle.⁹

ABDUCENS NERVE: CRANIAL NERVE VI

The **abducens nerve** innervates the lateral rectus muscle.

Abducens Nucleus

The **abducens nucleus** is located near the midline of the pons beside the floor of the fourth ventricle (see Figure 12-8). The fibers from the nucleus pass through the pons and exit in the groove between the pons and the medulla oblongata. The abducens nucleus also contains *internuclear neurons* that communicate with the nucleus for the contralateral medial rectus muscle in the oculomotor complex via the medial longitudinal fasciculus.³³ This is the pathway for conjugate horizontal eye movements. This pathway receives information

from higher CNS centers, including the paramedial pontine reticular formation, the cerebellum, and the vestibular nucleus. Thus, coordinated movement of the ipsilateral lateral rectus muscle and the contralateral medial rectus muscle results in conjugate horizontal eye movement.³³

Abducens Nerve Pathway

In its long, tortuous, intracranial course, the **abducens nerve** runs along the occipital bone at the base of the skull and up along the posterior slope of the petrous portion of the temporal bone, makes a sharp bend over the petrous ridge (see Figure 12-10), and enters the cavernous sinus.^{4,12,34} Within the sinus it lies near the lateral wall of the internal carotid artery⁵ (see Figure 12-6); it gives off small branches, possibly proprioceptive fibers, to the ophthalmic nerve. The abducens nerve enters the orbit through the superior orbital fissure *within* the common tendinous ring and innervates the lateral rectus muscle on the medial surface (see Figure 12-11).

SUPERIOR ORBITAL FISSURE

The trochlear, frontal, and lacrimal nerves and the superior ophthalmic vein are located in the superior orbital fissure *above* the muscle cone. The superior and inferior divisions of the oculomotor nerve, the abducens nerve, and the nasociliary nerve are located within the superior orbital fissure *and* the common tendinous ring. The inferior ophthalmic vein lies *below* the fissure *and* the tendinous ring (see Figure 8-15).

CONTROL OF EYE MOVEMENTS

Communication among areas of the CNS is necessary to produce controlled and coordinated eye movements. The **corticonuclear tract** contains fibers that run from the cerebral hemispheres to the nuclei of CNs III, IV, and VI; the **tectobulbar tract** connects the superior colliculus to the CN III, IV, and VI nuclei. The **medial longitudinal fasciculus** extends from the midbrain into the spinal cord and connects the vestibular nucleus, the oculomotor nucleus, the abducens nucleus, and the trochlear nucleus, providing a connection between eye movement control and the vestibular apparatus (see Figure 12-8).

FACIAL NERVE: CRANIAL NERVE VII

The **facial nerve** has two roots; the large motor root innervates the facial muscles, and the smaller root contains sensory and parasympathetic fibers. The sensory fibers carry taste sensations from the tongue. The parasympathetic nerves supply secretomotor fibers

to various glands of the face; those supplying the lacrimal gland are discussed in Chapter 14.

Facial Nucleus

The motor nucleus of the facial nerve is located in the reticular formation of the pons. The upper segment of the nucleus supplies the frontalis, procerus, corrugator superciliaris, and orbicularis muscles, and the lower segment supplies the remaining facial muscles.^{35,36}

Facial Nerve Pathway

The fibers leave the facial nucleus arch around the abducens nucleus and emerge as the **facial nerve** from the brain stem at the lower border of the pons. The facial nerve enters the internal acoustic foramen in the petrous portion of the temporal bone and runs through a canal in the bone. While in the temporal bone, parasympathetic fibers en route to the lacrimal gland are given off as the greater petrosal nerve.^{35,36} The motor fibers of the facial nerve emerge through the stylo-mastoid foramen, pass below the external auditory canal, travel over the mandibular ramus, and divide into several branches (Figure 12-12). The upper two—the temporal and zygomatic branches—supply the frontalis, procerus, corrugator, and orbicularis muscles.

The following Clinical Comments discuss damage to the cranial nerves, specifically the oculomotor, trochlear, and abducens nerves, caused by involvement of adjacent cranial and orbital structures and the resulting clinical presentation.

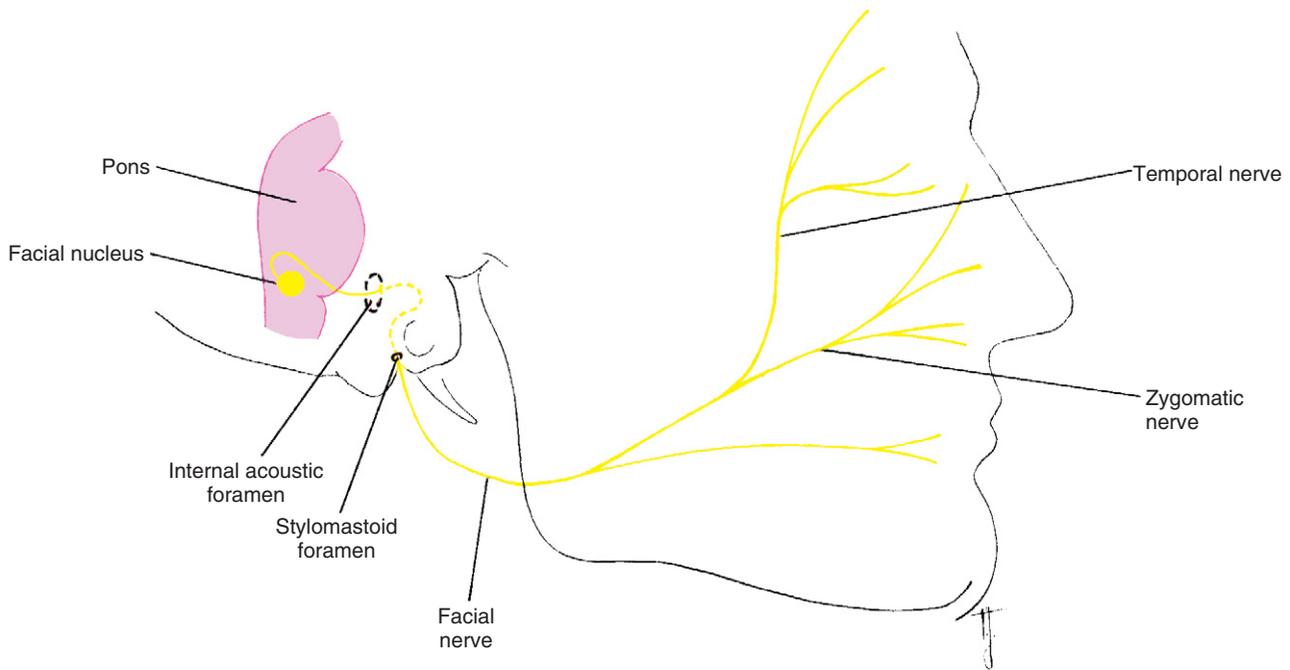
CLINICAL COMMENT: CRANIAL NERVE DAMAGE

Injury to sensory cranial nerve fibers results in anesthesia, a loss of sensation in the innervated area. Injury to a cranial motor nerve causes either a partial loss (paresis) or a total loss (paralysis) of muscle function. Paresis or paralysis of an extraocular muscle can result in diplopia if the involvement is acquired; in congenital involvement, diplopia usually is not a complaint, because the brain has learned to disregard the double image, resulting in suppression.

Nerve fibers can be damaged by a compromised blood supply caused by vascular diseases (e.g., hypertension, atherosclerosis, diabetes mellitus) or by space-occupying lesions (e.g., aneurysms, hemorrhages, tumors) that exert pressure on the nerve fibers. The location of the involvement will influence the presenting signs and symptoms.

In various studies of isolated extraocular nerve paralysis, the sixth cranial nerve was reported to be affected most often, and the fourth cranial nerve was affected least often.³⁷⁻³⁹ The tortuosity and length of the abducens nerve make it susceptible to compression and stretching injuries and may explain why it is damaged so frequently.¹⁴

Continued

**FIGURE 12-12**

Facial nerve pathway. Motor pathway of facial nerve to facial muscles of orbit.

A number of clinical signs and symptoms accompany damage to the motor nerves that innervate the extraocular muscles. Muscle paresis or paralysis will be evident in testing ocular motility (as described in Chapter 10). In acquired extraocular muscle impairment, a patient often attempts to minimize diplopia by carrying the head in a compensatory position. If a horizontal deviation is present, the head will be turned to the right or left. With a vertical deviation the head is raised or lowered, and if a torsional deviation occurs the head is tilted toward the shoulder. With right superior oblique involvement the head will be turned to the left, positioned down, and tilted toward the left shoulder^{40,41} (Figure 12-13).

CLINICAL COMMENT: OCULOMOTOR DAMAGE

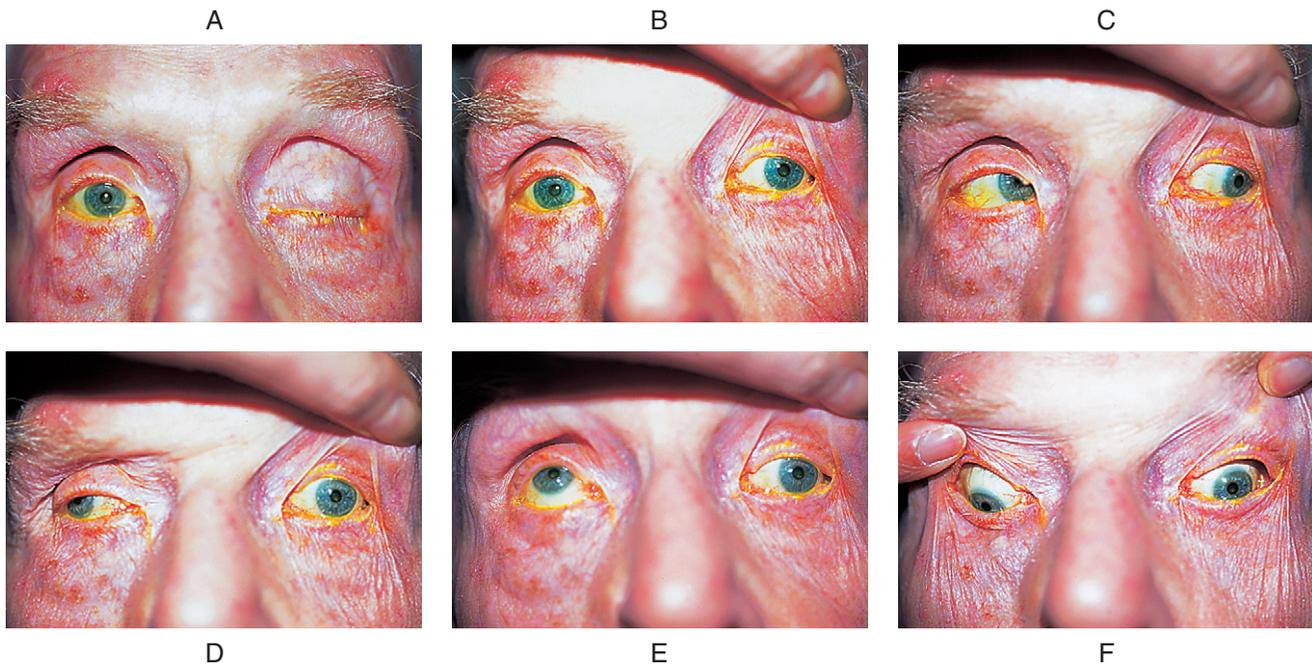
MIDBRAIN INVOLVEMENT. A lesion in the midbrain can affect the entire oculomotor nucleus or selectively affect only some subnuclei; however, such selective damage is unusual.²⁶ If the lesion affects the entire oculomotor nucleus, the muscles involved are the ipsilateral medial rectus, inferior rectus, and inferior oblique, contralateral superior rectus, and both levators. The ipsilateral superior rectus might be involved as well, because the decussating fibers pass through the contralateral superior rectus nucleus.²⁶ The trochlear nucleus is near the oculomotor nucleus, and if it too is involved, the contralateral superior oblique muscle will be affected. The clinical presentation would show the ipsilateral eye positioned out in primary position and only able to move in as far as the midline. The contralateral eye would be unable to elevate in abduction and unable to depress in adduction.

**FIGURE 12-13**

Patient tilts head toward the left shoulder and turns head to the left and down, resulting from right superior oblique dysfunction. (From Eskridge JB: *J Am Optom Assoc* 60(5):378, 1989.)

INTRACRANIAL INVOLVEMENT. The oculomotor nerve lies near several blood vessels in its intracranial path and frequently is affected by an aneurysm of the posterior communicating artery.⁴² An aneurysm of the superior cerebellar artery or the posterior cerebral artery could also impinge on the nerve, damaging fibers.

Continued

**FIGURE 12-14**

Third nerve palsy, left eye (OS). **A**, Lid ptosis. **B**, Primary gaze, eye positioned out. **C**, Normal abduction. **D**, Unable to adduct. **E**, Unable to elevate. **F**, Unable to depress. (From Kanski J]: *Clinical ophthalmology: a systematic approach*, ed 5, Oxford, England, 2003, Butterworth-Heinemann.)

Once the oculomotor nerve exits the midbrain, all its fibers supply the ipsilateral eye, and the dysfunction is unilateral. Damage to the nerve results in ptosis because of levator muscle paralysis; in primary position the eye is positioned out because of the unopposed action of the superior oblique and lateral rectus muscles (Figure 12-14, A and B). (Because the superior oblique muscle is unaffected, the eye also should be positioned down, but clinically this is not always evident.⁴³) The eye cannot adduct (Figure 12-14, D) and, in the abducted position, cannot move up or down (Figure 12-14, E and F).² In paralysis of the iris sphincter and ciliary muscle, the pupil will be dilated, and accommodation will not occur.

Incomplete lesions of the oculomotor nerve are possible. In external ophthalmoplegia the extraocular muscles are paralyzed and the intrinsic muscles are spared; in internal ophthalmoplegia the internal muscles are paralyzed and the extraocular muscles are spared. As the oculomotor nerve exits the midbrain, the parasympathetic fibers are superficial, and as the nerve nears the orbit, the parasympathetic fibers move into the center of the nerve and therefore are better protected. Sparing of the parasympathetic fibers in ischemic lesions may account for normal pupillary responses usually seen with diabetic ophthalmoplegia.^{26,44-46}

CAVERNOUS SINUS INVOLVEMENT. The lateral wall of the cavernous sinus contains the oculomotor nerve as well as the trochlear, ophthalmic, and maxillary nerves. A lesion that affects all these nerves would leave only the lateral rectus muscle still functioning. The eye would be positioned out in primary gaze and could move only from the lateral position to the midline. Anesthesia of the facial areas served by the ophthalmic and maxillary nerves would be present in addition to the impaired ocular motility.

ORBITAL INVOLVEMENT. Both divisions of the oculomotor nerve are located within the muscle cone, together with the abducens and nasociliary nerves. A retrobulbar tumor or inflammation involving these nerves would leave only the superior oblique muscle functional. In primary position the eye would be positioned downward and outward slightly and would be fairly immobile. Corneal sensitivity could be decreased because of nasociliary nerve involvement.

ABERRANT REGENERATION OF THE OCULOMOTOR NERVE. After injury the brain may attempt to repair a nerve, and some attempts may be misdirected, eliciting an unusual clinical presentation. Fibers going to the inferior oblique may sprout branches that also innervate the sphincter, causing pupillary constriction on elevation. Fibers innervating the medial rectus may send sprouts that innervate the sphincter, causing miosis with adduction or convergence.

**FIGURE 12-15**

Fourth nerve palsy OS, limitation in downgaze when adducted. (From Kanski JJ: *Clinical ophthalmology: a systematic approach*, ed 5, Oxford, England, 2003, Butterworth-Heinemann.)

CLINICAL COMMENT: TROCHLEAR DAMAGE

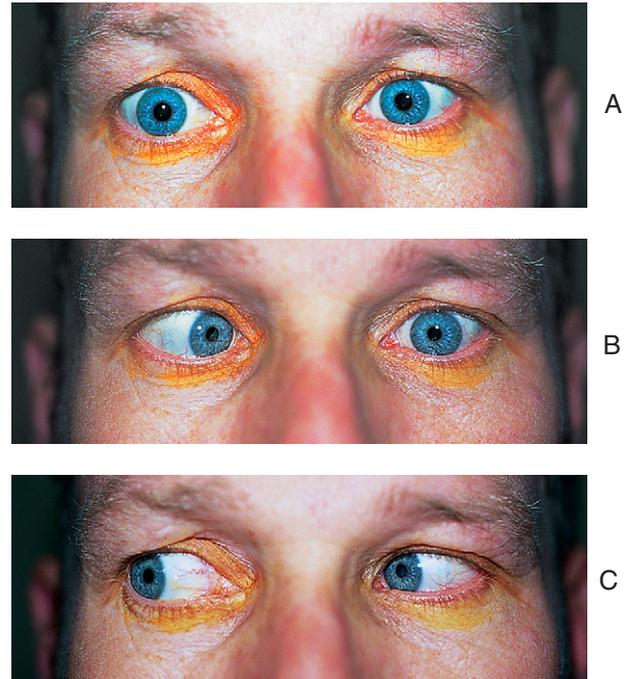
When the superior oblique muscle is affected by trochlear nerve damage, the eye is elevated in primary gaze and is unable to move down in the adducted position. The head may be tilted toward the opposite shoulder to compensate for the unopposed extorsion of the inferior oblique muscle⁴ (see Figure 12-13). Under the age of 10 years, palsies involving the trochlear nerve are usually congenital, and between 21 and 40 years of age the usual cause is trauma; otherwise the palsy may be idiopathic.⁴⁷⁻⁴⁹

MIDBRAIN INVOLVEMENT. Damage to the trochlear nucleus will affect the contralateral superior oblique muscle. Because of the proximity of the oculomotor nucleus, a lesion could affect both cranial nerve nuclei, resulting in the clinical presentation just discussed.

INTRACRANIAL INVOLVEMENT. For the most part, the trochlear nerve follows the same path as the oculomotor nerve and is susceptible to the same injuries. Damage to the trochlear nerve affects the ipsilateral superior oblique muscle, causing the eye to be elevated in primary gaze and unable to move down in the adducted position (Figure 12-15).

CAVERNOUS SINUS INVOLVEMENT. A lesion in the lateral wall of the cavernous sinus could affect the trochlear nerve. It could also affect the oculomotor, ophthalmic, and maxillary nerves, causing the previously described clinical presentation.

ORBITAL INVOLVEMENT. The trochlear nerve lies above the muscle cone near the frontal nerve, and injury affecting both nerves could impair the superior oblique muscle, limiting depression in the adducted position. Decreased sensitivity of the areas of the skin and scalp innervated by the branches of the frontal nerve might be observed.

**FIGURE 12-16**

Sixth nerve palsy, OS. **A**, Primary position, left eye positioned in. **B**, Unable to abduct; **C**, Normal adduction. (From Kanski JJ: *Clinical ophthalmology: a systematic approach*, ed 5, Oxford, England, 2003, Butterworth-Heinemann.)

CLINICAL COMMENT: ABDUCENS DAMAGE

Damage to the abducens nerve results in paralysis of the lateral rectus muscle; because of the unopposed action of the medial rectus muscle, a convergent strabismus is evident.⁵⁰ The eye will be unable to abduct (Figure 12-16). The patient might try to compensate for the diplopia by turning the face toward the paralyzed side.⁴

PONS INVOLVEMENT. Both the abducens and facial nuclei are located in the pons, and the fasciculus of the facial nucleus arches around the abducens nucleus. Damage here could affect the lateral rectus and the muscles of the forehead and the orbicularis. Symptoms might include inability to abduct the eye and lagophthalmos. The abducens nucleus also contains the internuclear neurons, so the patient may have a restriction when attempting to turn both eyes toward the side of the lesion. The contralateral medial rectus muscle may not be activated in this lateral gaze, but the patient will be able to converge.

INTRACRANIAL INVOLVEMENT. The course of the abducens nerve renders it particularly susceptible to increased intracranial pressure, which causes the brain stem to be displaced posteriorly, stretching the nerve over the bony prominence of the temporal bone.^{12,34,37} Fractures of the base of the skull and aneurysms of the basilar and carotid arteries can affect the abducens nerve.

Continued

CAVERNOUS SINUS INVOLVEMENT. *The abducens nerve is located near the internal carotid artery within the cavernous sinus. Often, it is the first nerve affected with an aneurysm of this vessel. A lateral rectus palsy with Horner's syndrome on the same side, suggesting sympathetic involvement, is indicative of cavernous sinus and internal carotid artery involvement.*

ORBITAL INVOLVEMENT. *The abducens nerve is located within the muscle cone. It accompanies the two divisions of the oculomotor nerve and the nasociliary nerve (with the resultant clinical presentation described earlier).*

REFERENCES

- Burton H: Somatic sensations from the eye. In Hart WM Jr, editor: *Adler's physiology of the eye*, ed 9, St Louis, 1992, Mosby, p 71.
- Warwick R: *Eugene Wolff's anatomy of the eye and orbit*, ed 7, Philadelphia, 1976, Saunders, p 275.
- Oliveira-Soto L, Efron N: Morphology of corneal nerves using confocal microscopy, *Cornea* 20(4):374, 2001.
- Wirtschafter JD: The peripheral courses of the third, fourth, fifth, sixth, and seventh cranial nerves. In Reeh MJ, Wobig JL, Wirtschafter JD, editors: *Ophthalmic anatomy*, San Francisco, 1981, American Academy of Ophthalmology, p 234.
- Müller LJ, Pels E, Vrensen GF: Ultrastructural organization of human corneal nerves, *Invest Ophthalmol Vis Sci* 37(4):476, 1996.
- Müller LJ, Pels E, Vrensen GF et al: Architecture of human corneal nerves, *Invest Ophthalmol Vis Sci* 38(5):985, 1997.
- Catania LJ: *Primary care of the anterior segment*, East Norwalk, Conn, 1988, Appleton & Lange, p 74.
- Berkow R, editor: *The Merck manual*, ed 14, Rahway, NJ, 1982, Merck, p 187.
- Bartlett JD, Jaanus SD: *Clinical ocular pharmacology*, ed 2, Boston, 1989, Butterworth-Heinemann, p 544.
- Schlaegel TF: Uveitis associated with viral infections. In Duane TD, Jaeger EA, editors: *Clinical ophthalmology*, Philadelphia, 1982, Harper & Row.
- Kanski JJ: *Clinical ophthalmology*, ed 3, London, 1994, Butterworth-Heinemann, p 111.
- Doxanas MT, Anderson RL: *Clinical orbital anatomy*, Baltimore, 1984, Williams & Wilkins, p 131.
- Feldon SE, Burde RM: The oculomotor system. In Hart WM Jr, editor: *Adler's physiology of the eye*, ed 9, St Louis, 1992, Mosby.
- Umansky J, Nathan H: The lateral wall of the cavernous sinus: with special reference to the nerves related to it, *J Neurosurg* 56:228, 1982.
- Nuza AB, Taner D: Anatomical variations of the intracavernous branches of the internal carotid artery with reference to the relationship of the internal carotid artery and sixth cranial nerve, *Acta Anat* 138:238, 1990.
- Beck RW, Smith CH: Trigeminal nerve. In Tasman W, Jaeger EA, editors: *Duane's foundations of clinical ophthalmology*, vol 1, Philadelphia, 1994, Lippincott.
- Warwick R, Williams PL, editors: *Gray's anatomy*, ed 35, Philadelphia, 1973, Saunders, pp 1001, 1006.
- Stott DG: Reflex bradycardia in facial surgery, *Br J Plast Surg* 42(5):595, 1989.
- Eustis HS, Eiswirth CC, Smith DR: Vagal responses to adjustable sutures in strabismus correction, *Am J Ophthalmol* 114(3):307, 1992.
- Hampl KE, Marsch SC, Schneider M et al: Vasovagal heart block following cataract surgery under local anesthesia, *Ophthalmic Surg* 24(6):422, 1993.
- Chong JL, Tan SH: Oculocardiac reflex in strabismus surgery under general anesthesia, *Singapore Med J* 31(1):38, 1990.
- Grover VK, Bhardwaj N, Shobana N et al: Oculocardiac reflex during retinal surgery using peribulbar block and nitrous narcotic anesthesia, *Ophthalmic Surg Lasers* 29(3):207, 1998 (abstract).
- Warwick R: Representation of the extraocular muscles in the oculomotor nucleus of the monkey, *J Comp Neurol* 98:449, 1953.
- Warwick R: Oculomotor organization. In Bender MB: *The oculomotor system*, New York, 1964, Harper & Row, p 173.
- Castro O, Johnson LN, Mamourian AC: Isolated inferior oblique paresis from brain stem infarction, *Arch Neurol* 47:235, 1990.
- Brazis PW: Localization of lesions of the oculomotor nerve: recent concepts, *Mayo Clin Proc* 66(10):1029, 1991.
- Bienfang DC: Crossing axons in the third nerve nucleus, *Invest Ophthalmol* 12:927, 1975.
- Marinkovic S, Marinkovic Z, Filipovic B: The oculomotor nuclear complex in humans: microanatomy and clinical significance, *Neurology* 38(2):135, 1989.
- Jampel RS, Mindel J: The nucleus for accommodation in the midbrain of the macaque, *Invest Ophthalmol* 6:40, 1967.
- Sacks JG: Peripheral innervation of the extraocular muscles, *Am J Ophthalmol* 95:520, 1983.
- Krewson W: Comparison of the oblique extraocular muscles, *Arch Ophthalmol* 32:204, 1944.
- Reeh MJ, Wobig JL, Wirtschafter JD: *Ophthalmic anatomy*, San Francisco, 1981, American Academy of Ophthalmology, p 75.
- Müri RM, Chermann JF, Cohen L et al: Ocular motor consequences of damage to the abducens area in humans, *J Neuroophthalmol* 16(3):191, 1996.
- Umansky F, Valarezo A, Elidan J: The microsurgical anatomy of the abducens nerve in its intracranial course, *J Neurosurg* 75(2):294, 1991.
- Monkhouse WS: The anatomy of the facial nerve, *Ear Nose Throat J* 69:677, 1990.
- Proctor B: The anatomy of the facial nerve, *Otolaryngol Clin North Am* 24:479, 1991.
- Rucker CW: The causes of paralysis of the third, fourth, and sixth cranial nerves, *Am J Ophthalmol* 63:1293, 1966.
- Rush JA, Younge BR: Paralysis of cranial nerves III, IV, and VI, *Arch Ophthalmol* 99:76, 1981.
- Tiffin PA, MacEwen CJ, Craig EA et al: Acquired palsy of the oculomotor, trochlear, and abducens nerves, *Eye* 10:377, 1996.
- Eskridge JB: Evaluation and diagnosis of incomitant ocular deviations, *J Am Optom Assoc* 60(5):375, 1989.
- Rubin MM: Trochlear nerve palsy simulating an orbital blowout fracture, *J Oral Maxillofac Surg* 50:1238, 1992.
- Troost BT, Glaser JS: Aneurysms, arteriovenous communications and related vascular malformations. In Glaser JS, editor: *Neuro-ophthalmology*, Hagerstown, Md, 1978, Harper & Row, p 319.
- Jampel RS: Ocular torsion and the function of the vertical extraocular muscles, *Am J Ophthalmol* 79:292, 1975.
- Goldstein JE, Cogan DG: Diabetic ophthalmoplegia with special reference to the pupil, *Arch Ophthalmol* 64:592, 1960.
- Gray LG: A clinical guide to third nerve palsy, *Rev Optom* 1:86, 1994.
- Ing EB, Leavitt JA, Younge BR: Incidence of pupillary involvement in ischemic oculomotor nerve palsies, *Ann Ophthalmol* 32(2):90, 2000.
- Burger LJ, Kalvin NH, Smith JL: Acquired lesions of the fourth cranial nerve, *Brain* 93:567, 1970.
- Young BR, Sutla F: Analysis of trochlear nerve palsies: diagnosis, etiology, and treatment, *Mayo Clin Proc* 52:11, 1977.
- Gundersen CA, Maxow ML, Avilla CW: Epidemiology of CN IV palsies, *Am Orthop J* 51:99, 2001.
- Galetta SL, Smith JL: Chronic isolated sixth nerve palsies, *Arch Neurol* 46:79, 1989.

▶ 13 *Visual Pathway*

The visual pathway consists of the series of cells and synapses that carry visual information from the environment to the brain for processing. It includes the retina, optic nerve, optic chiasm, optic tract, lateral geniculate nucleus (LGN), optic radiations, and striate cortex (Figure 13-1). The first cell in the pathway—a special sensory cell, the photoreceptor—converts light energy into a neuronal signal that is passed to the bipolar cell and the amacrine cell and then to the ganglion cell; all these cells and synapses lie within the retina. The axons of the ganglion cells exit the retina via the optic nerve, with the nasal fibers from each eye crossing in the optic chiasm and terminating in the opposite side of the brain. The optic tract carries these fibers from the chiasm to the LGN, where the next synapse occurs. The fibers leave the LGN as the optic radiations that terminate in the visual cortex of the occipital lobe. From various points in this pathway, information about the visual environment is transferred to related neurologic centers and to visual association areas.

This chapter discusses the structures of the visual pathway and orientation of the fibers within each structure, then briefly reviews characteristic field defects associated with specific locations in the visual pathway. Most of the current knowledge of the visual pathway is based on degeneration studies using laboratory animals, particularly monkeys and cats.¹⁻³ This type of investigation is based on the finding that damage to a neuron causes the cell and its processes to degenerate. After a small area of nerve tissue is damaged, researchers make serial sections of the tissue through which the neuronal processes are believed to pass. By examining these sections under the microscope, they identify the pathway by determining the location of the degenerating processes. In some studies, small lesions were made in the retina, and the degeneration was followed through the optic nerve, chiasm, and tract into the LGN.^{1,3} In other studies, lesions were made in the striate cortex, and the degeneration was followed through the optic radiations toward the LGN.² Whenever possible, reference to studies on the human pathway are cited.

ANATOMY OF VISUAL PATHWAY STRUCTURES

The anatomy of the retina and optic disc are discussed in Chapter 4.

OPTIC NERVE

The retinal nerve fibers make a 90-degree turn at the optic disc and exit as the **optic nerve**. This nerve consists of visual fibers, 90% of which will terminate in the LGN. Approximately 10% project to areas controlling pupil responses or the circadian rhythm.⁴ Various counts of the optic nerve fibers range from 1 million to 2.22 million, with their size ranging from small-diameter macular fibers to larger-caliber extramacular fibers.^{1,2,5-7}

The nerve is 5 to 6 cm long and can be divided into four segments on the basis of location: intraocular (0.7-1 mm), intraorbital (3 cm), intracranial (6-10 mm), and intracranial (10-16 mm).^{6,8,9}

The intraocular section of the optic nerve can be divided into prelaminar and laminar sections on the basis of association with the lamina cribrosa. In the prelaminar optic nerve, a glial tissue network provides structural support for the delicate nerve fibers; sheaths of astrocytes bundle the nerve fibers into fascicles, containing approximately 1000 fibers each.⁸ The optic nerve fibers are separated from the retinal layers by a ring of glial tissue, the *intermediary tissue (of Kuhnt)*. The continuation of this glial tissue, the *border tissue (of Jacoby)*, separates the choroid from the optic nerve fibers, and a ring of collagenous tissue of scleral derivation, the *marginal (or border) tissue (of Elschnig)*, lies outer to the glial sheaths.⁸ Tight junctions within the glial border tissue may prevent leakage from adjacent choriocapillaris into the optic nerve head.¹⁰ These layers are shown in Figure 13-2.

The intraorbital (postlaminar) length exceeds the distance from the globe to the apex of the orbit, giving the nerve a slight sine wave-shaped curve, allowing for full eye excursions without stretching the nerve.^{6,11} Within the orbit the nerve is surrounded by the rectus

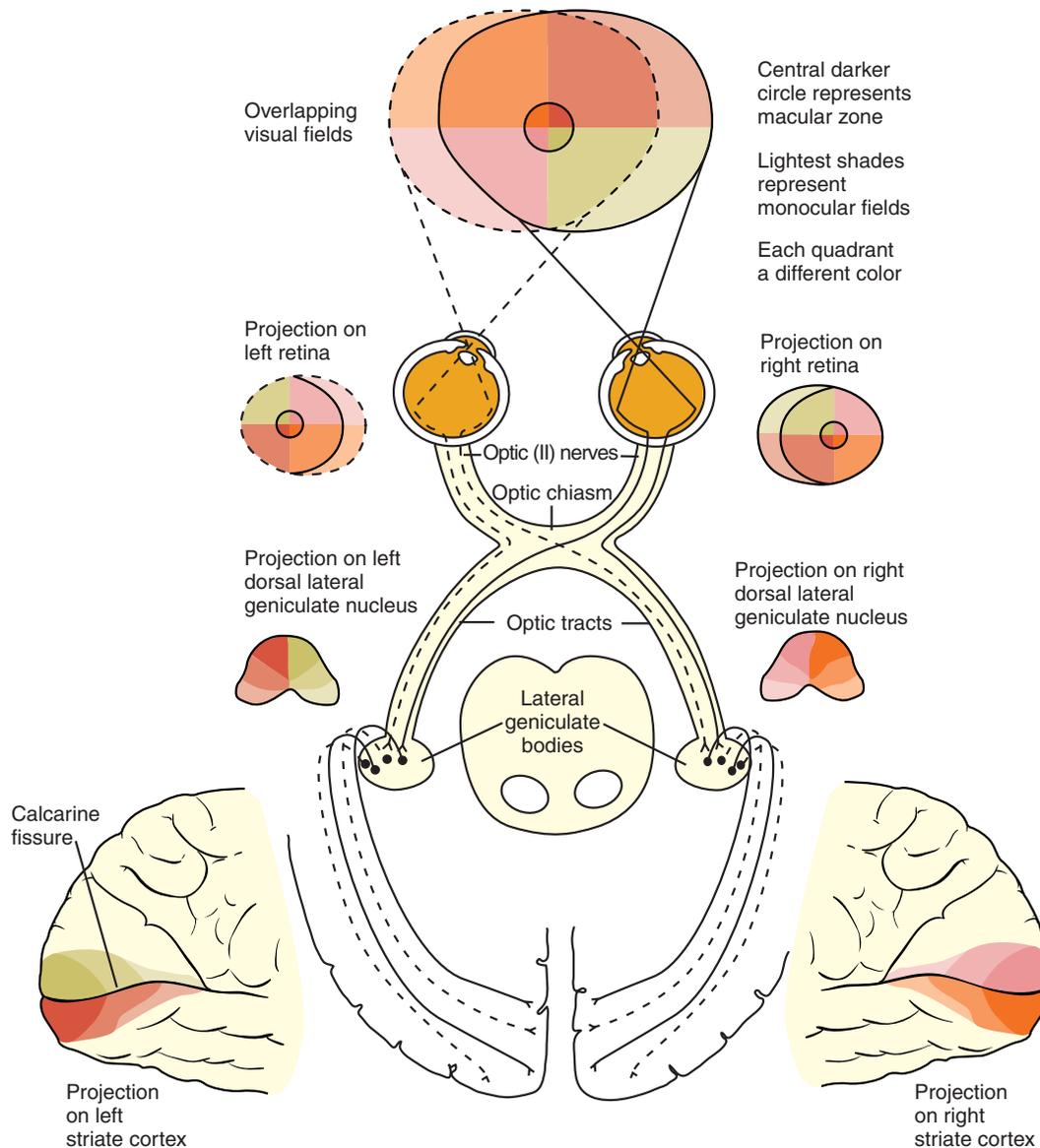


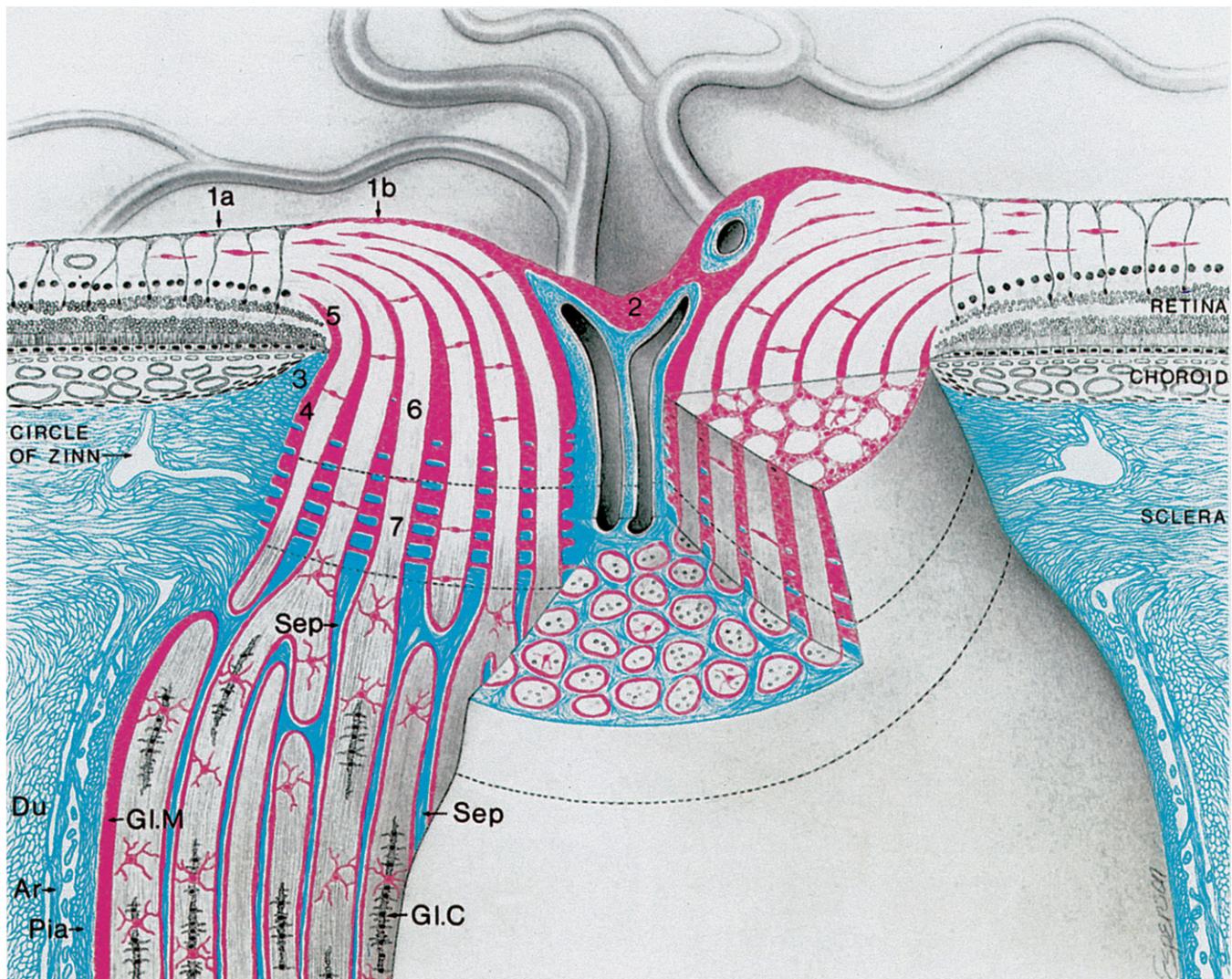
FIGURE 13-1
The visual pathway.

muscles; the sheaths of the superior and medial rectus muscles are adherent to the sheath of the optic nerve (which explains the pain associated with eye movements in optic neuritis).⁸

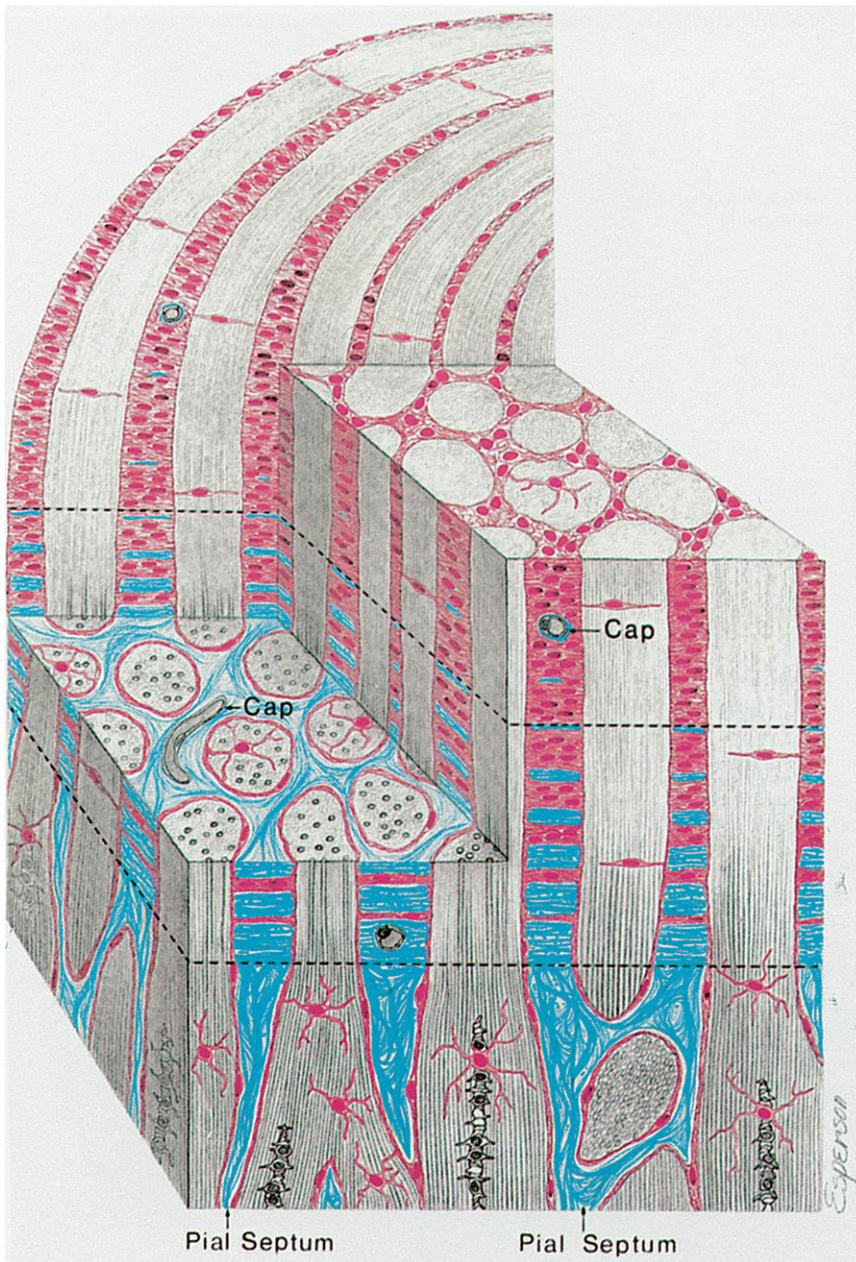
The optic nerve is surrounded by three meningeal sheaths continuous with the meningeal coverings of the cranial contents. The outermost sheath, the dura mater, is tough, dense connective tissue containing numerous elastic fibers.⁸ Next to it, the thin collagenous membrane of the arachnoid sends a fine network of trabeculae through the subarachnoid space and connects to the innermost layer, the pia mater. The subarachnoid space around the optic nerve is continuous with the intra-

cranial subarachnoid space and contains cerebrospinal fluid. The loose, vascular connective tissue of the pia mater branches, sending blood vessels and connective-tissue septa into the nerve (see Figure 13-2). All three of these layers fuse and become continuous with the sclera and with the periorbita.⁸ Of these sheaths only the pia continues along the intracranial optic nerve.¹⁰

As the unmyelinated retinal fibers pass through the scleral perforations of the lamina cribrosa, they become myelinated by oligodendrocytes since no Schwann cells exist in the central nervous system. It is postulated that the lamina cribrosa is a barrier to oligodendrocytes because these cells are not located in retinal tissue and

**FIGURE 13-2**

Intraocular and part of orbital optic nerve. Where retina terminates at optic disc edge, Müller cells (1a) are in continuity with astrocytes, forming internal limiting membrane of Elschnig (1b). In some specimens this membrane is thickened in central portion of disc, forming central meniscus of Kuhnt (2). At posterior termination of choroid on temporal side, border tissue of Elschnig (3) lies between astrocytes surrounding optic nerve canal (4) and stroma of choroid. On nasal side, choroidal stroma is directly adjacent to these astrocytes, known as border tissue of Jacoby, which is continuous with similar glial lining, intermediary tissue of Kuhnt (5), at termination of retina. Nerve fibers of retina are segregated into about 1000 bundles, or fascicles, by astrocytes (6). On reaching lamina cribrosa (upper dotted line), nerve fascicles (7) and surrounding astrocytes are separated by connective tissue (drawn in blue). This connective tissue is cribriform plate, an extension of scleral collagen and elastic fibers through optic nerve. External choroid also sends connective tissue to anterior part of lamina. At external part of lamina cribrosa (lower dotted line), nerve fibers become myelinated, and columns of oligodendrocytes (Gl.C) (black and white cells) and a few astrocytes (red-colored cells) are present in nerve fascicles. Astrocytes surrounding fascicles form thinner layer here than in lamellar and prelaminar portion. Bundles continue to be separated by connective tissue (septal tissue, derived from pia mater) all the way to optic chiasm (Sep). Mantle of astrocytes (Gl.M), continuous anteriorly with border tissue of Jacoby, surrounds optic nerve along its orbital course (Du, dura; Ar, arachnoid; Pia, pia mater). Central retinal vessels are surrounded by a perivascular connective tissue throughout its course in optic nerve. This central supporting connective tissue strand blends with connective tissue of cribriform plate in lamina cribrosa. (From Anderson D, Hoyt W: *Arch Ophthalmol* 82:506, 1969.)

**FIGURE 13-3**

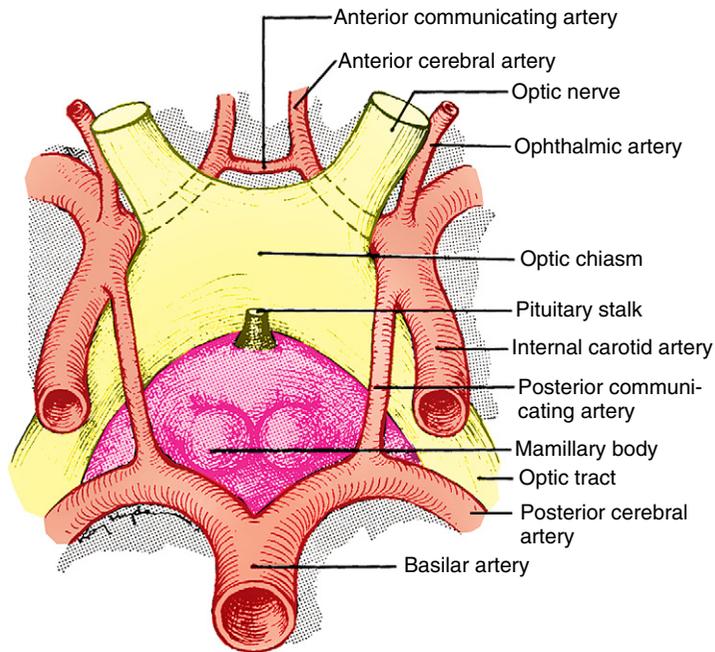
Prelaminar, laminar, and postlaminar optic nerve. Nerve bundles are drawn in black and white, astrocytes in red, oligodendrocytes in black and white, and connective tissue in blue. In prelaminar region, nerves coming from retina become segregated into bundles invested with tubelike layer of astrocytes, which are oriented, with their processes, perpendicular to nerve bundles. Capillaries (*Cap*) course within astrocyte tubes. As lamina cribrosa is reached (*upper dotted line*), nerve fascicles are separated by layer of astrocytes, which is covered by mantle of connective tissue containing collagen, elastic fibers, fibroblasts, and capillaries. In posterior lamina cribrosa (*lower dotted line*), nerves become myelinated, and columns of oligodendrocytes and a few astrocytes are found in fascicles. Astrocytes separating nerve fascicles in laminar and postlaminar regions form thinner layer than in prelaminar portion. Connective tissue of lamina cribrosa is continuous with pial septa. (From Anderson D: *Arch Ophthalmol* 82:800. 1969.)

myelination does not normally occur in the retina.¹⁰ A sheath of connective tissue branching from and continuous with the pia mater meningeal covering is added to the glial sheath of each fascicle posterior to the lamina (Figure 13-3). These additional tissues double the diameter of the optic nerve as it leaves the eye; the nerve is approximately 1.5 mm in diameter at the level of the retina and 3 mm after its exit from the globe. The septa that separate the fiber fascicles end near the chiasm.⁸ Astrocytes present in the optic nerve probably function similar to Müller cells of the retina; they provide structure, store glycogen, and regulate the extracellular concentration of certain ions.¹⁰

The anterior perforated substance, the root of the olfactory tract, and the anterior cerebral artery lie superior to the optic nerve in its intracranial path. The sphenoid sinus is medial, with only a thin plate of bone separating it from the nerve.⁸ The internal carotid artery is below and then lateral to the nerve, and the ophthalmic artery enters the dural sheath of the optic nerve as it passes through the optic canal.

OPTIC CHIASM

The **optic chiasm** is roughly rectangular, approximately 15 mm in its horizontal diameter, 8 mm anterior to

**FIGURE 13-4**

Relationship of optic chiasm to vessels of circle of Willis. (From Harrington DO: *The visual fields*, ed 5, St Louis, 1981, Mosby.)

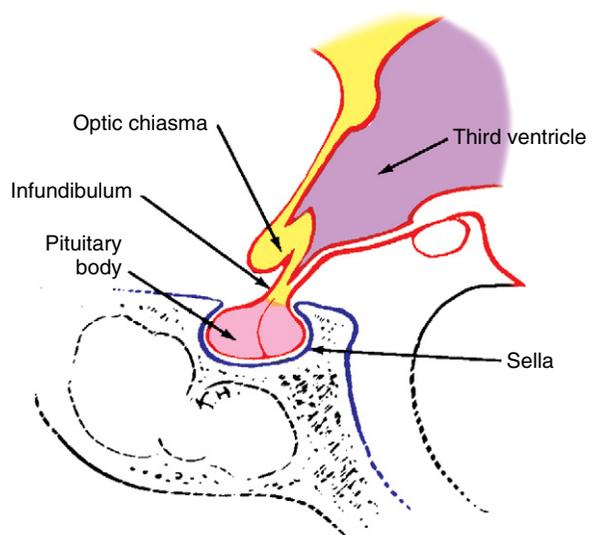
posterior, and 4 mm high.^{6,9,12} As with the optic nerve, the optic chiasm is surrounded by the meningeal sheaths and cerebrospinal fluid.

The chiasm lies within the circle of Willis, a circle of blood vessels that is a common location for aneurysms.⁶ The circle of Willis is an anastomotic group of anterior and posterior arteries that join the anterior circulation of the internal carotid arteries with the posterior circulation of the basilar artery (Figure 13-4). The internal carotid arteries supply the anterior cranial regions, including most of the cerebral hemispheres and orbital and ocular structures. The vertebral branches of the basilar artery supply the posterior regions, including the brain stem, occipital lobes, and inferomedial temporal lobes, thus supplying most of the ocular motor centers and the cortical visual areas.¹³ If the circle is complete, the anterior cerebral arteries are joined via the anterior communicating artery, and each internal carotid artery is joined to the ipsilateral posterior cerebral artery by a posterior communicating artery. The anterior cerebral and anterior communicating arteries are anterior to the chiasm, and an internal carotid artery lies on each lateral side of the chiasm.

Above the optic chiasm is the floor of the third ventricle, and approximately 1 cm below the chiasm is the pituitary gland (Figure 13-5). The position of the optic chiasm above the sella turcica (the fossa in which the pituitary gland sits) can vary from being directly above it (in 75% of the population) to a position referred to as **prefixed** (if the optic nerves are short and the gland lies below the posterior part of the chiasm) or **postfixed** (if the optic nerves are long and the gland is

situated toward the anterior of the chiasm).¹² The chiasm is anteriorly displaced in approximately 10% of individuals and posteriorly displaced in 15%.¹⁰

Posterior to the optic chiasm, the visual pathway continues into both the right and the left sides of the brain (the structures on only one side are described here).

**FIGURE 13-5**

Sagittal section through optic chiasm showing its relationship to third ventricle, pituitary body, pituitary stalk, sella turcica, and sphenoid sinus. (From Harrington DO: *The visual fields*, ed 5, St Louis, 1981, Mosby.)

OPTIC TRACT

The **optic tract** is a cylindrical, slightly flattened band of fibers approximately 3.5 mm high and 5.1 mm long that runs from the posterolateral corner of the optic chiasm to the LGN.⁹ Most of the fibers (which are still the axons of retinal ganglion cells) terminate in the LGN. Fibers from the retinal ganglion cells may branch so that the same cell sends fibers to various target structures or some axons may be destined for a specific structure. The afferent fibers of the pupillomotor reflex leave the optic tract before reaching the LGN and pass by way of the superior brachium to the pretectal nucleus in the midbrain. Other fibers project to several areas within the hypothalamus involved with the circadian rhythm, and others terminate in the superior colliculus. The rather poorly defined accessory optic system, including the nucleus of the optic tract, is involved in the optokinetic nystagmus response and receives information generated by retinal ganglion cells.⁴

The optic tract lies along the upper anterior and then the lateral surface of the cerebral peduncle and is parallel to the posterior cerebral artery. The globus pallidus is above, the internal capsule is medial, and the hippocampus is below the optic tract.⁸

LATERAL GENICULATE NUCLEUS

Information from all the sensory systems except the olfactory pass through the thalamus before being transferred to the cerebral cortex; visual information is processed in the LGN and then is relayed to higher cortical centers.¹⁴ The **lateral geniculate nucleus (LGN, lateral geniculate body)** is located on the dorsolateral aspect of the thalamus and resembles an asymmetric cone, the rounded apex of which is oriented laterally. The retinal axons terminate here. Most of the fibers that leave the LGN project to the visual cortex.

The LGN is a layered structure; the layers are piled on each other, with the larger ones draping over smaller ones, and some layers becoming fragmented and irregular. The cells within a layer are all of the same type, and three types have been identified according to size. *Magnocellular* layers contain large cells, *parvocellular* layers contain medium-sized cells, and *koniocellular* layers contain small cells. The number of layers present depends on the location of the plane through the structure. In the classic textbook presentation of the LGN, six layers are seen. Two magnocellular layers are located inferiorly and numbered 1 and 2, and four parvocellular layers are above them and numbered 3, 4, 5, and 6 (Figure 13-6). Below each of these six layers lies a koniocellular layer (Figure 13-7). The retinal ganglion cells that project to each of these layers differ in a number of their characteristics.¹⁵

The LGN is not a simple relay station; it also receives input from cortical and subcortical centers and reciprocal

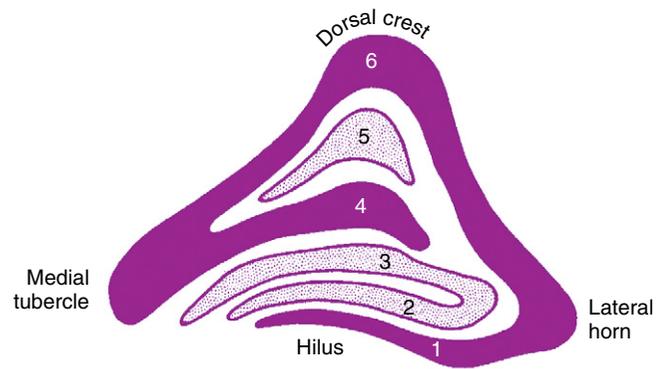


FIGURE 13-6

Laminae in right lateral geniculate nucleus. Crossed retinal projections terminate in laminae 1, 4, and 6. Uncrossed projections terminate in laminae 2, 3, and 5. Selective partial involvement of one or more of these laminae will produce asymmetric homonymous visual field defects, depending on the extent of laminar damage. (From Harrington DO: *The visual fields*, ed 5, St Louis, 1981, Mosby.)

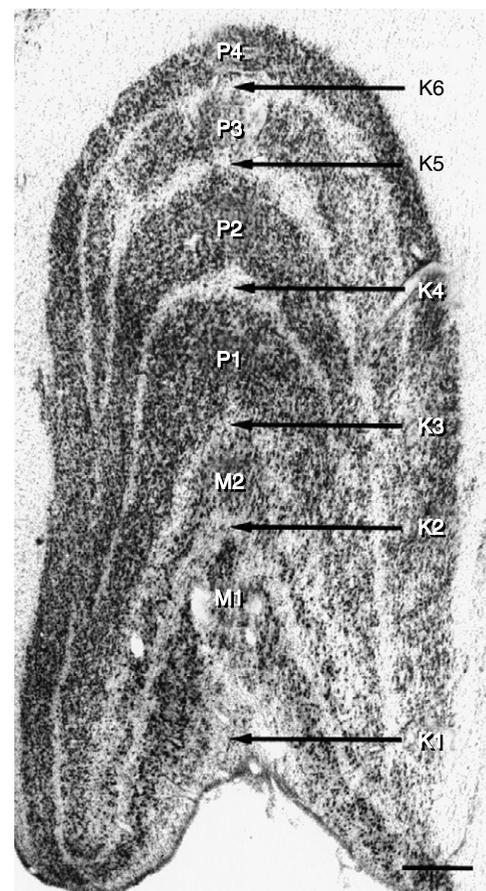
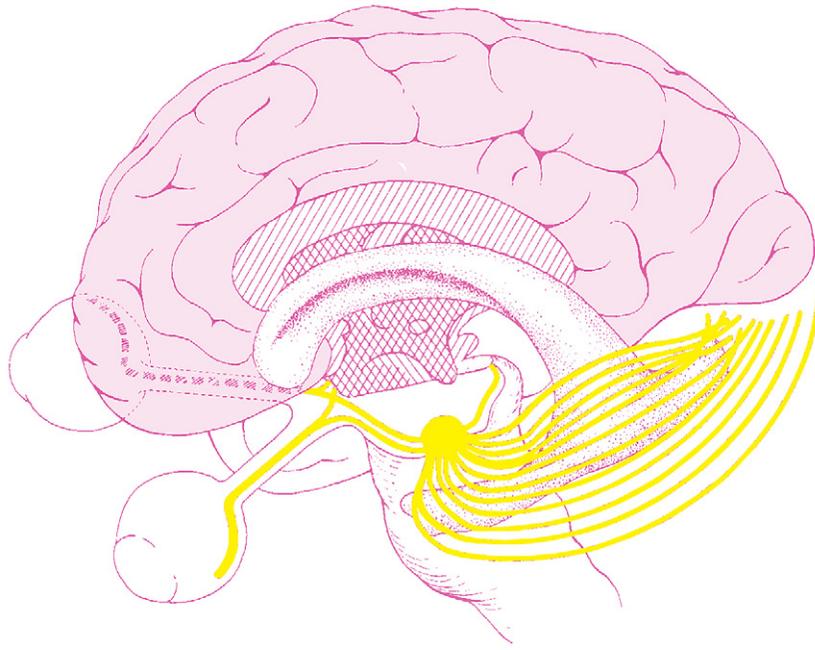


FIGURE 13-7

Coronal section through lateral geniculate nucleus of macaque monkey showing parvocellular (P), magnocellular (M), and koniocellular (K) layers. At this plane there are four P layers, two M layers and six K layers. (From Casagrande VA, Ichida JM: In Kaufman PL, Alm A, editors: *Adler's physiology of the eye*, ed 10, St Louis, 2003, Elsevier.)

**FIGURE 13-8**

The visual pathway from retina to calcarine fissure of occipital lobe. Cutaway view from gross dissections shows distribution of visual fibers in optic radiation. (From Harrington DO: *The visual fields*, ed 5, St Louis, 1981, Mosby.)

innervation from the visual cortex and is a center of complex processing.^{6,17} It regulates the flow of visual information ensuring that the most important is sent to the cortex.¹⁶ The optic tract enters the LGN anteriorly; the internal capsule is lateral, the medial geniculate nucleus is medial, and the inferior horn of the lateral ventricle is posterolateral to the LGN.⁸ The axons leave the LGN as the optic radiations.

OPTIC RADIATIONS (GENICULOCALCARINE TRACT)

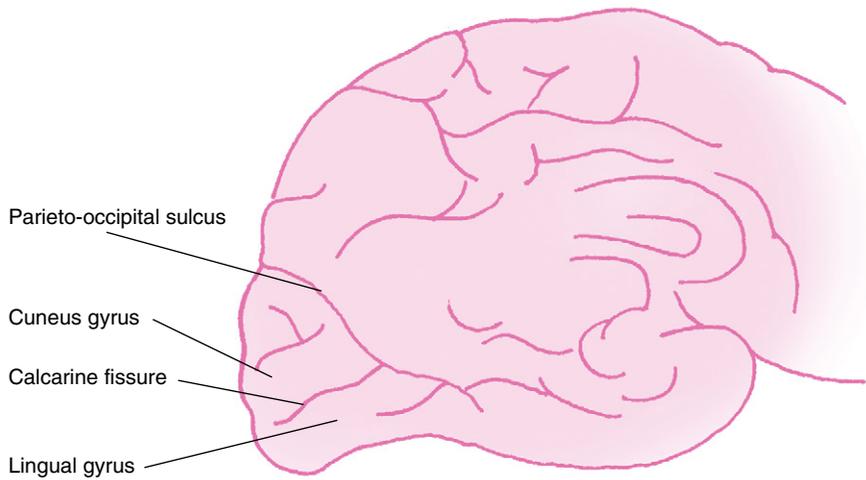
The **optic radiations** spread out fanwise as they leave the LGN, deep in the white matter of the cerebral hemispheres, sweeping laterally and inferiorly around the anterior tip of the temporal horn of the lateral ventricle (Figure 13-8). Some fibers loop into the temporal lobe before passing back to the parietal lobe en route to the occipital lobe. Within the parietal lobe the fibers pass lateral to the occipital horn of the lateral ventricle before terminating in the striate cortex.^{8,18}

PRIMARY VISUAL CORTEX (STRIATE CORTEX)

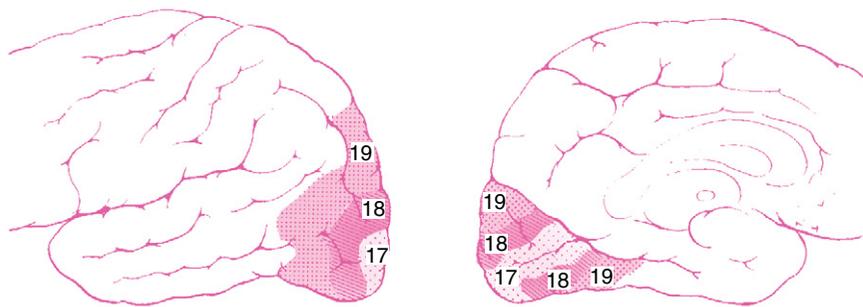
The **primary visual cortex** (Brodmann area 17 or, according to more recent nomenclature, V1), is located

almost entirely on the medial surface of the occipital lobe; just a small portion (perhaps 1 cm long) extends around the posterior pole onto the lateral surface. The visual cortex is called also the **striate cortex** because a white myelinated fiber layer, the white stria of Gennari, is characteristic of this area.⁶ The **calcarine fissure** extends from the parieto-occipital sulcus to the posterior pole, dividing the visual cortex into an upper portion (the **cuneus gyrus**) and a lower part (the **lingual gyrus**) (Figure 13-9); most of the primary visual cortex is buried in the tissue within the calcarine fissure.¹⁹

The primary visual cortex has a thickness of about 2 mm and is organized into horizontal layers and vertical columns. Layer I, the most superficial layer, contains a few scattered neurons. Layer II contains neurons that send axons only to deeper cortical layers. Layer III contains neurons that communicate with both near and far cortical locations. Layer IV contains the stria of Gennari and is subdivided into strata, one of which receives information from the magnocellular layers and another that receives information from the parvocellular layers.^{20,21} Layer IV sends axons to more superficial visual cortex as well as other visual cortical areas. Layer V sends axons to the superior colliculus and other areas in the brain stem. Layer VI sends projections back to the LGN.¹⁶

**FIGURE 13-9**

Medial surface of cerebral cortex showing striate cortex of occipital lobe.

**FIGURE 13-10**

Visual area, or striate cortex, in occipital lobe. Lateral and medial views show Brodmann areas 17 (striate area), 18 (parastriate area), and 19 (peristriate area). Area 17 is sharply delineated cortical termination of visual pathway. (From Harrington DO: *The visual fields*, ed 5, St Louis, 1981, Mosby.)

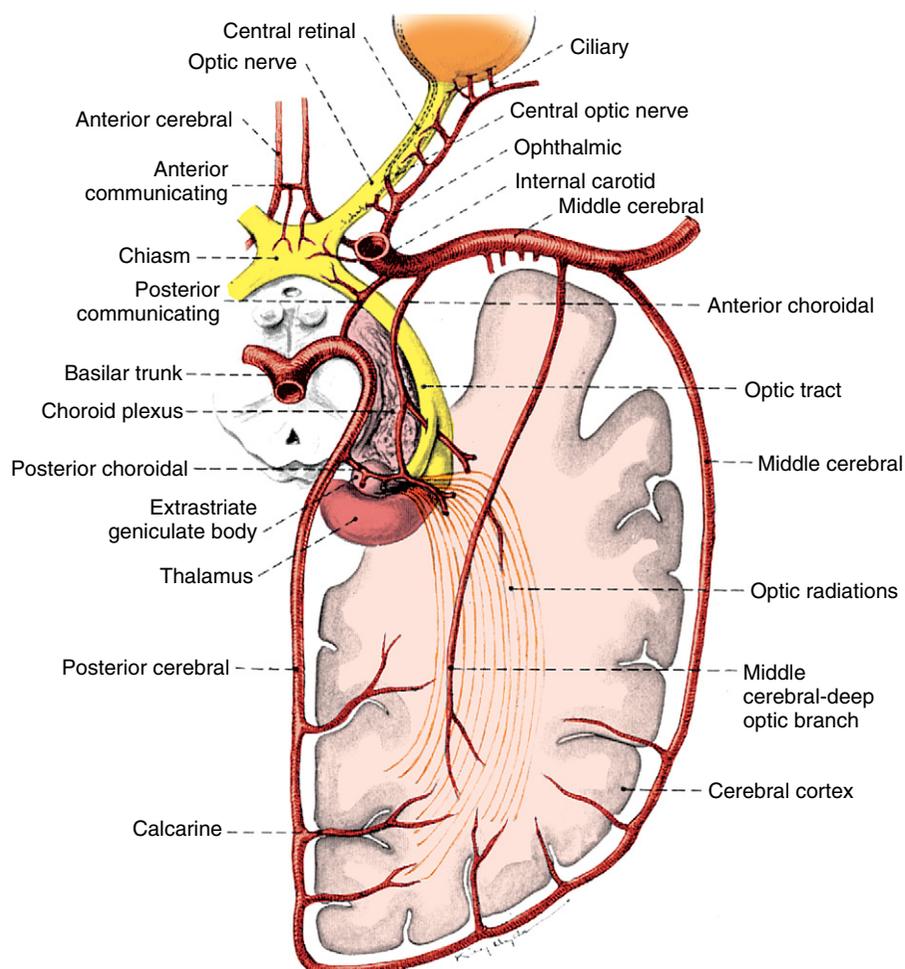
Certain cortical regions are active during motion stimulation, whereas others are active during color vision.²² The magnocellular areas probably mediate movement detection and low-spatial-frequency contrast sensitivity, and the parvocellular areas likely mediate color and high-spatial-frequency contrast sensitivity, although this generalization oversimplifies the properties.²³⁻²⁶

Cells are also distributed in a vertical organization, according to the eye of origin, forming alternating parallel ocular dominance columns.^{21,27,28} These columns are lacking in the area of the cortex that represents the physiologic blind spot since this region receives information exclusively from one eye.¹⁴ A second system of columns, specific for stimulus orientation, responds on the basis of the direction of a light slit or edge.²¹ Contour analysis and binocular vision are two functions of the visual cortex, and such processing is a function of both its horizontal and its vertical organization. The cells within the striate cortex are activated only by input from the LGN, although other cortical areas have input into the striate cortex.^{16,29,30}

The striate cortex communicates with the superior colliculus and the frontal eye fields. The superior

colliculus, which has a complete retinotopic map of the contralateral field of vision, also receives communication from fibers exiting the posterior optic tract. It does not analyze sensory information for perception but is important for visual orientation, foveation, and the control of saccadic eye movements.^{14,31} The frontal eye fields, in the frontal lobe, receive fibers from the striate cortex that contribute to the control of conjugate eye movements. Both voluntary and reflex ocular movements are mediated in this area, as are pupillary responses to near objects (see Chapter 14).⁸

The striate cortex combines and analyzes the visual information relayed from the LGN and transmits this information to the higher **visual association areas** (the **extrastriate cortex**), which provide further interpretation.¹⁴ These areas surround the striate cortex, and are located on the lateral aspects of the occipital cortex. Historically called **Brodmann areas 18 and 19** (Figure 13-10), these areas now are known to contain several distinct cortical areas (designated **V2, V3, V4, and V5**) in which visual processing occurs. A study involving the macaque monkey has identified 32 such areas associated with visual processing.¹⁴ The visual and visual association areas in one hemisphere are connected to

**FIGURE 13-11**

Vascular supply of visual pathway from retina to occipital cortex. (From Harrington DO: *The visual fields*, ed 5, St Louis, 1981, Mosby.)

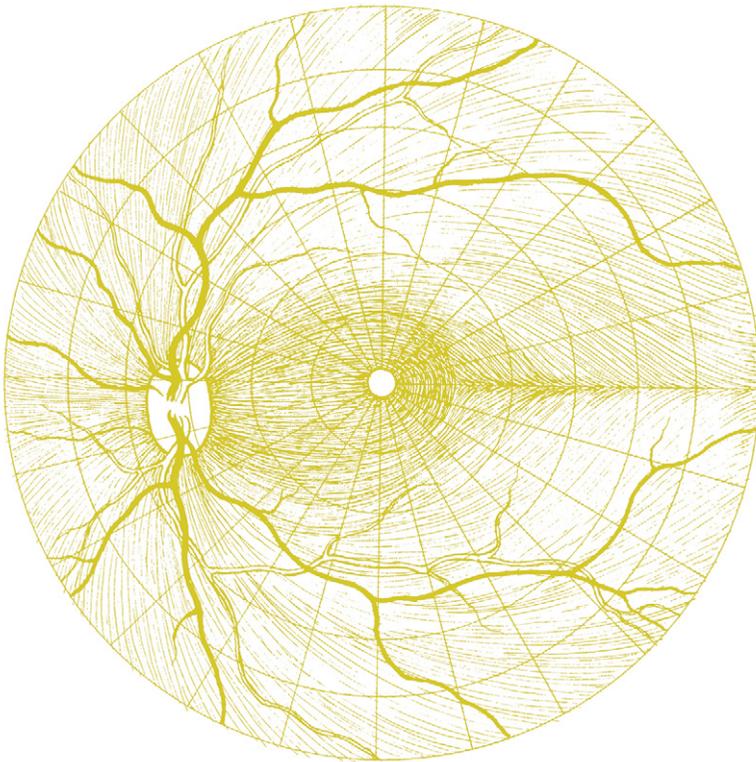
the corresponding areas in the other hemisphere through the posterior portion of the corpus callosum.⁶ Magnetic resonance imaging (MRI) techniques that are sensitive to changes in blood flow and oxygenation occurring with neuronal activity can be used to study the human visual system in vivo. Innovative studies are attempting (1) to identify the areas of visual cortex and associated visual areas activated during visual stimulation and visual processing, (2) to detect the storage areas for learned visual patterns, and (3) to establish the pathway of activation in the cortex for recall and recognition of a visual pattern.³²⁻³⁸

BLOOD SUPPLY TO THE VISUAL PATHWAY

The structures of the visual pathway have an extensive blood supply. Figure 13-11 shows many of the involved vessels. The outer retinal layers receive nutrition from the choroid, whereas the inner retina is supplied by the central retinal artery. The circle of Zinn, the anastomotic

ring of branches of the short ciliary arteries, and peripapillary vessels supply the optic disc.⁶ The optic nerve capillaries from the choroidal supply are composed of nonfenestrated endothelium joined by zonula occludens, thus the vessels perfusing the nerve head are part of the blood-brain barrier.¹⁰ Pial vessels supply the optic nerve throughout its length; the intraorbital portion is supplied by branches from the ophthalmic artery, and the intracranial optic nerve is nourished by branches of the ophthalmic, anterior cerebral, anterior communicating, and internal carotid arteries.^{6,8}

The blood supply to the optic chiasm is rich and anastomotic, with arterioles from the circle of Willis forming capillary beds at two levels.^{39,40} The superior network is supplied by the anterior cerebral and anterior communicating arteries, whereas the inferior network is supplied by the internal carotid, posterior cerebral, and posterior communicating arteries.^{6,8,12,13} The anterior choroidal artery, a branch of the internal carotid, is a primary supplier of the optic tract, although

**FIGURE 13-12**

Nerve fiber pattern of retina in its relationship to retinal vascular tree. (From Harrington DO: *The visual fields*, ed 5, St Louis, 1981, Mosby.)

small branches from the middle cerebral artery also contribute.^{6,8,12,41,42} The blood supply to the LGN is derived from the anterior choroidal artery and the lateral choroidal and posterior choroidal branches of the posterior cerebral artery.^{8,41,43}

The optic radiations can be divided into three sections: (1) the anterior radiations, which pass laterally over the inferior horn of the ventricle, are supplied by the anterior choroidal artery and the middle cerebral artery; (2) the middle group of fibers passing lateral to the ventricle is supplied by the deep optic branch of the middle cerebral artery; and (3) branches of the posterior cerebral artery, including the calcarine branch, supply the posterior radiations as they spread out in the occipital lobe. Branches from the middle cerebral artery also contribute.^{6,8,12} The calcarine branch of the posterior cerebral artery is the major blood supply for the striate cortex, often supplemented by the posterior temporal or parieto-occipital branch of the posterior cerebral artery or the occipital branch of the middle cerebral artery.^{6,8,12,44}

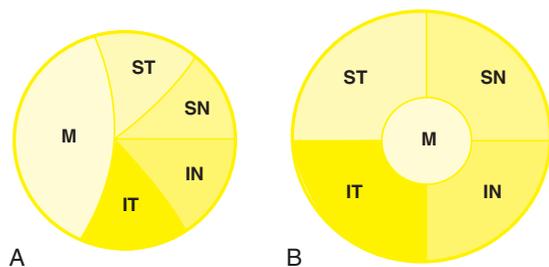
FIBER ORIENTATION AND VISUAL FIELDS

With the eye looking straight ahead and fixating on an object, one is able to detect other objects around the point of regard, although the details may not be

discernible. This entire visible area is termed the **visual field**. Information from the visual field is taken in by the retina and processed through the afferent visual sensory pathway. The location and orderly arrangement of the fibers throughout this pathway have been extensively studied. Damage in this afferent visual pathway will cause a defect in the visual field. Knowledge of the fiber patterns in the pathway can help to identify the location of the lesion on the basis of the resultant visual field defect.

RETINA

The axons of the retinal ganglion cells form characteristic patterns in the nerve fiber layer. The group of fibers that course from the macular area to the optic disc is called the **papillomacular bundle**. The superior and inferior temporal fibers, separated at the 180th meridian by the **horizontal retinal raphe**, must arch superiorly and inferiorly around the macular area, forming characteristic arcuate patterns in their course to the optic disc; the temporal retinal vessels usually do not cross the horizontal raphe either. The nasal fibers can travel directly to the optic disc and are described as radiating (Figure 13-12). Nasal and temporal fibers are separated by a theoretic vertical line passing through the center of the fovea. The long nerve fibers, from peripheral retina, are more vitread in location than are the short

**FIGURE 13-13**

A, Surface of optic disc showing orientation of nerve fibers as they enter disc. **B**, Coronal section showing orientation of nerve fibers in optic nerve proximal to chiasm. (Right disc and nerve viewed from front.) *ST*, Superior temporal; *SN*, superior nasal; *IT*, inferior temporal; *IN*, inferior nasal; *M*, macular.

peripapillary fibers, with extensive intermingling in the prelaminar optic nerve.⁴⁵

OPTIC DISC

All of the axons in the nerve fiber layer come together at the optic disc, creating a specific pattern. The nasal fibers radiate directly to the nasal side of the disc, whereas the papillomacular bundle courses directly to the temporal side of the disc.⁴⁵⁻⁴⁷ The fibers from the superior temporal retina arch around the papillomacular bundle to enter the superior pole of the disc; fibers from the inferior temporal retina curve below the papillomacular bundle to the inferior pole.⁴⁷ The macular fibers take up approximately one third of the disc, although the macular area encompasses only one twentieth of the retinal area.^{1,8} The temporal fibers occupy approximately one third of the disc, as do the nasal fibers (Figure 13-13, A). The boundaries between each set of fibers are not always clear-cut in all parts of the pathway. The fibers from peripheral retina are more superficial than those coming from central retina.⁴⁷

OPTIC NERVE

Near the lamina cribrosa the fibers have the same orientation as they do in the disc, but within a short distance the macular fibers move to the center of the nerve.^{3,8} The rest of the fibers take up their logical positions: superior temporal fibers in the superior temporal optic nerve, inferior temporal fibers in the inferior temporal nerve, superior nasal fibers in the superior nasal nerve, and inferior nasal fibers in the inferior nasal optic nerve (Figure 13-13, B).

OPTIC CHIASM

In the optic chiasm the nasal fibers cross (decussate); the ratio of crossed to uncrossed fibers in the chiasm is approximately 53 to 47.⁴⁸ The crossing pattern depends on processes that occur during embryologic development, with certain molecular guides directing the path taken by nerve fibers. The inferior nasal retinal fibers are inferior in the anterior chiasm; they cross to the other side, and many loop into the terminal part of the opposite optic nerve before turning to run back through the chiasm into the contralateral optic tract¹ (Figure 13-14). These anterior loops (**anterior knees of Wilbrand**) bring fibers from the opposite eye into the posterior optic nerve.⁴⁹ Some investigators believe that these “knees” are artifacts and suggest that the fibers shift into such a location after loss from fiber degeneration.⁵⁰

The superior nasal fibers enter the superior chiasm, where they cross and then leave the chiasm in the contralateral optic tract; some of these fibers loop posteriorly into the optic tract on the same side before crossing. The fibers were historically called the **posterior knees of Wilbrand**^{1,8} (see Figure 13-14). The fibers from the temporal retina course directly back through the chiasm into the optic tract. The nasal macular fibers cross primarily in the posterior aspect of the chiasm.⁶

A few fibers have been identified that exit the posterior of the chiasm and enter the hypothalamus. Studies suggest that these fibers represent light-dark input, affecting the circadian rhythm.^{6,51}

OPTIC TRACT

As the fibers leave the chiasm in the optic tract, the crossed and uncrossed fibers intermingle. The superior fibers (the fibers from both the ipsilateral superior temporal retina and the contralateral superior nasal retina) move to the *medial* side of the tract. The fibers from the inferior retina (ipsilateral inferior temporal retinal fibers and contralateral inferior nasal retinal fibers) occupy the *lateral* area of the tract.^{1,3} Figure 13-15 shows the regrouping that occurs as the fibers pass through the chiasm and into the optic tract. The macular fibers, crossed and uncrossed, are located between these two groups¹ (Figure 13-16).

LATERAL GENICULATE NUCLEUS

Fibers from the superior retinal quadrants terminate in the *medial* aspect of the LGN, whereas fibers from the inferior retinal quadrants terminate in the *lateral* aspect.⁸ A dorsal wedge, composing two thirds to three fourths of the LGN, represents the macula.^{3,52,53} Based on animal study mapping, each of the magnocellular and parvocellular layers receives input from just one

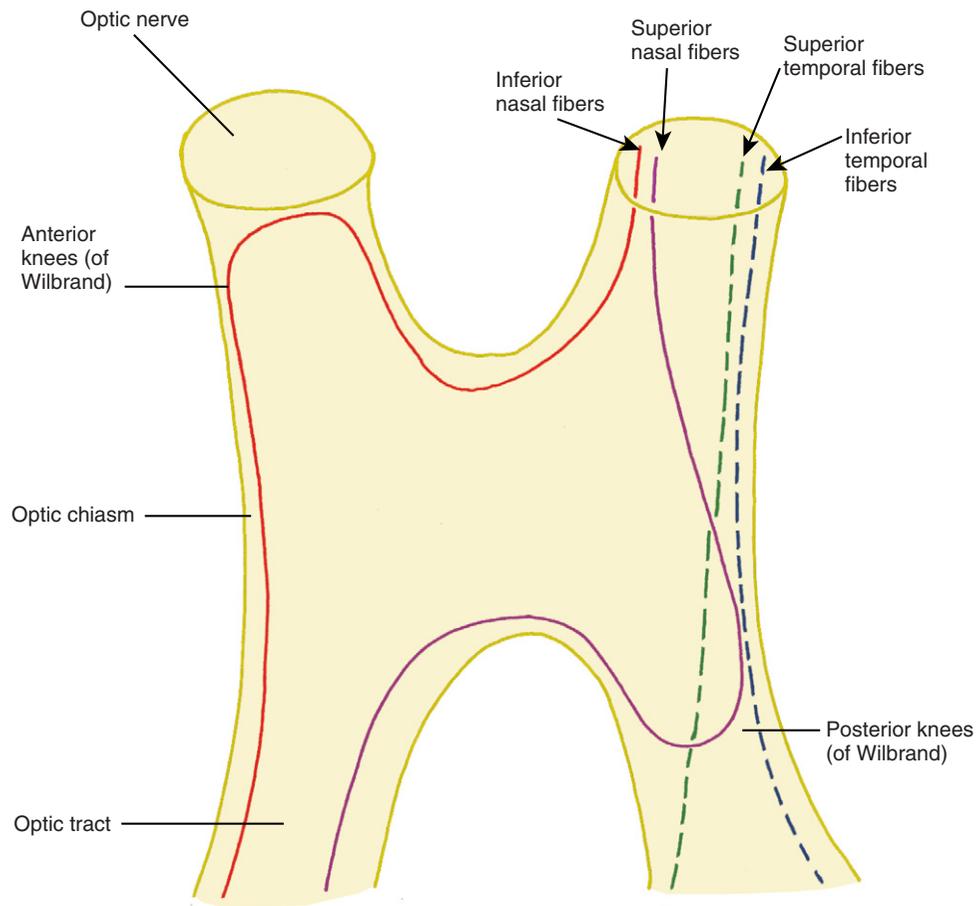


FIGURE 13-14

Fiber orientation through optic chiasm. Temporal fibers (*dotted lines*) pass through chiasm and exit in ipsilateral optic tract. Nasal fibers (*solid lines*) cross in chiasm to exit in contralateral optic tract.

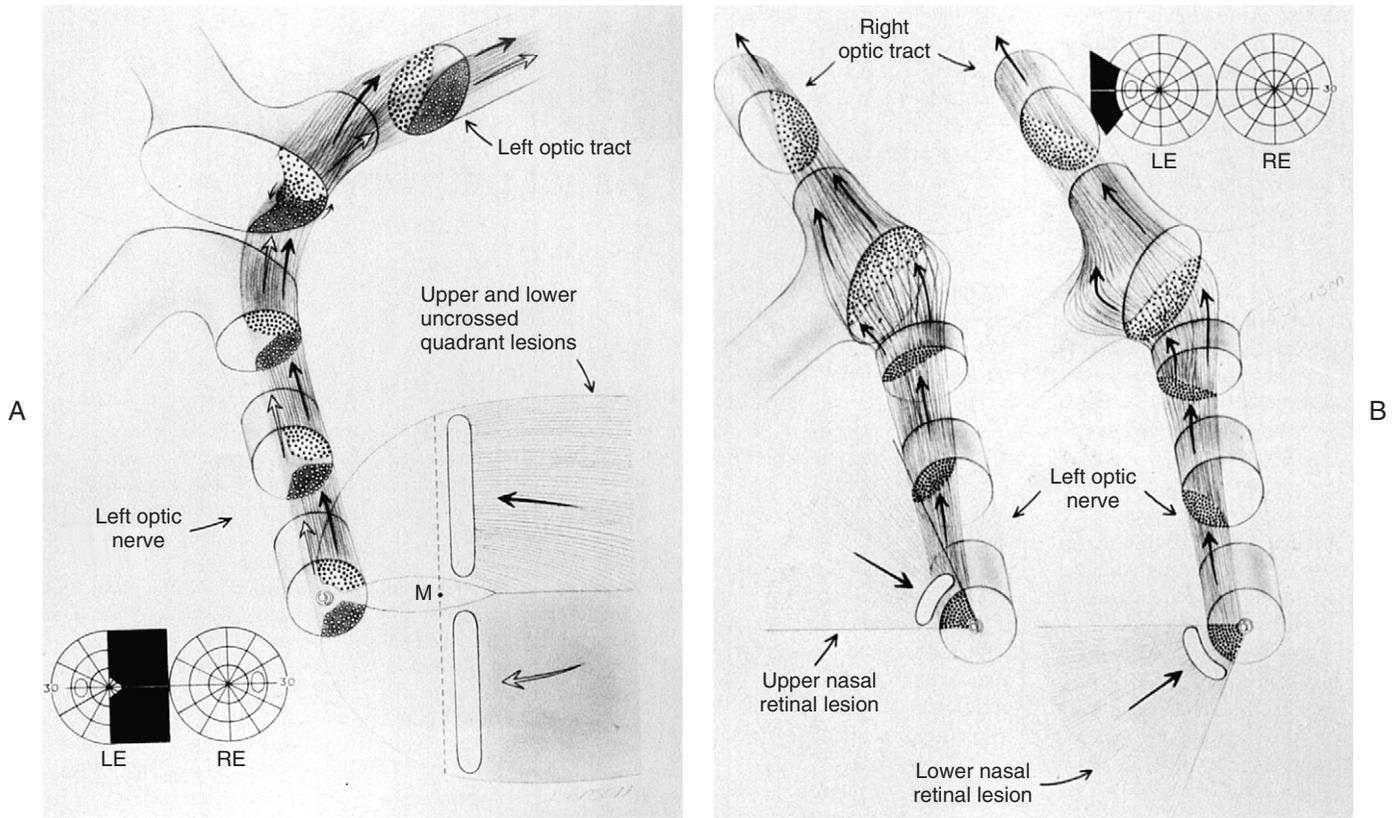


FIGURE 13-15

A, Course of uncrossed retinal ganglion cell axons through optic nerve, chiasm, and tract of monkey. Left retina is represented below on right. Vertical white bars are lesions made by photocoagulator; macula (*M*) has not been damaged. Hypothetic visual field defect produced by these lesions is shown in lower left. **B**, Course of crossed retinal ganglion cell axons. Photocoagulator lesions in left retina are indicated by white crescents in retinal diagrams at bottom of figure; hypothetic visual field defects produced by these lesions are shown at upper right. *LE*, Left eye; *RE*, right eye. (From Hoyt WF, Luis O: *Arch Ophthalmol* 68:428, 1962.)

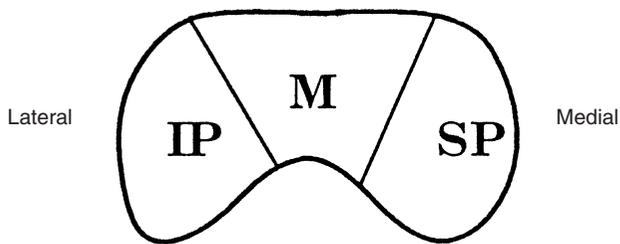
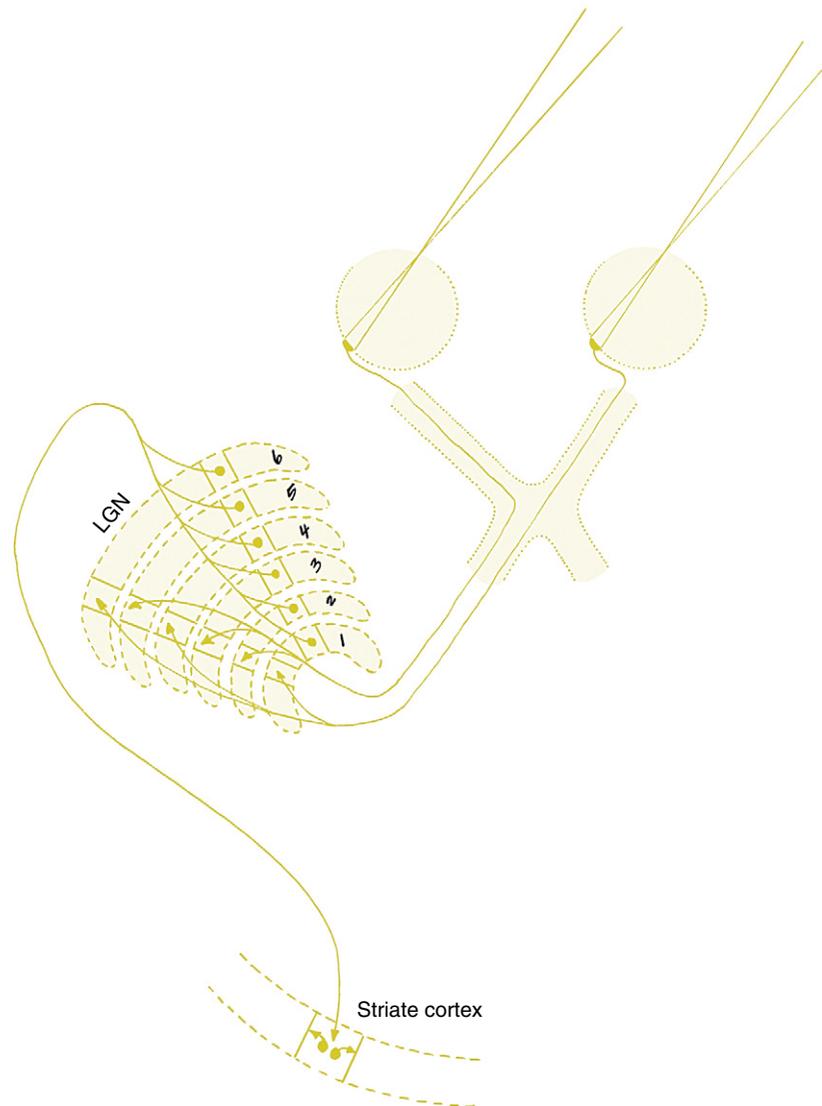


FIGURE 13-16

Coronal section showing orientation of nerve fibers in optic tract. *IP*, Inferior peripheral; *M*, macular; *SP*, superior peripheral.

eye: Layers 1, 4, and 6 receive fibers from the *contralateral nasal retina*, whereas layers 2, 3, and 5 receive *ipsilateral temporal retinal fibers*⁴⁸ (Figure 13-17). Most of the structure, including the wedge representing the macula, contains all layers, although in the far medial and lateral aspects, some of the layers merge.^{6,52}

The anatomic structure of the human LGN is similar to that of the monkey, so detailed maps of the monkey LGN have been applied to the human structure.⁵⁴ Each layer of the LGN contains a retinotopic map or representation of the contralateral hemifield of vision. A **retinotopic map** is a "point-to-point localization" of the retina.¹⁴ These maps are stacked on one another, such

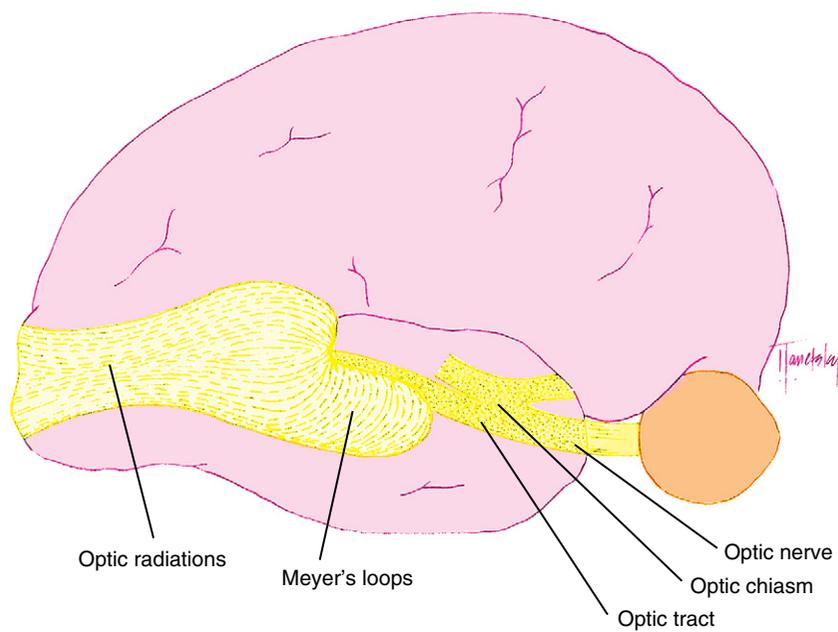
**FIGURE 13-17**

Retinotopic map representation in lateral geniculate nucleus (or body, *LGN*). Fibers from ipsilateral (temporal) retina terminate in layers 2, 3, and 5. Fibers from contralateral (nasal) retina terminate in layers 1, 4, and 6. Fibers that originate in neighboring areas of all layers of *LGN* terminate in same place in striate cortex.

that if a line (called a line of projection) were passed through all six layers, perpendicular to the surface, the intercepted cells all would be carrying information about the same point in the visual field. This alignment is so precise that there is a gap in each contralateral layer along the line of projection that corresponds to the location of the optic disc.¹⁵ Thus the fibers that carry information from the same site in the visual field of each eye terminate in adjacent layers of the *LGN*, right next to one another⁸ (see Figure 13-17). The fibers course through the posterior limb of the internal capsule as they leave the *LGN* to form the optic radiations.

OPTIC RADIATIONS

The fibers leaving the lateral aspect of the *LGN*, representing inferior retina, follow an indirect route to the occipital lobe. They pass into the temporal lobe and loop around the tip of the temporal horn of the lateral ventricle, forming **Meyer's loops**, before continuing into the parietal lobe; these fibers form the inferior radiations^{8,18} (Figure 13-18). Fibers from the medial aspect of the *LGN*, representing superior retina, form the superior radiations. The fibers from the macula are situated between the superior and inferior fibers.

**FIGURE 13-18**

Location of optic radiations in cerebral hemisphere. Meyer's loops pass into temporal lobe before passing into parietal lobe.

STRIATE CORTEX

The superior radiations terminate in the area of the striate cortex above the calcarine fissure, the cuneus gyrus, and the inferior radiations terminate in the region below the calcarine fissure, the lingual gyrus. Thus, the cuneus gyrus receives projections from *superior retina* and the lingual gyrus from *inferior retina*. Only one third of the striate cortex is on the surface of the occipital lobe; the majority is buried within the calcarine fissure, and only a small portion is on the posterolateral aspect of the occipital posterior pole.⁵⁵

Fibers from the macular area terminate in the most *posterior* part of the striate cortex, with the superior macular area represented in the cuneus gyrus and the inferior macula represented in the lingual gyrus. The macular projection might extend onto the posterolateral surface of the occipital cortex. The macular area representation occupies a relatively large portion of striate cortex compared with the small macular area in the retina. The macular cells are densely packed, and macular fibers are small caliber. Because macular function involves sharp, detailed vision, the macular representation in the striate cortex is more extensive than the representation of peripheral retinal areas. The most *anterior* part of the striate cortex, the part adjacent to the parietal lobe, represents the periphery of the nasal retina, corresponding to an area of visual field, the temporal crescent, that is seen by one eye only.

Retinotopic representation is present in the striate cortex. Those fibers that are adjacent to one another in

the layers of the LGN project to the same area in the visual cortex (see Figure 13-17). That is, corresponding points from the two retinas (ipsilateral temporal and contralateral nasal) that represent the same target in the visual field will project to the same place in the primary visual cortex. All the cells in a column respond to a stimulus presented at a particular point in the visual field, and cells in adjacent columns respond to a point in adjacent visual field.

CLINICAL COMMENT: VISUAL FIELD TESTING

The visual field is tested monocularly with the patient looking straight ahead at a fixation point and responding when a target is seen anywhere in the area surrounding that fixation point, usually described to the patient as "seen out of the corner of your eye." The field can be divided into four quadrants by a vertical line and a horizontal line that intersect at the point of fixation. The point of fixation is seen by the fovea and is eccentric, because the temporal field is slightly larger than the nasal field. Inversion and reversal of the field are caused by the optical system of the eye. The superior field is imaged on the inferior retina and the inferior field on the superior retina; the nasal field is imaged on the temporal retina and the temporal field on the nasal retina (Figure 13-19). This orientation is maintained in the cortex, where the superior field is projected onto the visual cortex inferior to the calcarine fissure, and where the inferior visual field is projected onto the cortex superior to the calcarine fissure.

The reader is cautioned to be aware of the difference between visual fibers and visual fields. Both can be described as nasal, temporal, superior, and inferior.

Continued

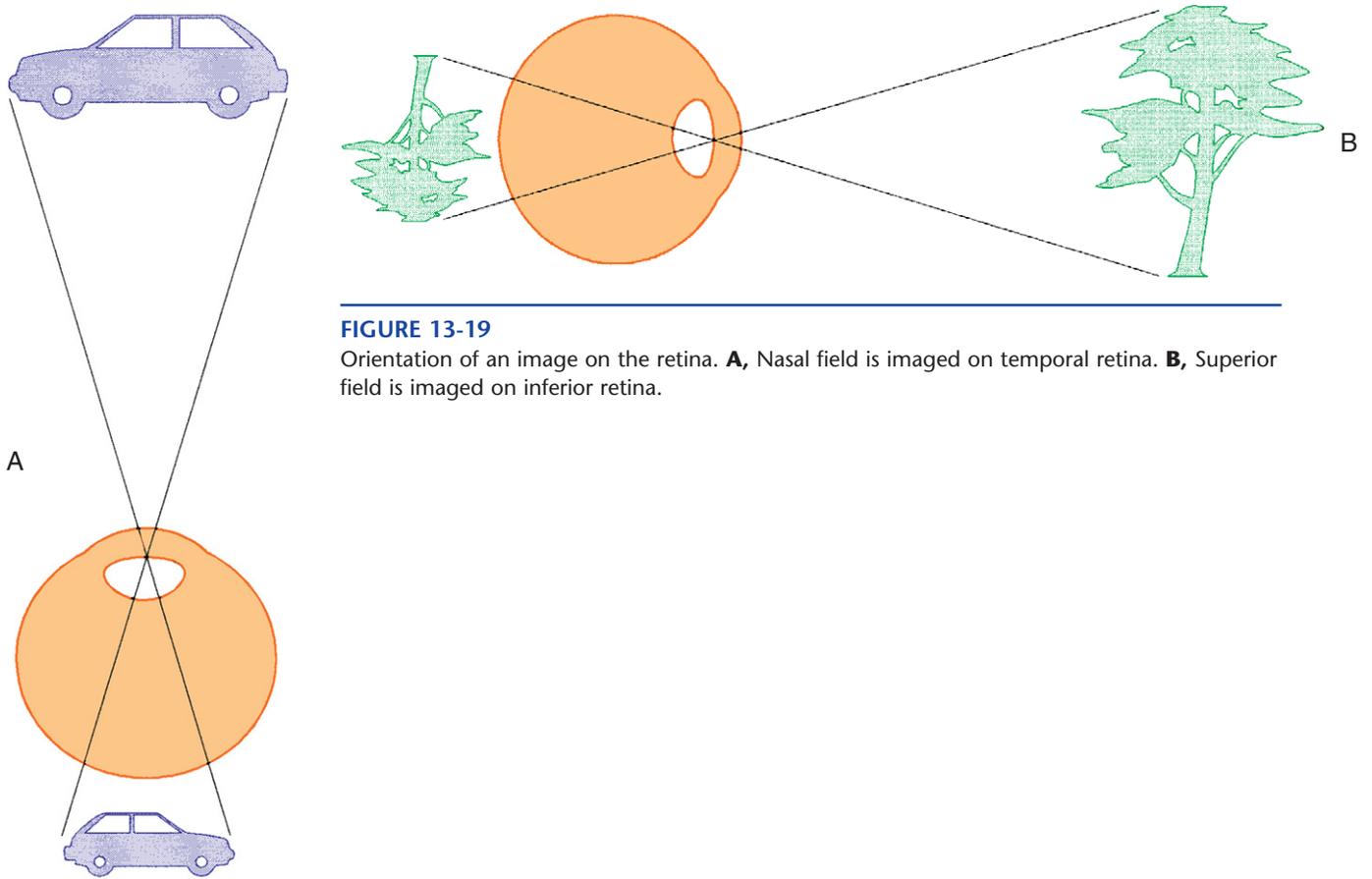


FIGURE 13-19

Orientation of an image on the retina. **A**, Nasal field is imaged on temporal retina. **B**, Superior field is imaged on inferior retina.

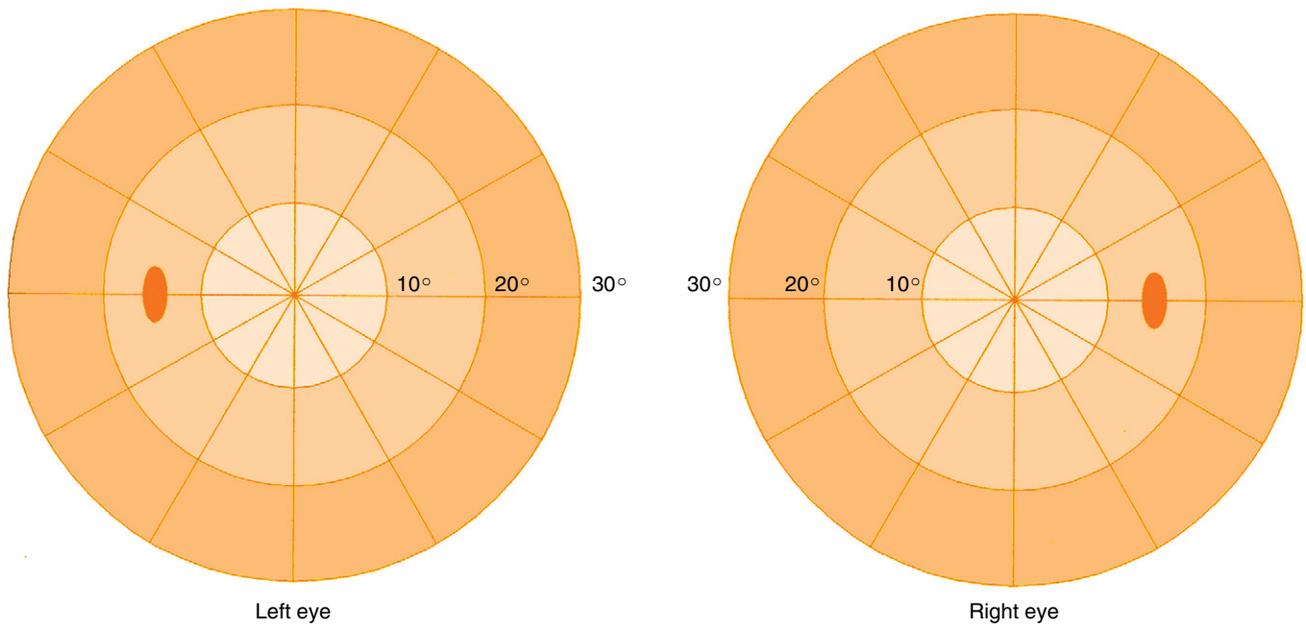


FIGURE 13-20

Central visual field plots showing scotoma of physiologic blind spot in the temporal field.

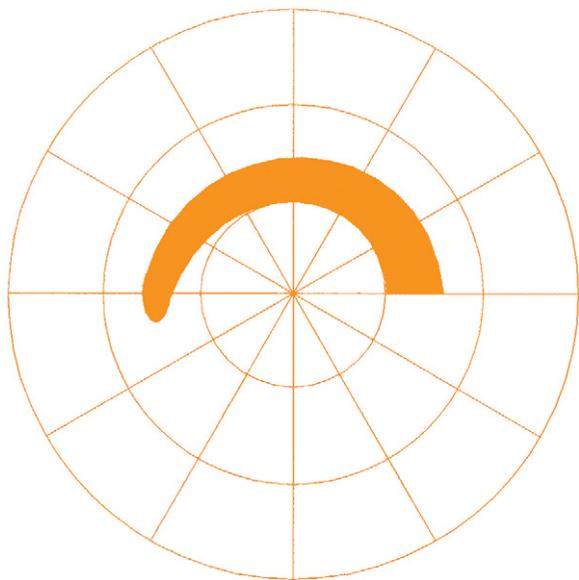


FIGURE 13-21

Visual field plot showing arcuate scotoma in field of left eye. Note nasal step.

The visual field seen by the right eye is nearly the same as that seen by the left eye. The nasal part of the field for one eye is the same as the temporal part of the field seen by the other eye, with the exception of the far temporal periphery, which is called the **temporal crescent**. The temporal crescent is imaged on the nasal retina of one eye but not on the temporal retina of the other because of the prominence of the nose. Within each temporal field is an absolute scotoma, the **physiologic blind spot**, a result of the lack of photoreceptors in the optic disc (Figure 13-20).

Because the fibers that emanate from nasal retina cross in the chiasm, the postchiasmal pathway carries information from the contralateral temporal field and the ipsilateral nasal field. These combined areas can be described as the **contralateral hemifield** (i.e., the right postchiasmal pathway carries information from the left side of the visual field for both eyes). Thus, the left side of the field is “seen” by the right striate cortex, paralleling the involvement of the right hemisphere in the motor and sensory activities of the left side of the body. Similarly, objects in the right side of the field are “seen” by the left striate cortex (see Figure 13-1).

Note that reference to the “left side of the visual field” is not the same as the “visual field of the left eye.”

A defect that affects the nasal field of one eye and the temporal field of the other eye is described as **homonymous**.

A defect in the field of just one eye must be caused by a disruption anterior to the chiasm. If there is a defect in the fields of both eyes, there are two lesions, one in each prechiasmal pathway, or there is a single lesion in the chiasm or the postchiasmal pathway, where the fibers for the two eyes are brought together. The pattern of the defect as well as associated signs or symptoms might aid in determining the location of the damage.

CLINICAL COMMENT: CHARACTERISTIC VISUAL FIELD DEFECTS

The regular fiber orientation in each structure of the visual pathway can be correlated with a specific pattern of visual field loss. A lesion of the choroid or outer retina will cause a field defect that is similar in shape to the lesion and is in the corresponding location in the field (e.g., if the lesion is in the superior nasal retina, the defect will be in the inferior temporal field).

A lesion in the nerve fiber layer will cause a field defect corresponding to the location and configuration of the affected nerve fiber bundle. One of the disease processes that affects the nerve fiber layer is glaucoma. If temporal retinal fibers are affected, an arcuate defect can be produced that curves around the point of fixation from the blind spot to termination at the horizontal nasal meridian (Figure 13-21). This abrupt edge (at the horizontal meridian) is called a **nasal step** and results from the configuration of the fibers at the temporal retinal raphe. Less often, a lesion affects a nasal bundle of nerves, producing a wedge-shaped defect emanating from the physiologic blind spot into the temporal field.

Injury to the optic nerve is accompanied by a visual field defect, a relative afferent pupillary defect, and atrophy of the affected nerve fibers, which eventually is manifested at the disc. The small-diameter, tightly packed fibers of the macula have the greatest metabolic need and often are affected first in both compressive and ischemic lesions.¹²

The optic chiasm brings all the visual fibers together; lesions of the chiasm usually will show bitemporal or binasal defects. The most common cause of a bitemporal field defect is a pituitary gland tumor, and a visual field defect is often the first clinical sign (Figure 13-22, A). A patient may not recognize the field loss because the nasal field of one eye overlaps the temporal field of the other eye. The crossed fibers seem to be damaged first in compressive lesions such as a tumor.¹⁴ This susceptibility to damage might be attributable to the purported weak blood supply of the median portion of the chiasm. Consequently, the crossed fibers also are more susceptible to ischemia in a vascular event.⁴⁰ Involvement of both lateral sides of the chiasm, producing a binasal defect, might be caused by an aneurysm of the internal carotid artery that impinges on the chiasm and displaces it against the other internal carotid artery (Figure 13-22, B).

A single lesion at the optic chiasm and its junction with the optic nerve might be characterized by a central defect in the field of the eye on the same side as the lesion, as well as a superior temporal defect in the field of the opposite eye, because of the inferior nasal fibers that loop into the optic nerve from the contralateral eye.

A homonymous field defect will be produced by a single lesion in the postchiasmal pathway, as the nasal fibers of the contralateral eye join the temporal fibers of the ipsilateral eye; visual acuity usually is not affected because one-half the fovea is sufficient for 20/20 Snellen acuity.¹⁴ In this lesion the field loss is present on the side of the field contralateral to the lesion. Other signs or symptoms accompanying a homonymous defect can help the diagnostician determine more exactly the site of the lesion.

Continued

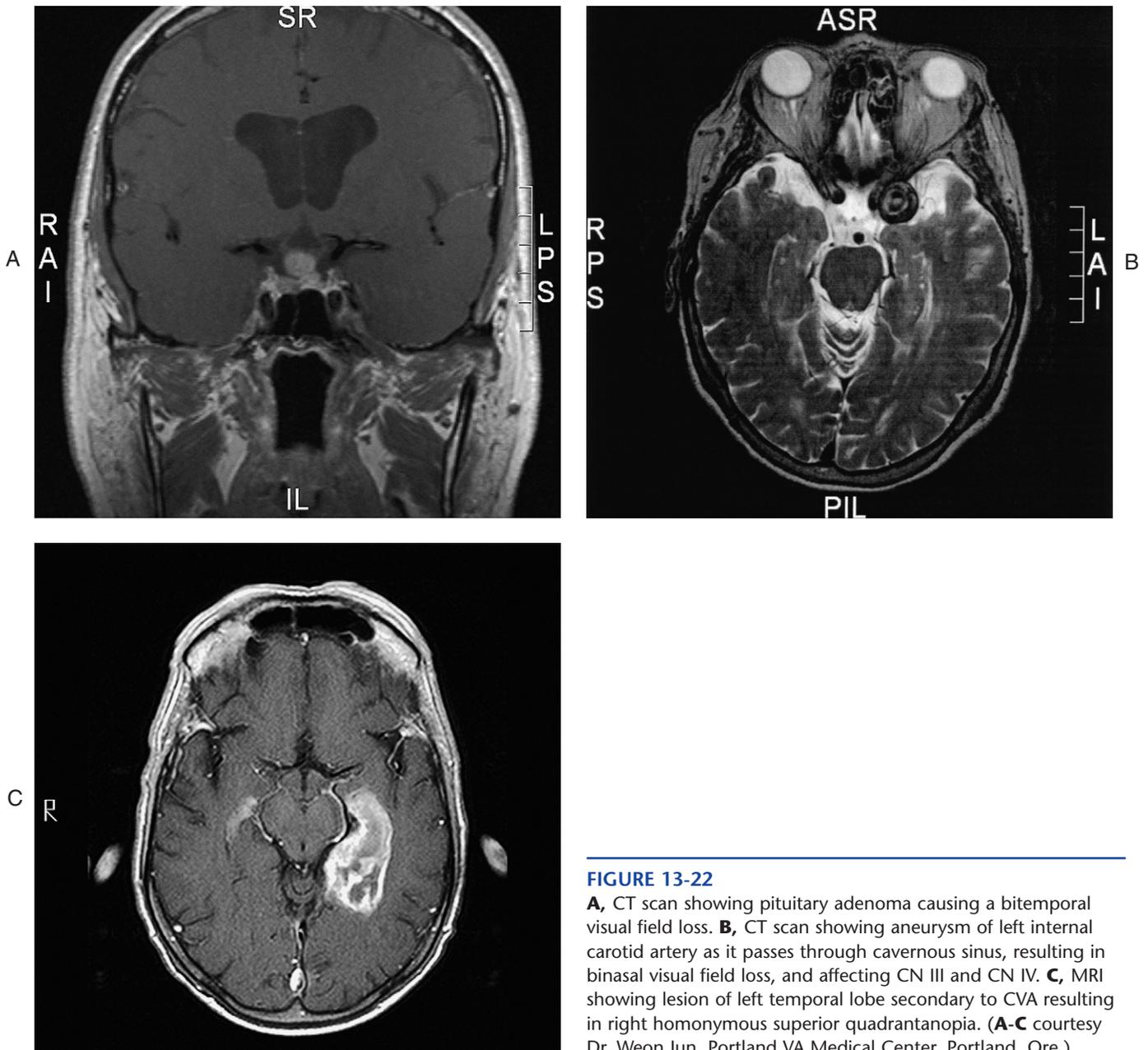


FIGURE 13-22

A, CT scan showing pituitary adenoma causing a bitemporal visual field loss. **B**, CT scan showing aneurysm of left internal carotid artery as it passes through cavernous sinus, resulting in binasal visual field loss, and affecting CN III and CN IV. **C**, MRI showing lesion of left temporal lobe secondary to CVA resulting in right homonymous superior quadrantanopia. (**A-C** courtesy Dr. Weon Jun, Portland VA Medical Center, Portland, Ore.)

A lesion involving the optic tract eventually will produce optic nerve atrophy, which usually becomes evident as optic disc pallor. Because the optic tract is relatively small in cross section, a lesion often damages all of the fibers, causing a homonymous field defect that affects the entire half of the field; if a partial hemianopia results, the defects will be incongruent.⁵⁶ The defects in a homonymous field are **congruent** if the two defects are similarly shaped and are **incongruent** if the defect shapes are dissimilar. Because crossed fibers outnumber uncrossed fibers, a lesion of the optic tract may be accompanied by a relative afferent pupillary defect of the contralateral eye.¹⁴

A lesion in the LGN would affect the contralateral field and eventually also cause optic atrophy; however, there would be no associated pupillary defect. Because of the point-to-point localization in the LGN, lesions here produce moderately to completely congruent field defects.⁴¹

Damage to the optic radiations or cortex does not normally cause atrophy of the optic nerve because it does not involve the fibers of the retinal ganglion cells. A lesion of the optic radiations causes a contralateral homonymous field defect and, because the fibers are so spread out, the defect often affects only one quadrant. If a lesion of the

Continued

temporal lobe involves Meyer's loop, a superior quadrant field defect will result; parietal lobe lesions more commonly cause inferior field defects (Figure 13-22, C).¹⁴

The characteristic feature of a defect in the occipital lobe is congruency. Congruency depends on how closely fibers from corresponding points of each eye and carrying the same visual field information are positioned to one another at the site of the lesion. As the fibers reach the occipital lobe and finally the striate cortex, the fibers emanating from corresponding points in the field come together to form a point-to-point representation of the field. Therefore, a lesion here will cause a congruent defect.

Figure 13-23 depicts examples of various visual field defects.

When visual association areas within the occipital, temporal, and parietal lobes are involved, higher cortical visual processes may be affected. Lesions of the parietal lobe can cause abnormal optokinetic nystagmus and affect visual attention; temporal lobe lesions can cause olfactory hallucinations, formed visual hallucinations, or déjà vu phenomenon; injury involving the occipitotemporal cortex can affect object and facial recognition.⁵⁷ Blindsight occurs when there seems to be some sight in a hemifield but there is no conscious awareness of the sight. That is, a motor reflex response can be elicited with presentation of an unexpected stimulus in the affected field, but the patient has no awareness of the vision. It is likely that subcortical visual responses are mediated at the level of the superior colliculus and that the reflex does not initiate from the visual cortex.

Striate Cortex Maps

Early work correlating the visual field to striate cortex was done by Holmes and Lister,⁵⁸ who studied injured soldiers from World War I and attempted to match visual field defects with injuries from shrapnel to the occipital lobe. The Holmes map was the most detailed source showing the representation of the visual field in human striate cortex. The macular portion extends from the posterior pole forward, with the periphery of the field represented in anterior occipital lobe and the unioocular temporal crescent in the most anterior aspect of the striate cortex adjacent to the parieto-occipital sulcus. However, detailed mapping of monkey striate cortex using electrophysiologic methods revealed discrepancies between monkey and human data. These findings suggested that either monkey cortex and human cortex were not as alike as believed or the Holmes map required some modification.

Technologies such as MRI have been used to study the human cortex, allowing more direct correlation of a lesion with a field defect. Some investigators suggest revision of the Holmes map⁵⁵ shown in Figure 13-24. The primary change concerns the extent of the area depicting macular representation. A much greater area of the visual cortex is thought to be taken up by macular projection,⁵⁵ with the central 30 degrees of the visual

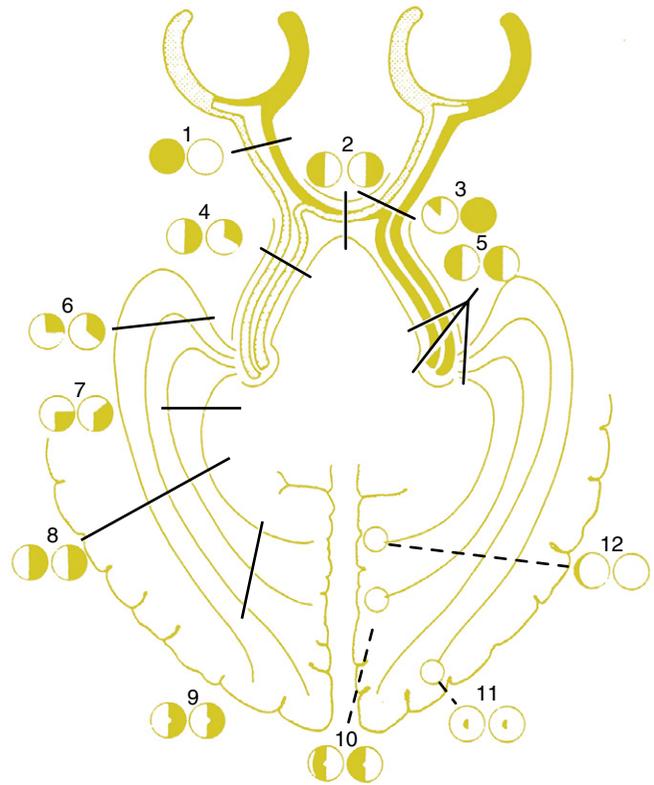
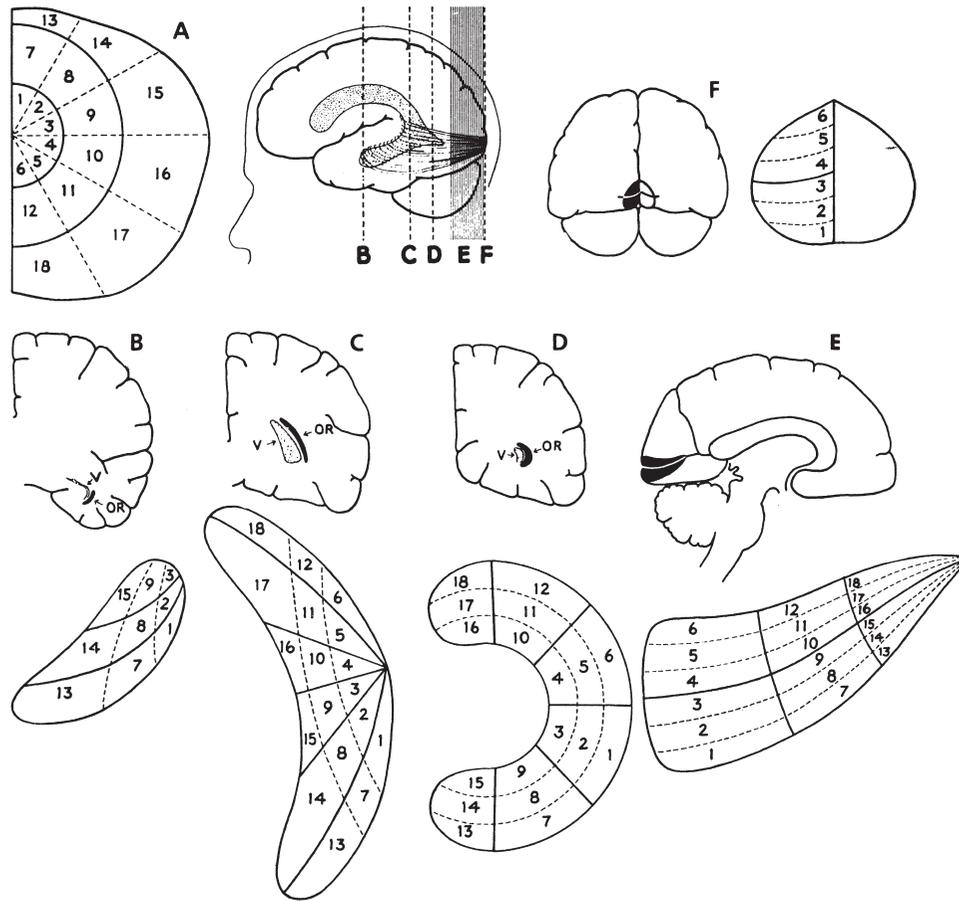


FIGURE 13-23

Visual field defects. Visual pathway is shown, as are sites of interruption of nerve fibers and resulting visual field defects. 1, Complete interruption of left optic nerve, resulting in complete loss of visual field for left eye. 2, Interruption in midline of optic chiasm, resulting in bitemporal hemianopia. 3, Interruption in right optic nerve at junction with chiasm, resulting in complete loss of visual field for right eye and superior temporal loss in field for left eye (due to anterior knees). 4, Interruption in left optic tract, causing incongruent right homonymous hemianopia. 5, Complete interruption in right optic tract, lateral geniculate nucleus, or optic radiations, resulting in total left homonymous hemianopia. 6, Interruption in left optic radiations involving Meyer's loop, causing incongruent right homonymous hemianopia. 7, Interruption in optic radiations in left parietal lobe, causing incongruent right homonymous hemianopia. 8, Interruption of all left optic radiations, resulting in total right homonymous hemianopia. 9, Interruption of fibers in left anterior striate cortex, resulting in right homonymous hemianopia with macular sparing. 10, Interruption of fibers in right striate cortex, resulting in left homonymous hemianopia with macular and temporal crescent sparing. 11, Interruption of fibers in right posterior striate cortex, resulting in left macular homonymous hemianopia. 12, Interruption of fibers in right anterior striate cortex, resulting in left temporal crescent loss. (From Hart WM Jr, editor: *Adler's physiology of the eye*, ed 9, St Louis, 1992, Mosby.)

**FIGURE 13-24**

Schematic representation of architecture of geniculocalcarine pathway with projection of striate cortex and nerve fiber bundles of optic radiation onto visual field. **A**, Right homonymous half-field divided into sectors and concentric zones representing projection of various bundles of optic radiations in temporal and parietal lobes and in striate cortex in occipital lobe. **B**, **C**, and **D**, Coronal sections (seen from in front) through temporal, parietal, and parieto-occipital lobes of left cerebral hemisphere showing planes of section, relationship of optic radiations to lateral ventricle, and division of visual fiber bundles in optic radiations into sectors and concentric zones corresponding to their projection onto visual field. Note in plane of section through temporal loop of Meyer (**B**) that only lower half of radiations are represented; in planes **B** and **C**, that section anterior radiations, macular fibers (1 to 6) are laminated on lateral surface of radiations; and in plane **D**, that section's posterior radiations, macular fibers are interposed between and completely separate upper and lower peripheral fibers. **E**, Medial view of left cerebral hemisphere showing striate cortex divided according to its projection on right homonymous half-field. **F**, View from behind striate cortex at posterior tip of left occipital pole showing projection of macular portion of right homonymous defect. (From Harrington DO, Drake MV: *The visual fields; text and atlas of clinical perimetry*, ed 6, St Louis, 1990, Mosby.)

field represented in approximately 83% of the striate cortex.⁵⁵ Other imaging studies more closely agree with the Holmes map and show that the central 15 degrees of vision occupies 37% of the surface area of the striate cortex.⁵⁹ Some discrepancies may result from the nature of the lesion because an MRI may overestimate the actual area involved when edema is present.⁵⁹

Macular Sparing

Macular sparing occurs when an area of central vision remains within a homonymous field defect. Because fixational eye movements of 1 to 2 degrees do occur during the visual field examination, the area spared within the defect should involve at least 3 degrees in order for macular sparing to be confirmed clinically.⁴⁴ Because the macular area often was spared in homonymous defects caused by occipital lobe lesions, it once was supposed that the entire macula was represented in both sides of the striate cortex. We now know that this is not the case. However, even in the presence of an extensive lesion, some of the macular projection area might remain unaffected, either because the posterior pole of the occipital lobe has such an extensive blood supply or because the macular projection covers a very large area.¹⁴ Macular sparing can also be explained by the size and overlap of the receptive field of the retinal ganglion cells subserving the vertical meridian.⁶⁰

AGING WITHIN THE VISUAL PATHWAY

Neural cell death occurs throughout all structures of the visual pathway, although the extent varies significantly within the population.⁶¹ Age is accompanied by a decrease in the extent of the visual field, caused both by loss of cells and by a decrease in the transparency of the ocular media.^{12,62} The ability to perceive accurately the speed of moving objects declines with age, and animal studies have identified an age-related difference in temporal processing speed at the level of the visual cortex.⁶³ This decline in accurately perceiving the speed of moving objects may contribute to the higher incidence of automobile accidents among the elderly population.

REFERENCES

- Hoyt WF, Osman L: Visual fiber anatomy in the infrageniculate pathway of the primate, *Arch Ophthalmol* 68:124, 1962.
- Polyak S: *The vertebrate visual system*, Chicago, 1957, University of Chicago Press.
- Brouwer B, Zeeman WP: The projection of the retina in the primary optic neuron in monkeys, *Brain* 49, 1926.
- Boyd JD, Gu Q, Matsubara JA: Overview of the central visual pathways. In Kaufman PL, Alm A, editors: *Adler's physiology of the eye*, ed 10, St Louis, 2003, Elsevier, p 641.
- Jonas JB, Schmidt AM, Muller-Bergh JA et al: Human optic nerve fiber count and optic disc size, *Invest Ophthalmol Vis Sci* 33(6):2012, 1992.
- Sadun AA, Glaser JS: Anatomy of the visual sensory system. In Tasman W, Jaeger EA, editors: *Duane's foundations of clinical ophthalmology*, vol 1, Philadelphia, 1994, Lippincott.
- Milekberg FS, Drance SM, Schulzer M et al: The normal human optic nerve, *Ophthalmology* 96:1325, 1989.
- Warwick R: *Eugene Wolff's anatomy of the eye and orbit*, ed 7, Philadelphia, 1976, Saunders, p 325.
- Parravano JG, Toledo A, Kucharczyk W: Dimensions of the optic nerves, chiasm, and tracts: MR quantitative comparison between patients with optic atrophy and normals, *J Comput Assist Tomogr* 17(5):688, 1993.
- Levin LA: Optic nerve. In Kaufman PL, Alm A, editors: *Adler's physiology of the eye*, ed 10, St Louis, 2003, Elsevier, p 603.
- Unsold R, Hoyt WF: Band atrophy of the optic nerve, *Arch Ophthalmol* 98:1637, 1980.
- Harrington DO: *The visual fields*, ed 5, St Louis, 1981, Mosby.
- Borchert MS: Vascular anatomy of the visual system, *Ophthalmol Clin North Am* 9(3):327, 1996.
- Horton JC: The central visual pathways. In Hart WM Jr, editor: *Adler's physiology of the eye*, ed 9, St Louis, 1992, Mosby, p 728.
- Casagrande VA, Ichida JM: The lateral geniculate nucleus. In Kaufman PL, Alm A, editors: *Adler's physiology of the eye*, ed 10, St Louis, 2003, Elsevier, p 655.
- Casagrande VA, Ichida JM: The primary visual cortex. In Kaufman PL, Alm A, editors: *Adler's physiology of the eye*, ed 10, St Louis, 2003, Elsevier, p 669.
- Lachica EA, Casagrande VA: The morphology of collicular and retinal axons ending on small relay (W-like) cells of the primate lateral geniculate nucleus, *Vis Neurosci* 10(3):403, 1993.
- Krolak-Salmon P, Guenot M, Tiliket C et al: Anatomy of optic nerve radiations as assessed by static perimetry and MRI after tailored temporal lobectomy, *Br J Ophthalmol* 84(8):884, 2000.
- Gilbert CD, Kelly JP: The projections of cells in different layers of the cat's visual cortex, *J Comp Neurol* 163:81, 1975.
- Hubel DH, Wiesel TN: Laminar and columnar distribution of geniculocortical fibers in the macaque monkey, *J Comp Neurol* 146:421, 1972.
- Horton JC, Dagi LR, McCrane EP et al: Arrangement of ocular dominance columns in human visual cortex, *Arch Ophthalmol* 108(7):1025, 1990.
- Zeki S, Watson JD, Lueck CJ et al: A direct demonstration of functional specialization in human visual cortex, *J Neurosci* 11(3):641, 1991.
- Livingstone MS, Hubel DH: Segregation of form, color, movement, and depth: anatomy, physiology, and perception, *Science* 240:740, 1988.
- Hockfield S, Tootell RB, Zaremba S: Molecular differences among neurons reveal an organization of human visual cortex, *Proc Natl Acad Sci USA* 87(8):3027, 1990.
- Hubel DH, Livingstone MS: Color and contrast sensitivity in the lateral geniculate body and primary visual cortex in the macaque monkey, *J Neurosci* 10(7):2223, 1990.
- Silverman SE, Trick GL, Hart WM Jr: Motion perception is abnormal in primary open-angle glaucoma and ocular hypertension, *Invest Ophthalmol Vis Sci* 31(4):722, 1990.
- Hubel DH, Wiesel TN: Receptive fields and functional architecture of monkey striate cortex, *J Physiol* 195:215, 1968.
- Hubel DH, Wiesel TN, Stryker MP: Anatomical demonstration of orientation columns in macaque monkey, *J Comp Neurol* 177:361, 1978.

29. Boyd JD, Matsubara JA: Extrastriate cortex. In Kaufman PL, Alm A, editors: *Adler's physiology of the eye*, ed 10, St Louis, 2003, Elsevier, p 686.
30. Catani M, Jones DK, Donato R et al: Occipito-temporal connections in the human brain, *Brain* 126(pt 9):2093, 2003.
31. Wurtz RH: Vision for the control of movement: the Friedenwald Lecture, *Invest Ophthalmol Vis Sci* 37:2310, 1996.
32. Roland E, Gulyás B, Seitz RJ et al. Functional anatomy of storage, recall, and recognition of a visual pattern in man, *Neuroreport* 1:53, 1990.
33. Belliveau JW, Kennedy DN Jr, McKinstry RC et al: Functional mapping of the human visual cortex by magnetic resonance imaging, *Science* 254(5032):716, 1991.
34. Belliveau JW, Kwong KK, Kennedy DN et al: Magnetic resonance imaging mapping of brain function: human visual cortex, *Invest Radiol* 27(suppl 2):59, 1992.
35. Kwong KK, Belliveau JW, Chesler DA et al: Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation, *Proc Natl Acad Sci USA* 89(12):5675, 1992.
36. Menon RS, Ogawa S, Kim SG et al: Functional brain mapping using magnetic resonance imaging: signal changes accompanying visual stimulation, *Invest Radiol* 27(suppl 2):47, 1992.
37. Le Bihan D, Turner R, Zeffiro TA et al: Activation of human primary visual cortex during visual recall: a magnetic resonance imaging study, *Proc Natl Acad Sci USA* 90(24):11802, 1993.
38. Ogawa S, Menon RS, Tank DW et al: Functional brain mapping by blood oxygenation level-dependent contrast magnetic resonance imaging: a comparison of signal characteristics with a biophysical model, *Biophys J* 64(3):803, 1993.
39. Francois J, Neetens A, Collette JM: Vascularization of the optic pathway, *Br J Ophthalmol* 42:80, 1958.
40. Lao Y, Gao H, Zhong Y: Vascular architecture of the human optic chiasma and bitemporal hemianopia, *Chin Med Sci J* 9(1):38, 1994.
41. Ferreira A, Braga FM: Microsurgical anatomy of the anterior choroidal artery, *Arq Neuropsiquiatr* 48(4):448, 1990 (abstract).
42. Margo CE, Hamed KM, McCarty J: Congenital optic tract syndrome, *Arch Ophthalmol* 109(8):1120, 1991.
43. Luco C, Hoppe A, Schweitzer M et al: Visual field defects in vascular lesions of the lateral geniculate body, *J Neurol Neurosurg Psychiatry* 55(1):12, 1992.
44. McFadzean R, Brosnahan D, Hadley D et al: Representation of the visual field in the occipital striate cortex, *Br J Ophthalmol* 78(3):185, 1994.
45. Ogden TE: Nerve fiber layer of the macaque retina: retinotopic organization, *Invest Ophthalmol Vis Sci* 24:85, 1983.
46. Hoyt WF, Tudor RC: The course of parapatillary temporal retinal axons through the anterior optic nerve, *Arch Ophthalmol* 69:503, 1963.
47. Ballantyne AJ: The nerve fiber pattern of the human retina, *Trans Ophthalmol Soc UK* 66:179, 1946.
48. Kupfer C, Chumbley L, Downer J et al: Quantitative histology of optic nerve, optic tract, and lateral geniculate body of man, *J Anat* 101:393, 1967.
49. Wilbrand HL: Schema des verlaufs der sehnervenfasern durch das chiasma, *Z Augenheilk* 59:135, 1927.
50. Jeffery G: Architecture of the optic chiasm and the mechanisms that sculpt its development, *Physiol Rev* 81(4):1393, 2001.
51. Moore RY: Retinohypothalamic projection in mammals: a comparative study, *Brain Res* 49:403, 1973.
52. Kupfer C: The projection of the macula in the lateral geniculate body of man, *Am J Ophthalmol* 54:597, 1962.
53. Hickey TL, Guillery RW: Variability of laminar patterns in the human lateral geniculate body, *J Comp Neurol* 183:221, 1979.
54. Malpeli JG, Baker FH: The representation of the visual fields in the lateral geniculate body of *Macaca mulatta*, *J Comp Neurol* 161:569, 1975.
55. Horton JC, Hoyt WF: The representation of the visual field in human striate cortex, *Arch Ophthalmol* 109:816, 1991.
56. Reese BE, Cowey A: Fibre organization of the monkey's optic tract. II. Noncongruent representation of the two half-retinae, *J Comp Neurol* 295(3):401, 1990.
57. Balcer LJ: Anatomic review and topographic diagnosis, *Ophthalmol Clin North Am* 14:1, 2001.
58. Holmes G, Lister WT: Disturbances of vision from cerebral lesions with special reference to the cortical representation of the macula, *Brain* 39:34, 1916.
59. Wong AM, Sharpe JA: Representation of the visual field in the human occipital cortex, *Arch Ophthalmol* 117(2):208, 1999.
60. Reinhard J, Trauzettel-Klonsinski S: Nasotemporal overlap of retinal ganglion cells in humans: a functional study, *Invest Ophthalmol Vis Sci* 44(4):1568, 2003.
61. Hirose T, Katsumi O: Functional changes: psychophysical and electrophysiologic measurements. In Albert DM, Jakobiec FA, editors: *Principles and practice of ophthalmology*, Philadelphia, 1994, Saunders, p 728.
62. Trobe JD, Glasser JS: *The visual field manual: a practical guide to testing and interpretation*, Gainesville, Fla, 1983, Triad.
63. Mendelson JR, Wells EF: Age-related changes in the visual cortex, *Vis Res* 42:695, 2002.

Autonomic Innervation of Ocular Structures

The autonomic nervous system innervates smooth muscles, glands, and the heart and consists of (1) the sympathetic system, which, when stimulated, prepares the body to face an emergency, and (2) the parasympathetic system, which maintains and restores the resting state. Balance is maintained between these two systems and is particularly evident in those structures innervated by both systems. The ocular structures innervated by the autonomic nervous system are the iris muscles, ciliary muscle, smooth muscles of the eyelids, choroidal and conjunctival blood vessels, and the lacrimal gland.

AUTONOMIC PATHWAY

The sympathetic pathway originates in the lateral gray column of the thoracic and upper lumbar segments (T-1 through L-2) of the spinal cord; sympathetic innervation for ocular structures originates in segments T-1 through T-3. The parasympathetic pathway originates in the midbrain, pons, medulla, and sacral spinal cord; parasympathetic innervation of ocular structures originates in the midbrain and pons.

The autonomic efferent pathway consists of two neurons. The cell body of the first, the preganglionic neuron, is located in the brain or spinal cord, whereas the cell body of the second is in a ganglion outside the central nervous system. The preganglionic fiber, which generally is myelinated, terminates in an autonomic ganglion, where a synapse occurs. The postganglionic fiber, which usually is nonmyelinated, exits the ganglion and innervates the target structure. Sympathetic ganglia usually are located near the spinal column, whereas parasympathetic ganglia are located near the target structure.

Ocular structures supplied by the sympathetic system are the iris dilator, ciliary muscle, smooth muscle of the lids, lacrimal gland, and choroidal and conjunctival blood vessels.¹⁻⁵ Ocular structures supplied by the parasympathetic system are the iris sphincter, ciliary muscle, lacrimal gland, and blood vessels.

SYMPATHETIC PATHWAY TO OCULAR STRUCTURES

Sympathetic fibers are controlled by the hypothalamus through a pathway that terminates in the lateral column of the cervical spinal cord. The fiber from the preganglionic neuron leaves the spinal cord in one of the first three thoracic nerves via the ventral root and enters the sympathetic ganglion chain located adjacent to the vertebrae (Figure 14-1). These **preganglionic fibers** then ascend in the sympathetic chain to a synapse in the **superior cervical ganglion**, located near the second and third vertebrae.^{6,7}

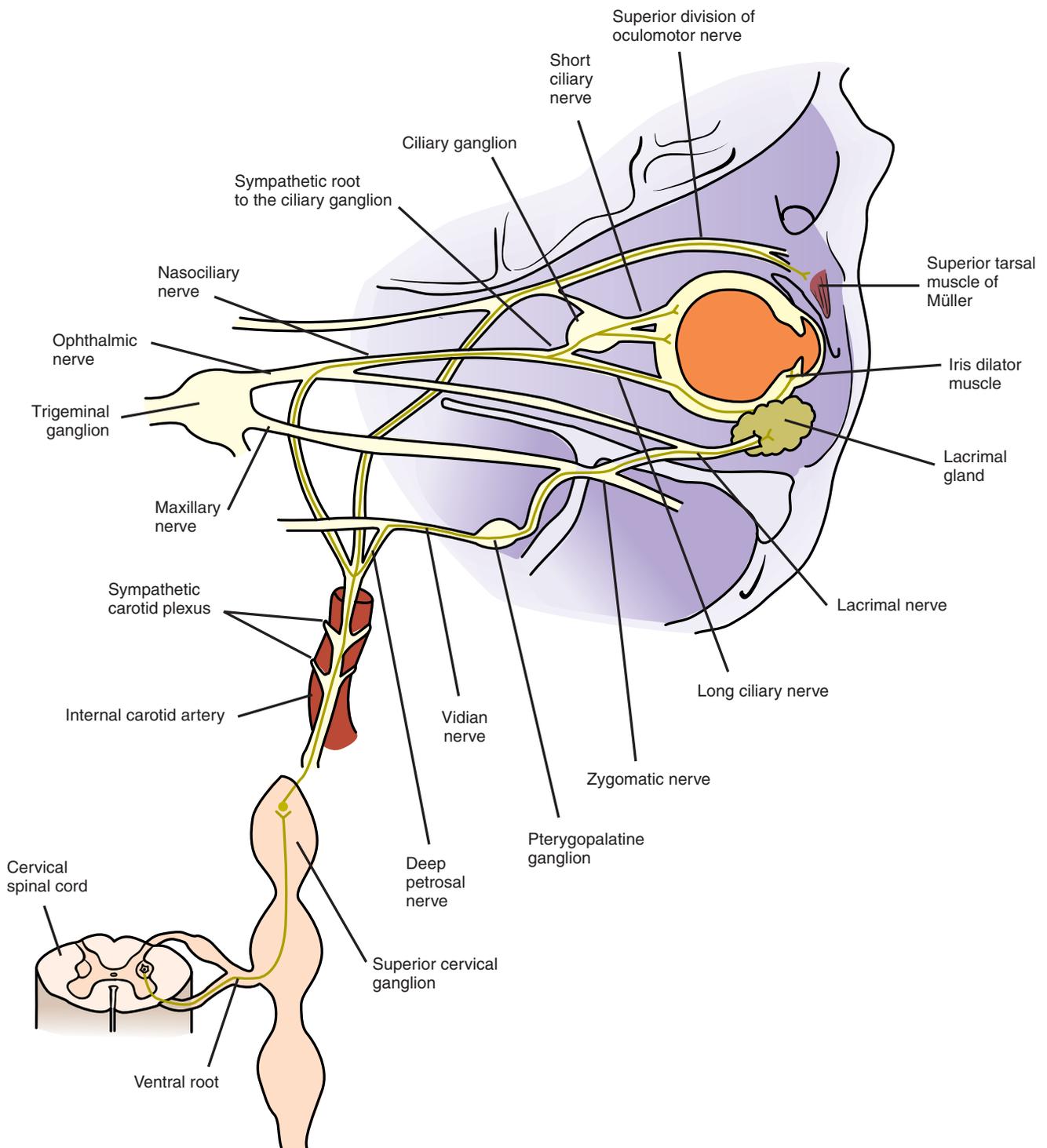
The **postganglionic fibers** leave the ganglion, form the carotid plexus around the internal carotid artery, and enter the skull through the carotid canal. The network of fine sympathetic fibers destined for orbital structures leaves the plexus in the cavernous sinus and takes multiple pathways to the target structures. The fibers most often described in the literature are presented here.

Some of these sympathetic fibers travel with the ophthalmic division of the trigeminal nerve from the cavernous sinus into the orbit.⁸ Once in the orbit the sympathetic fibers follow the nasociliary nerve and then travel with the long ciliary nerves to innervate the iris dilator and the ciliary muscle⁸⁻¹¹ (see Figure 14-1).

Other fibers from the carotid plexus follow this same route to the nasociliary nerve and then branch to the ciliary ganglion as the sympathetic root; these fibers pass through the ganglion without synapsing. They enter the globe as the short ciliary nerves to innervate the choroidal blood vessels. Alternately, the sympathetic root to the ciliary ganglion may emanate directly from the internal carotid plexus. The pathway to the conjunctival vasculature may be through either the long or the short ciliary nerves.

Other fibers from the carotid plexus join the oculomotor nerve and travel with it into the orbit to innervate the smooth muscle of the upper eyelid. These fibers follow the same path as the superior division of the oculomotor nerve as it supplies the levator muscle⁸ (see Figure 14-1).

Sympathetic stimulation activates the iris dilator, causing pupillary dilation and thereby increasing retinal

**FIGURE 14-1**

Sympathetic innervation to iris dilator, Müller's muscle, blood vessels, and lacrimal gland.

illumination, and exhibits a small inhibitory effect on the ciliary muscle.^{1-3,5,12-15} It also causes vasoconstriction of the choroidal and conjunctival vessels and widening of the palpebral fissure by stimulating the smooth muscle of the eyelids.

PARASYMPATHETIC PATHWAY TO OCULAR STRUCTURES

The preganglionic neuron in the parasympathetic pathway to the intrinsic ocular muscles is located in the

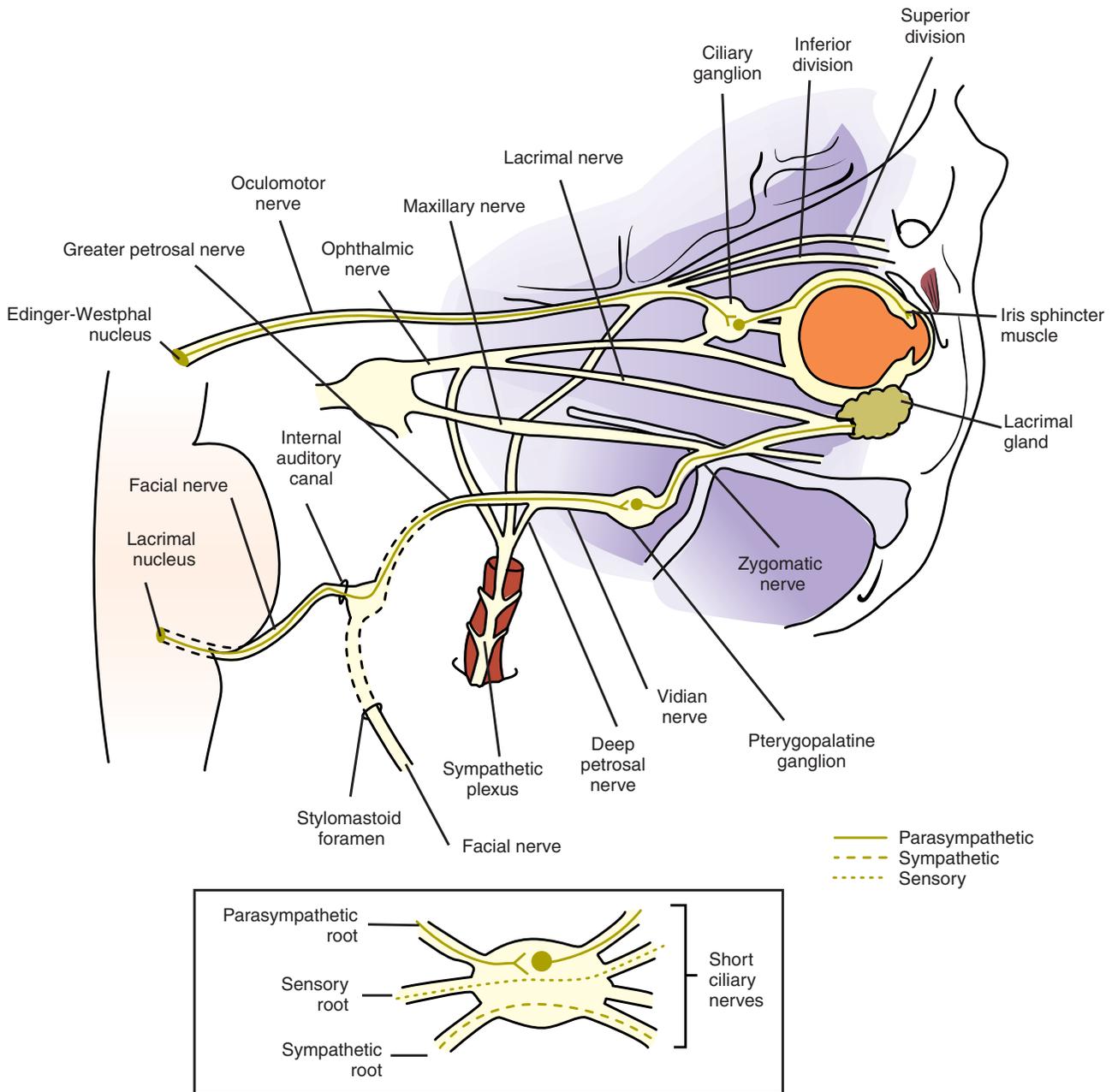


FIGURE 14-2

Parasympathetic innervation to sphincter and ciliary muscles and lacrimal gland. Inset shows sensory, sympathetic, and parasympathetic fibers into ciliary ganglion; only parasympathetic fibers synapse. Each short ciliary nerve carries all three types of fibers.

midbrain in the **parasympathetic accessory third-nerve nucleus**, also called the **Edinger-Westphal nucleus**. The **preganglionic fibers** leave the nucleus with the motor fibers of the oculomotor nerve and follow the inferior division of that nerve into the orbit.¹⁶ The parasympathetic fibers leave the inferior division and enter

the ciliary ganglion as the parasympathetic root¹⁷⁻¹⁹ (Figure 14-2).

The **ciliary ganglion** is a small, somewhat flat structure, 2 mm long and 1 mm high, located within the muscle cone between the lateral rectus muscle and the optic nerve, approximately 1 cm anterior to the

optic canal.^{9,20} Three roots are located at the posterior edge of the ganglion: the parasympathetic root, mentioned above; the sensory root, which carries sensory fibers from the globe and joins with the nasociliary nerve; and the sympathetic root, which supplies the blood vessels. Only the parasympathetic fibers synapse in the ciliary ganglion; the sensory and sympathetic fibers pass through without synapsing (see Figure 14-2).

The short ciliary nerves, located at the anterior edge of the ciliary ganglion, carry sensory, sympathetic, and parasympathetic fibers. The **postganglionic parasympathetic fibers**, which are myelinated,¹⁷ exit the ganglion in the short ciliary nerves, enter the globe, and travel to the anterior segment of the eye to innervate the sphincter and ciliary muscles. Most of the fibers innervate the ciliary body; only approximately 3% supply the iris sphincter.^{17,18} The two groups of neurons likely share some characteristics and differ in others, but specifics have not been identified.²¹

Parasympathetic stimulation causes pupillary constriction, thus decreasing retinal illumination and reducing chromatic and spheric aberrations. It also causes contraction of the ciliary muscle, enabling the eye to focus on near objects in accommodation.

CLINICAL COMMENT: IRIS EQUILIBRIUM

The iris contains muscles innervated by both autonomic systems. The parasympathetic system innervates the sphincter, and the sympathetic system innervates the dilator. The parasympathetic and sympathetic nerves are in some state of balance in the normal, healthy, awake individual, and the size of the pupil changes constantly, reflecting this balance. This physiologic pupillary unrest is called hippus. During sleep the pupils are small because the sympathetic system shuts down and the parasympathetic system predominates.

CLINICAL COMMENT: INHIBITION OF CILIARY MUSCLE

Parasympathetic activation causes contraction of the ciliary muscle in accommodation. Many investigators, using pharmacologic,^{22,23} electrophysiologic,²⁴ and anatomic^{17,25,26} evidence, have demonstrated the presence of both sympathetic receptors and fibers in animals and humans.^{27,28} The sympathetic effect on the ciliary muscle appears to be a small, slow inhibition that is a function of the level of parasympathetic activity.¹⁻⁵

AUTONOMIC INNERVATION TO LACRIMAL GLAND

The efferent autonomic pathway to the lacrimal gland follows a complex route. Fibers controlling the parasympathetic innervation originate in the pons in an area within the nucleus for cranial nerve VII designated as the lacrimal nucleus. These preganglionic fibers exit the pons with the motor fibers of the facial nerve, enter the internal auditory canal, and pass through the geniculate ganglion of the facial nerve without synapsing. They leave the ganglion as the **greater petrosal nerve**, which exits the petrous portion of the temporal bone.²⁹ The greater petrosal nerve is joined by the **deep petrosal nerve**, composed of sympathetic postganglionic fibers from the carotid plexus. The greater petrosal and the deep petrosal nerves together form the **vidian nerve (nerve of the pterygoid canal)** (see Figures 14-1 and 14-2).

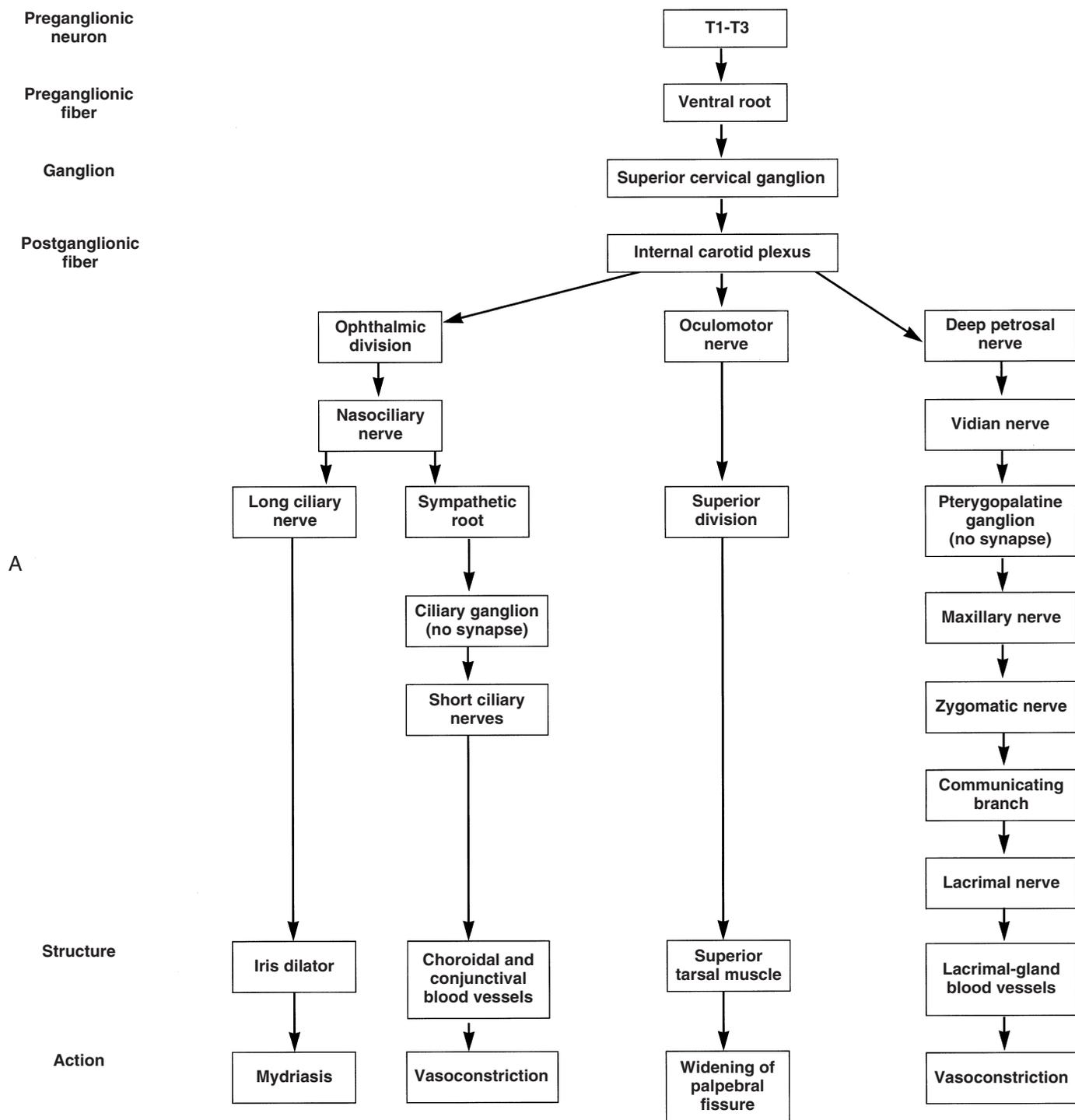
The vidian nerve enters the pterygopalatine ganglion, where the parasympathetic fibers synapse. The **pterygopalatine ganglion** (also called the **sphenopalatine ganglion**) lies in the upper portion of the pterygopalatine fossa (see Figure 12-5). It is a parasympathetic ganglion because it contains parasympathetic cell bodies and synapses; sympathetic fibers pass through without synapsing.

The autonomic fibers (all of which are now postganglionic) leave the ganglion, join with the maxillary branch of the trigeminal nerve, pass into the zygomatic nerve, and then form a communicating branch to the lacrimal nerve (see Figures 14-1 and 14-2). An alternate pathway bypasses the zygomatic nerve and travels from the ganglion directly to the gland.³⁰ The parasympathetic fibers that innervate the lacrimal gland are of the secretomotor type and thus cause increased secretion. The sympathetic fibers innervate the blood vessels of the gland and cause vasoconstriction. Sympathetic stimulation might indirectly cause decreased production of lacrimal gland secretion because of the restricted blood flow. Parasympathetic stimulation causes increased lacrimation. Figure 14-3 provides a flow chart of the common autonomic nerve pathways to orbital structures.

Sympathetic fibers from the zygomatic nerve also branch into the lower eyelid to innervate Müller's muscle of the lower lid.³¹

Parasympathetic innervation to the choroidal blood vessels is believed to emanate directly from the sphenopalatine ganglion through a network of fine nerves, the **rami oculares**.³² Parasympathetic activation presumably causes vasodilation, which might raise intraocular pressure.^{30,33}

Irritation of any branch of the trigeminal nerve activates a reflex afferent pathway, precipitating increased lacrimation.^{7,34}



A

FIGURE 14-3

Flow chart of autonomic nervous system. **A**, Sympathetic innervation.

Continued

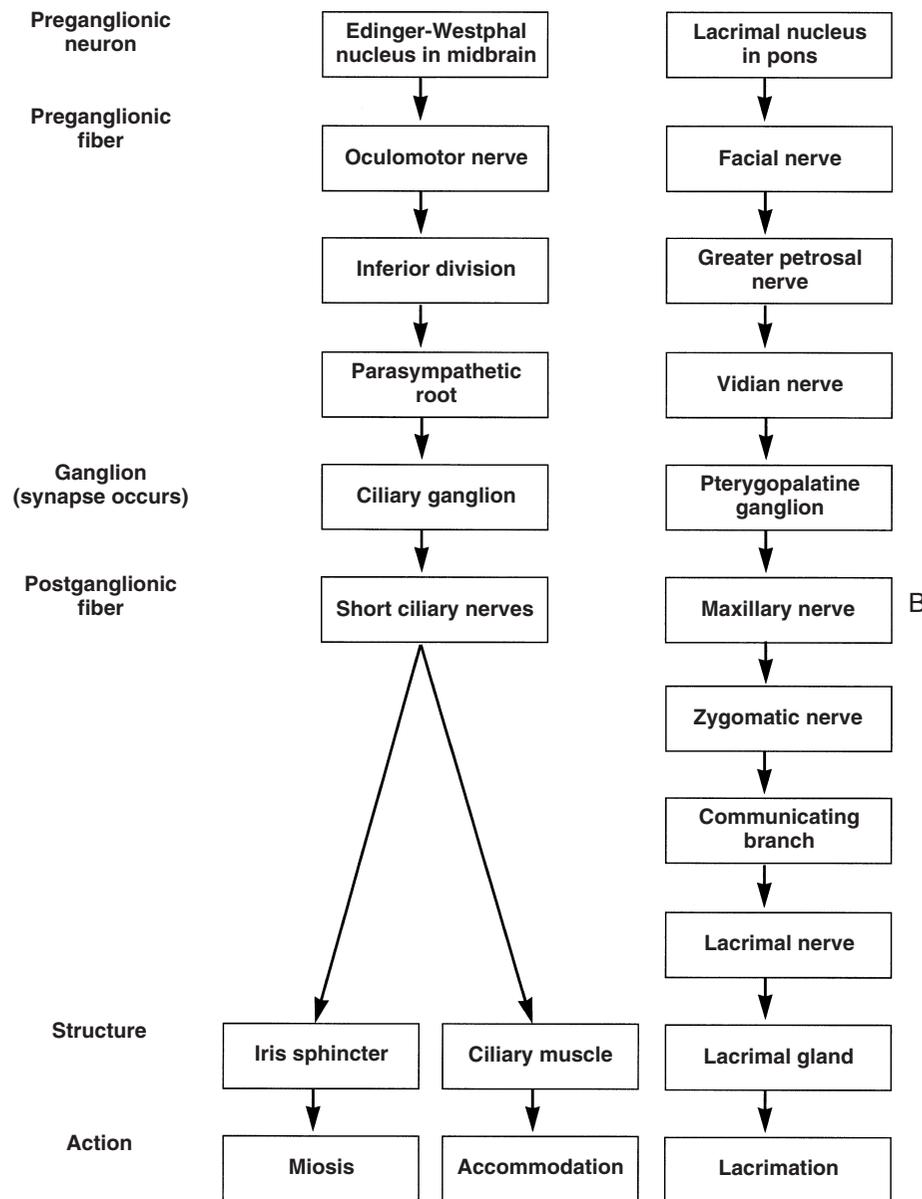


FIGURE 14-3 cont'd

B, Parasympathetic innervation.

CLINICAL COMMENT: CORNEAL REFLEX

Corneal touch initiates the three-part corneal reflex: lacrimation, miosis, and a protective blink (Figure 14-4). The pain sensation elicited by the touch travels to the trigeminal ganglion and then into the pons as the trigeminal nerve. Communication from the trigeminal nucleus to the Edinger-Westphal nucleus causes activation of the sphincter muscle. Communication to the facial nerve nucleus activates the motor pathway to the orbicularis muscle, causing the blink, and communication to the lacrimal nucleus and the parasympathetic pathway to the lacrimal gland stimulates increased lacrimation.

PHARMACOLOGIC RESPONSES OF INTRINSIC MUSCLES

Pharmacologic agents can alter autonomic responses. Topical ophthalmic drugs, which readily pass through the cornea, can be used to activate the intrinsic ocular muscles.

After a brief discussion of neurotransmitters and drug types relative to iris musculature, this section presents specific drugs that induce mydriasis or miosis, as well as

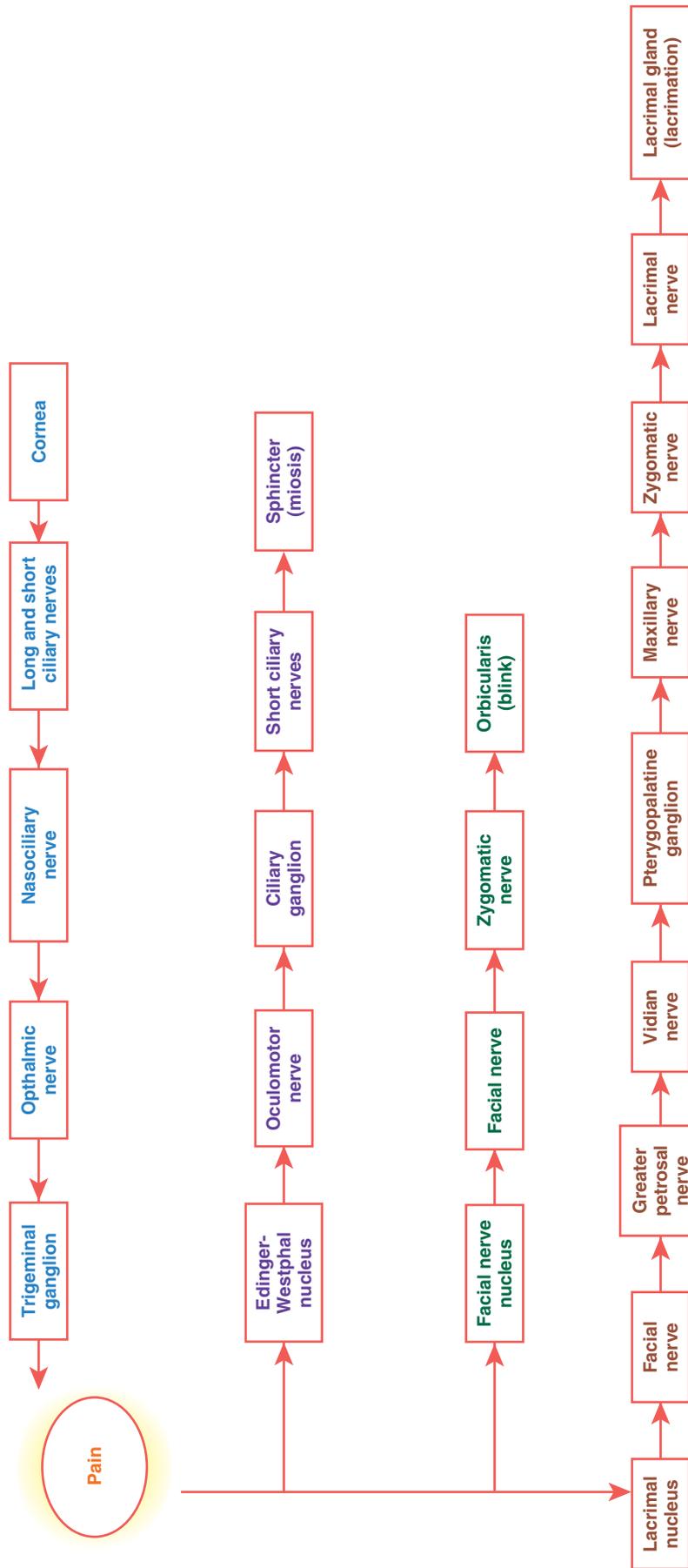
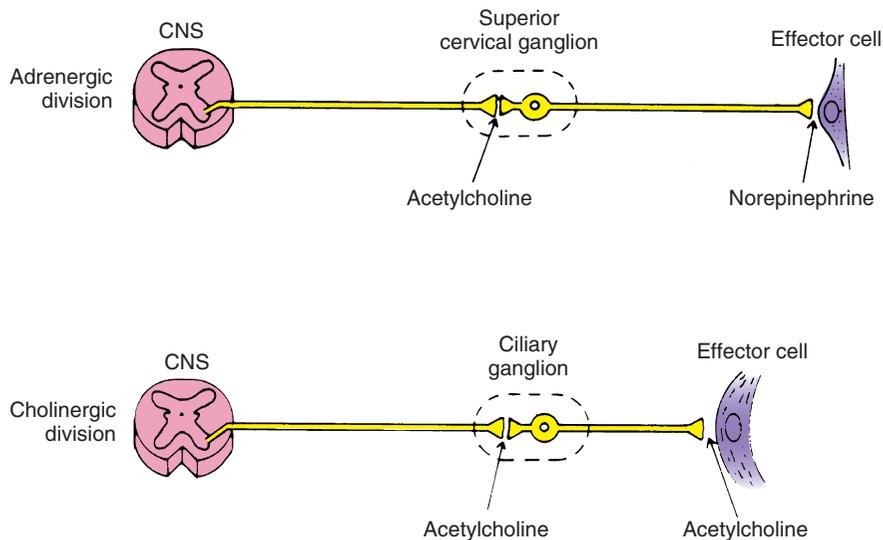


FIGURE 14-4 Corneal touch reflex. Pathways involved when pain from the cornea results in the reflex actions of miosis, blink, and lacrimation.

**FIGURE 14-5**

Autonomic neurotransmitters at their sites of action. CNS, Central nervous system. (From Bartlett JD, Jaanus SD: *Clinical ocular pharmacology*, ed 2, Boston, 1989, Butterworth-Heinemann.)

drugs used in the differential diagnosis of certain pupillary abnormalities. The reader is encouraged to review a text on pharmacology for detailed information.

NEUROTRANSMITTERS

When an action potential reaches the terminal end of an axon, a neurotransmitter is released that activates either the next fiber in the pathway or the target structure, the effector. In the sympathetic pathway the neurotransmitter released by the preganglionic fiber is **acetylcholine**, and the neurotransmitter released by the postganglionic fiber is **norepinephrine**. In the parasympathetic system both preganglionic and postganglionic fibers secrete acetylcholine (Figure 14-5). Fibers that release acetylcholine are called **cholinergic**, and fibers that release norepinephrine are called **adrenergic**.

The neurotransmitter binds to effector sites on the muscle and initiates a contraction. The neurotransmitter then is released from the muscle and is either inactivated or taken back up by the nerve ending, thus preventing continual muscle spasm; further muscle contraction should occur only with another action potential and release of additional transmitter. At the cholinergic neuromuscular junction, acetylcholinesterase hydrolyzes and inactivates acetylcholine; at the adrenergic neuromuscular junction, norepinephrine is recycled, taken back up by the nerve ending.

DRUGS: AGONISTS AND ANTAGONISTS

A drug that replicates the action of a neurotransmitter is called an **agonist**. A **direct-acting agonist** is usually structurally similar to the transmitter and duplicates the action of the neurotransmitter by acting on the receptor sites of the effector. An **indirect-acting agonist** causes the action to occur either by exciting the nerve fiber, thereby causing release of the transmitter, or by preventing the recycling or reuptake of the transmitter, thus allowing it to continue its activity. **Antagonists** either block the receptor sites or block the release of the neurotransmitter, thus preventing action of the effector.

Ophthalmic Agonist Agents

Epinephrine and *phenylephrine* are direct-acting adrenergic agonists that bind to sites on the dilator muscle, causing contraction³⁵ (Figure 14-6). *Hydroxyamphetamine* and *cocaine* are indirect-acting adrenergic agonists. Hydroxyamphetamine causes the release of norepinephrine from the nerve ending, thus indirectly initiating muscle contraction. Cocaine prevents the reuptake of norepinephrine by the nerve ending; thus, norepinephrine remains at the neuromuscular junction and can continue to activate the dilator.³⁵

Pilocarpine is a direct-acting cholinergic agonist that directly stimulates the sites on the iris sphincter and

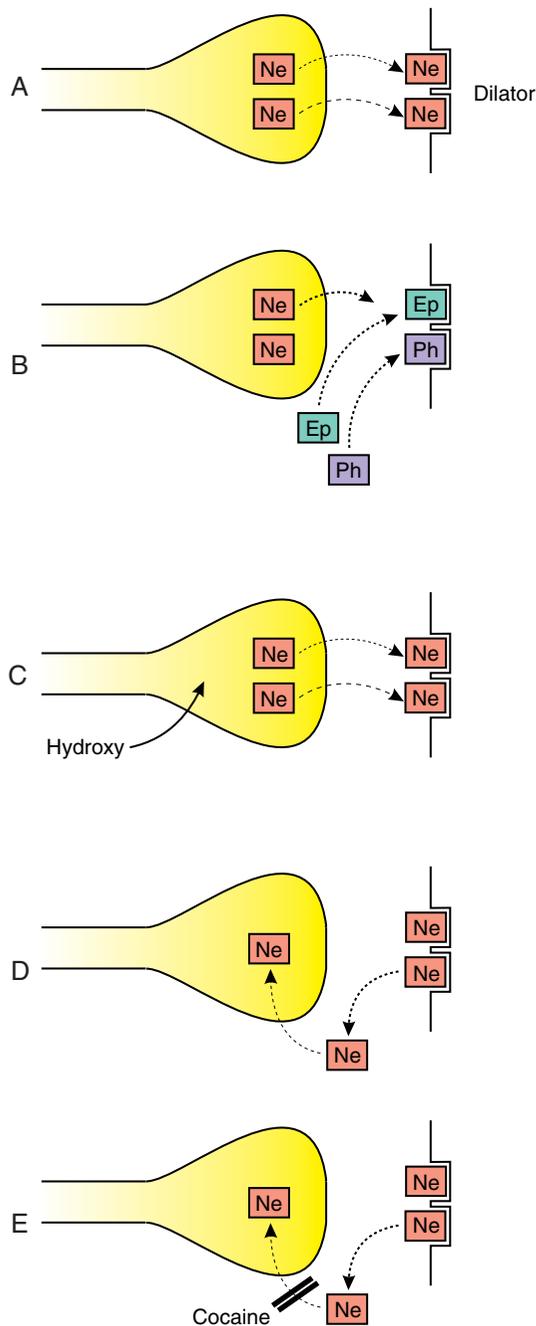


FIGURE 14-6

Adrenergic neuromuscular junction and actions of adrenergic agonists. **A**, Norepinephrine (Ne) is released by axon terminal and binds to sites on iris dilator muscle, causing contraction. **B**, Epinephrine (Ep) and phenylephrine (Ph) are direct-acting adrenergic agonists that bind to those same sites on iris dilator muscle, causing contraction. **C**, Hydroxyamphetamine (Hydroxy) is an indirect-acting adrenergic agonist that acts on nerve fiber, causing release of Ne. **D**, Once released from effector site, Ne is taken back up by nerve ending. **E**, Cocaine, an indirect-acting adrenergic agonist, prevents reuptake of Ne, allowing it to remain in neuromuscular junction and rebind to effector site.

ciliary muscle, causing contraction³⁵ (Figure 14-7). *Physostigmine* is an indirect-acting cholinergic agonist that inhibits acetylcholinesterase.³⁵ Therefore, acetylcholine is not broken down but remains in the junction, and the sphincter and ciliary muscle contraction continues in a spasm.

Ophthalmic Antagonist Agents

Dapiprazole is an adrenergic antagonist that blocks receptor sites, thereby preventing norepinephrine from activating the dilator muscle. *Atropine*, *cyclopentolate*, and *tropicamide* are cholinergic antagonists that compete with acetylcholine by blocking sphincter and ciliary muscle sites, thereby inhibiting miosis and accommodation³⁵ (Figure 14-8).

CLINICAL COMMENT: DRUG-INDUCED MYDRIASIS

For maximum pupillary dilation to occur, the dilator muscle should be activated and the sphincter muscle should be inhibited. This end is achieved by the combination of a direct-acting adrenergic agonist and a cholinergic antagonist. A common procedure for a dilated fundus examination involves the use of 2.5% phenylephrine and 1% tropicamide. Phenylephrine-induced mydriasis can be reversed with dapiprazole, which blocks the dilator receptor sites and prevents phenylephrine activity.

ACCOMMODATION-CONVERGENCE REACTION (NEAR-POINT REACTION)

The accommodation-convergence reaction is not a true reflex but rather a synkinesis or an association of three occurrences: convergence, accommodation, and miosis. As an object is brought near along the midline, the medial rectus muscles contract to move the image onto each fovea; the ciliary muscle contracts to keep the near object in focus; and the sphincter muscle constricts to decrease the size of the pupil, thereby improving depth of field.

Each of these actions can occur without the others. If plus lenses are placed in front of each eye, pupillary constriction and convergence occur without accommodation. If a base-in prism is placed in front of each eye, pupillary constriction and accommodation occur without convergence.³⁶

The afferent pathway for this reaction follows the visual pathway to the striate cortex. From the striate cortex, information is sent to the frontal eye fields, which communicate with the oculomotor nucleus and the Edinger-Westphal nucleus through a pathway that

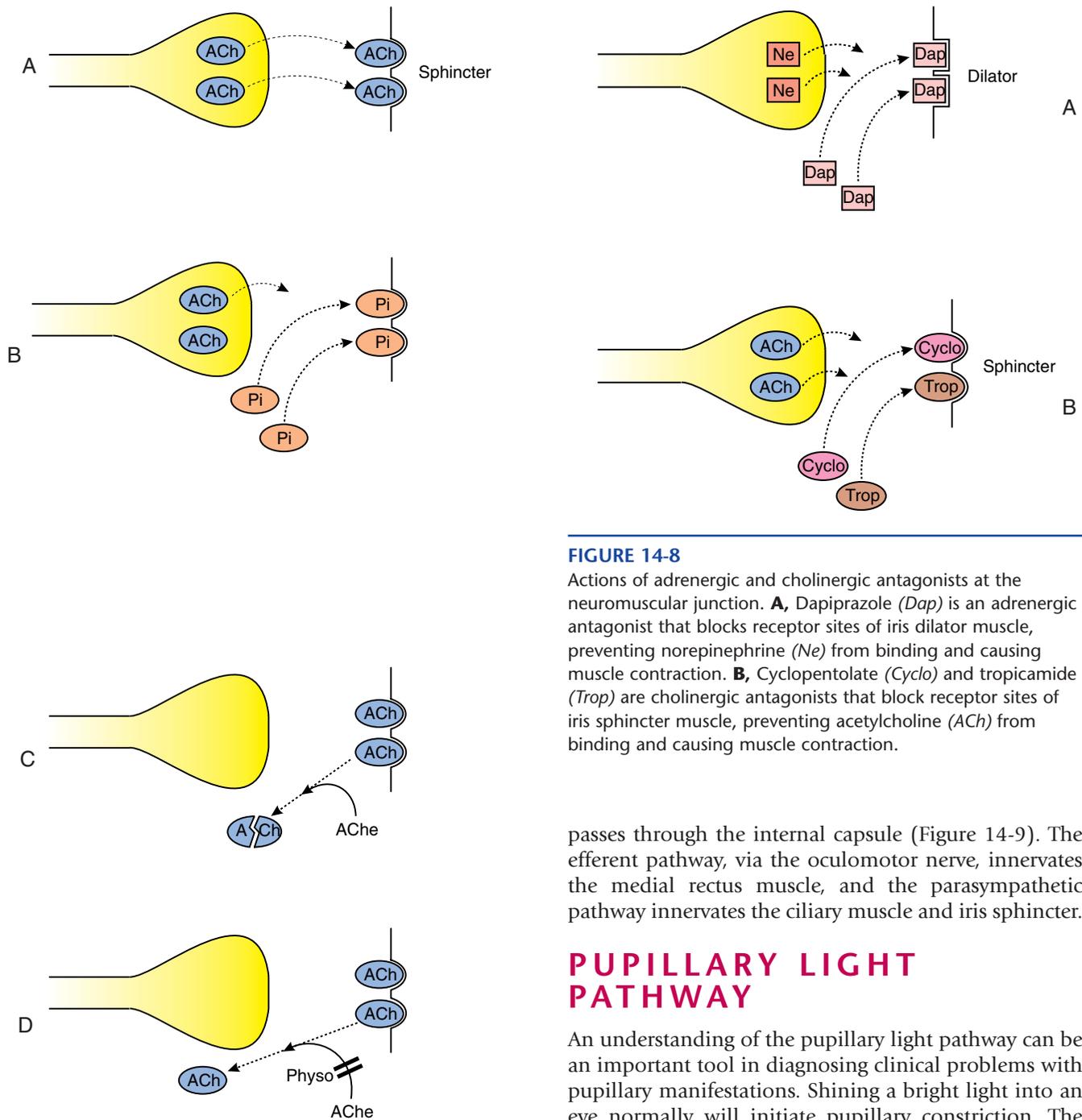


FIGURE 14-7 Cholinergic neuromuscular junction and actions of cholinergic agonists. **A**, Acetylcholine (ACh) is released by axon terminal and binds to sites on iris sphincter muscle, causing contraction. **B**, Pilocarpine (Pi) is a direct-acting cholinergic agonist that binds to those sites on iris sphincter muscle, causing contraction. **C**, Once released from effector site, ACh is broken down by acetylcholinesterase (AChE), which prevents ACh from rebinding to site. **D**, Physostigmine (Physo) is an indirect-acting cholinergic agonist that inhibits AChE, allowing ACh to remain active in the neuromuscular junction.

FIGURE 14-8 Actions of adrenergic and cholinergic antagonists at the neuromuscular junction. **A**, Dapiprazole (Dap) is an adrenergic antagonist that blocks receptor sites of iris dilator muscle, preventing norepinephrine (Ne) from binding and causing muscle contraction. **B**, Cyclopentolate (Cyclo) and tropicamide (Trop) are cholinergic antagonists that block receptor sites of iris sphincter muscle, preventing acetylcholine (ACh) from binding and causing muscle contraction.

passes through the internal capsule (Figure 14-9). The efferent pathway, via the oculomotor nerve, innervates the medial rectus muscle, and the parasympathetic pathway innervates the ciliary muscle and iris sphincter.

PUPILLARY LIGHT PATHWAY

An understanding of the pupillary light pathway can be an important tool in diagnosing clinical problems with pupillary manifestations. Shining a bright light into an eye normally will initiate pupillary constriction. The afferent fibers that carry this information are called **pupillary fibers**, to distinguish them from visual fibers, which carry visual information. For some time it was unclear whether there were two separate sets of fibers or whether the pupillary fibers were branches of the visual fibers.³⁶ It now seems that both theories are somewhat correct. One classification model groups retinal ganglion cells as W, X, and Y cells. The W cells project to the pretectum, carrying pupillary afferent information, and project to the colliculi, carrying information for reflexive eye movements. The Y cells send collateral

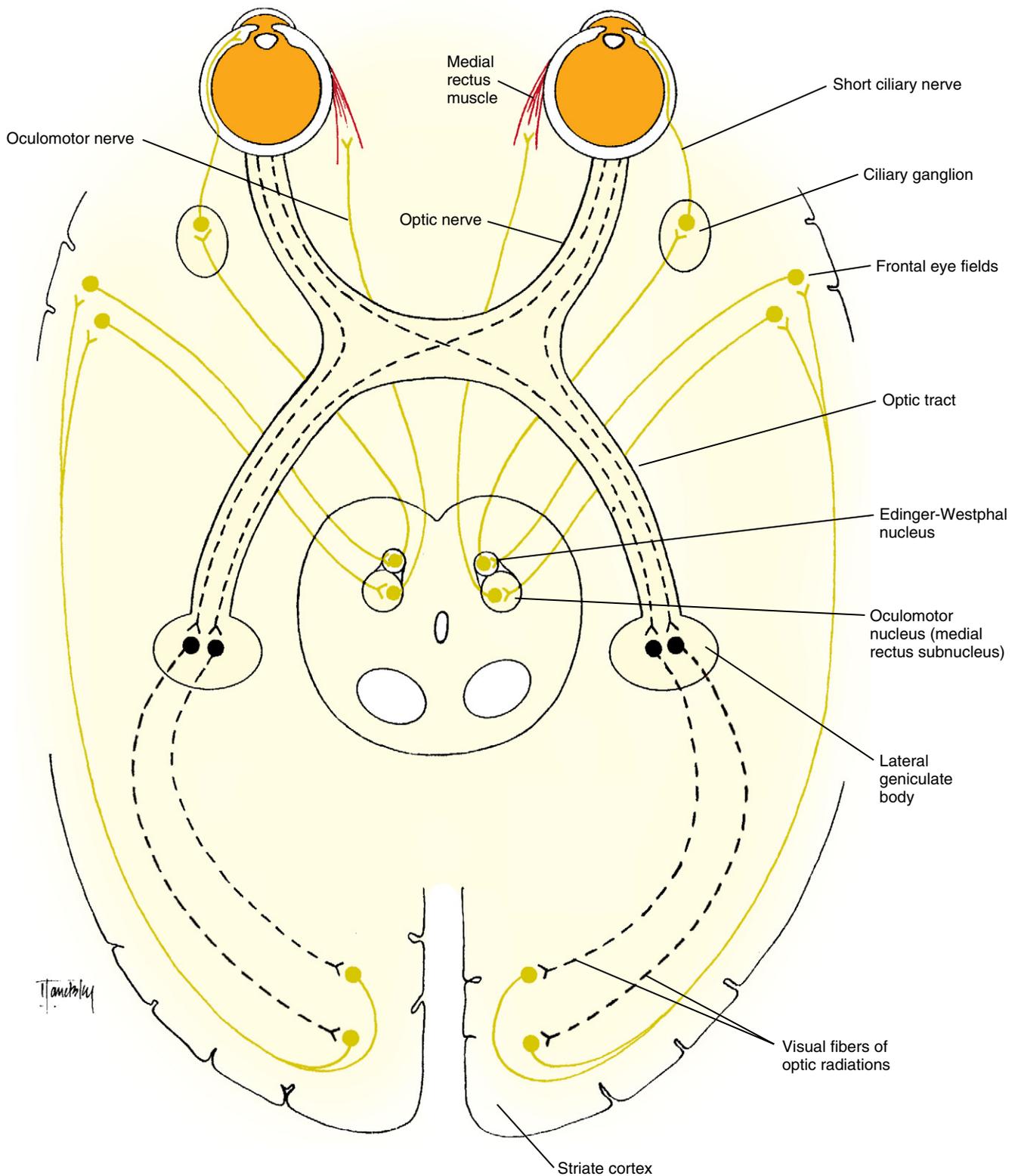


FIGURE 14-9

The near pupillary response. Dotted lines indicate visual pathway fibers carrying visual information from the eye to the visual cortex. Solid lines indicate pathway from the striate cortex to the frontal eye fields, then to the oculomotor nucleus, and from there to the medial rectus, ciliary, and sphincter muscles.

branches to the pretectum and to the colliculi. The X cells primarily carry visual information to the lateral geniculate nucleus, with a few having collateral fibers projecting to the midbrain.²¹

The afferent pupillary light pathway parallels the visual pathway as far as the posterior optic tract, with the nasal fibers crossing in the chiasm. The pupillary fibers exit in the posterior third of the optic tract and travel within the brachium of the superior colliculus to an area of the midbrain known as the **pretectal nucleus**, located near the superior colliculus. Synapse occurs, and the fibers that leave the pretectal region travel to the two Edinger-Westphal nuclei, distributing about equally to both.³⁶ The fibers that cross to the opposite Edinger-Westphal nucleus travel in the **posterior commissure** (Figure 14-10).

The efferent parasympathetic pathway from the Edinger-Westphal nucleus to the sphincter and ciliary muscles is described earlier under *Parasympathetic Pathway to Ocular Structures*. As the third nerve leaves the midbrain the pupillomotor fibers generally lie in a superior position, but as the nerve leaves the cavernous sinus and enters the orbit, the pupillomotor fibers move into an inferior position and travel in the inferior division of the oculomotor nerve.³⁶

While the parasympathetic system is activated, an inhibition of the dilator muscle apparently occurs. When light is removed from the eye and the Edinger-Westphal neurons stop firing, the preganglionic sympathetic fibers are no longer inhibited, their firing rate increases, and the dilator muscle increases in tone.²¹ The fibers that carry the inhibition message from the retina likely pass through an accessory optic system to the cervical spinal cord. There is similar inhibition of the parasympathetic innervation while the sympathetic nerves cause dilator contraction. These inhibitory fibers course through the midbrain.²¹

CLINICAL COMMENT: PUPILLARY LIGHT RESPONSE

In assessment of the pupillary light pathway, both the direct response and the consensual response are tested. When a bright light is directed into the eye, both a direct response (constriction of the ipsilateral iris) and a consensual response (constriction of the contralateral iris) occur. The consensual response occurs because of the two crossings of the fibers in the pathway: The nasal retinal fibers cross in the chiasm, and approximately half the fibers from each pretectal nucleus cross in the posterior commissure.

DISRUPTION IN THE AFFERENT PATHWAY

A disruption in the afferent pathway will affect both direct and consensual responses. For example, in the

presence of a disruption in the right afferent pathway, a light directed into the right eye will cause a poor response in both the right and the left eyes, although both responses would be normal if the light were directed into the left eye. If the damage to the afferent pathway is complete (i.e., all the fibers from one eye are affected), there would be no direct and no consensual response when light is directed into the affected eye. More often, only some fibers are damaged, such that the abnormal pupillary responses might be recognized only when compared to the normal pupillary responses; thus the term **relative afferent pupillary defect (RAPD)** is applied.

Disruption can occur anywhere in the afferent pathway: retina, optic nerve, chiasm, optic tract, or superior brachium. The swinging-flashlight test can be used to determine the presence of an RAPD. Damage posterior to the crossing in the chiasm might not be evident with the swinging-flashlight test unless the damage affects a great number of fibers from one eye and significantly fewer fibers from the other eye.³⁷ There are more crossed (contralateral) fibers in the optic tract than uncrossed (ipsilateral); therefore, with a complete optic tract lesion the pupillary constrictions may be greater with light into the ipsilateral eye than with light into the contralateral eye.

CLINICAL COMMENT: SWINGING-FLASHLIGHT TEST

The patient is asked to fixate on a distant object, and then the practitioner swings a light from eye to eye, several times rhythmically, taking care to illuminate each pupil for an equal length of time, about 2 or 3 seconds. If both pathways are normal, little or no change in pupil size will be noted; the eye will not recover from the consensual response before it is subjected to the direct light beam. The normal, symmetric response is characterized by equal pupillary constriction in both eyes when the light is presented to either eye. An abnormal response is characterized by larger pupils when the light is directed into the affected eye than when the light is directed into the normal eye (Figure 14-11).

As the intensity of the light increases, stronger constrictions occur with light presented to a normal eye. There is a threshold, however, beyond which no increase occurs. A very bright light can be used for detecting subtle defects; however, the luminance level should be recorded because a future change in the measured RAPD might reflect only a different light condition.^{38,39}

CLINICAL COMMENT: AFFERENT PUPILLARY DEFECT IN CATARACT

It would appear likely that a dense cataract would cause an RAPD because less light penetrates a cataract to stimulate the retina. In a clinical situation, however, a dense cataract has been found to cause an RAPD in the contralateral eye.^{40,41} Light scattered back to the retina from the lens opacity probably produces an enhanced pupillary response, which is manifested as an RAPD of the contralateral eye.

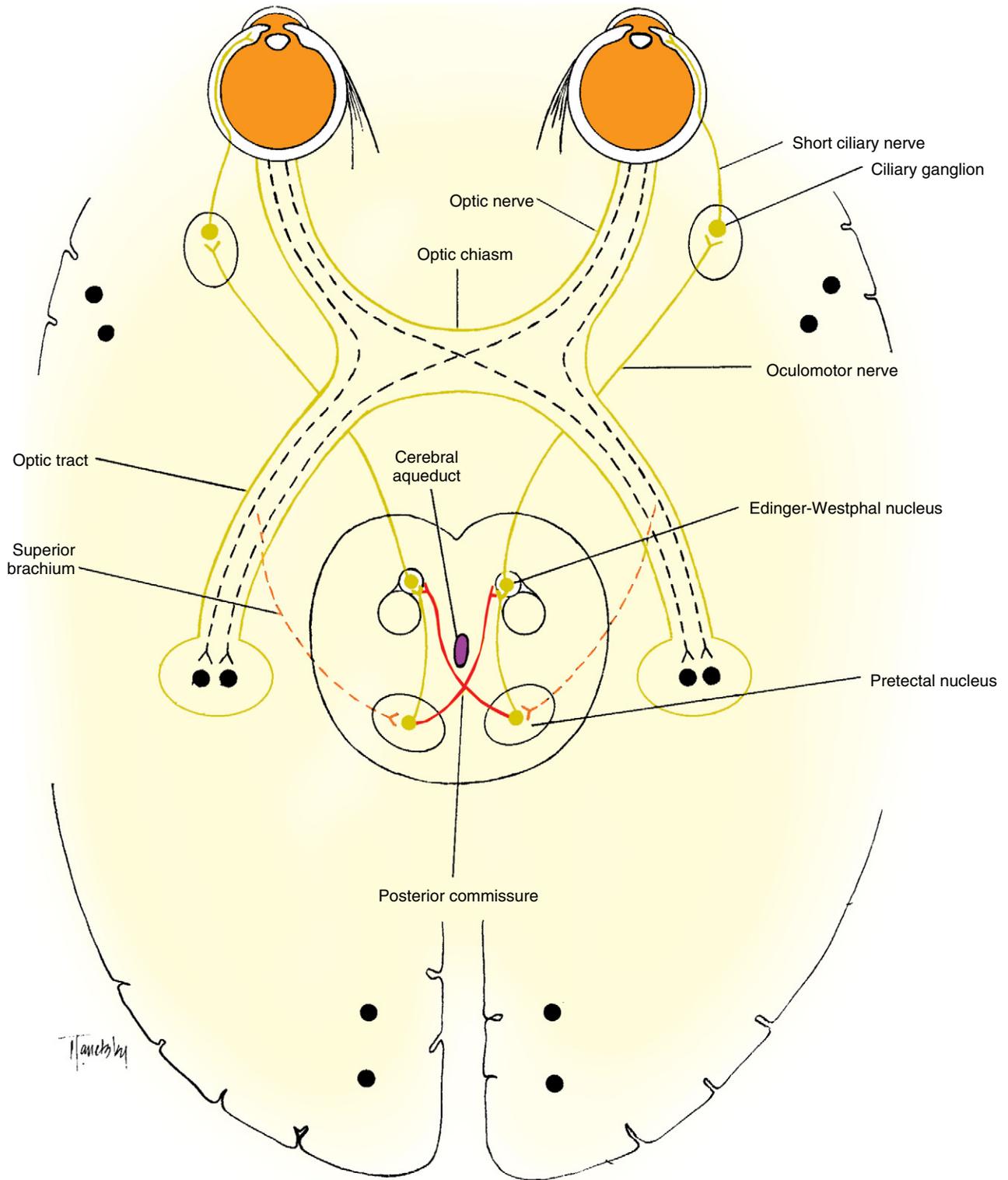
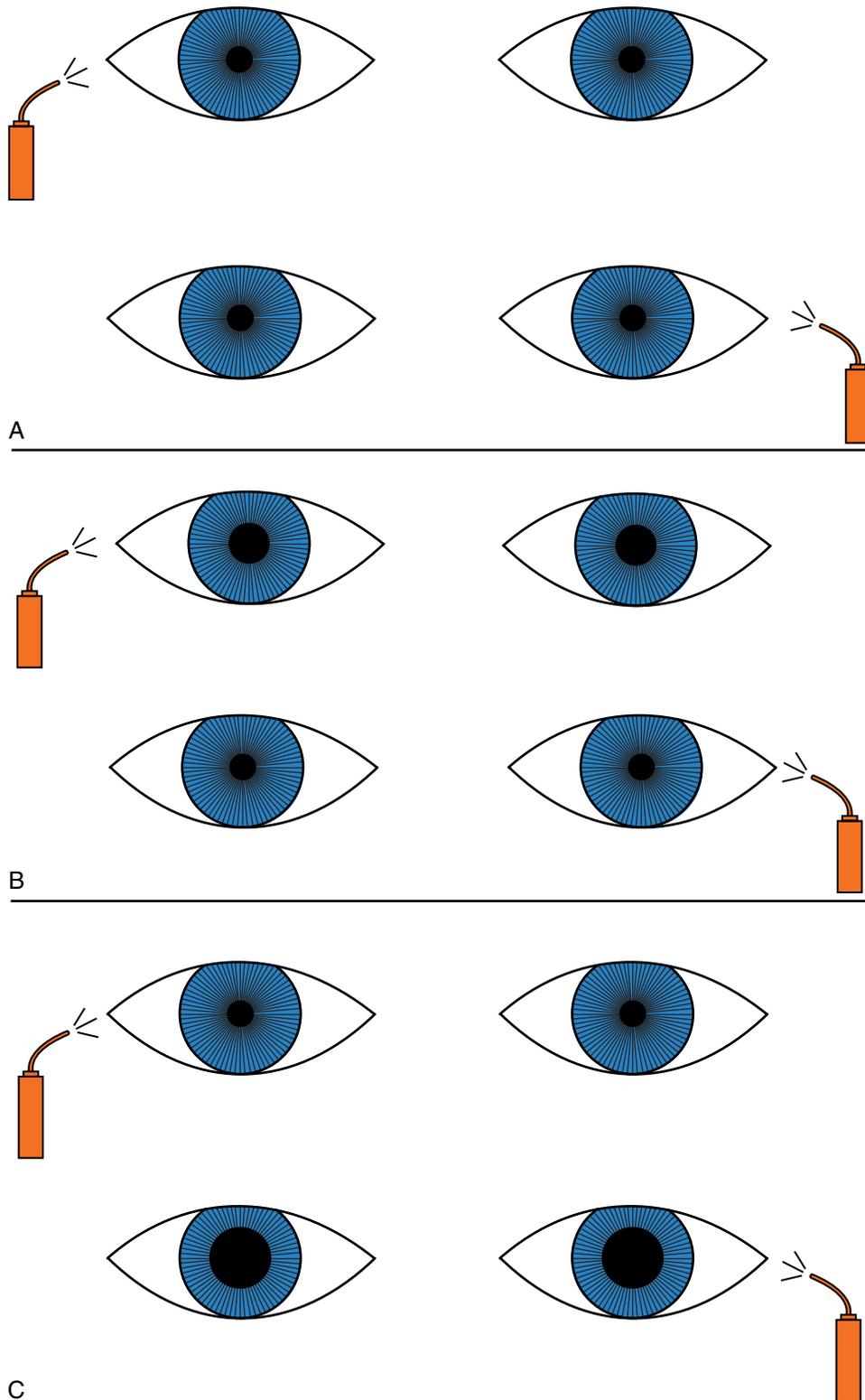


FIGURE 14-10 The pupillary light pathway. Dotted lines indicate the afferent pathway and solid lines the efferent pathway.

**FIGURE 14-11**

Swinging-flashlight test. **A**, Response is equal and symmetric, indicating no relative pupillary defect. **B**, Response is unequal, with both pupils growing larger as light is directed into the right eye, indicating a grade 1+ (relative afferent pupillary defect, right eye (RAPD OD)). **C**, Unequal pupillary response in which both pupils enlarge as light is directed into the left eye, indicating a grade 3+ relative afferent pupillary defect, left eye (RAPD OS).

CLINICAL COMMENT: OPTIC NEURITIS

The most common site of damage in an RAPD is the optic nerve. Ninety percent of patients with optic neuritis exhibit an RAPD during some stage of the disease.³⁶

DISRUPTION WITHIN THE CENTRAL NERVOUS SYSTEM

A lesion in the midbrain can involve the pretectal nucleus, the fibers leaving the nucleus, or the parasympathetic Edinger-Westphal nucleus. Damage to the pretectal nucleus might not cause a pupillary defect as fibers from the other pretectal nucleus still supply both parasympathetic nuclei.

Injury to the dorsal tegmentum of the midbrain that interrupts the fibers from the pretectal nuclei to the parasympathetic third-nerve nucleus, if limited to one side and affecting all fibers into that Edinger-Westphal nucleus, results in a pupil that shows a poor direct and consensual response but does constrict with the near response. This pupillary response is commonly called the **Argyll-Robertson pupil** and is said to show a “light-near dissociation.”⁴² Since the fibers carrying the message for the near reaction approach the Edinger-Westphal nucleus from a more ventral location, they do not pass through the affected area of midbrain. Since the path-

way from the frontal eye fields is intact and the efferent path is viable, the sphincter and ciliary muscle still will constrict to a near object.⁴³ In the Argyll-Robertson pupil, the retained near response exceeds the best direct-light response (Figure 14-12), and when the patient looks from near to distant, the pupils redilate briskly.

Because the fibers that carry inhibitory feedback to the parasympathetic nucleus also pass through the dorsal midbrain, miosis is a component of the Argyll-Robertson syndrome and is evident in darkness, with the affected pupil smaller than would be seen in the normal individual.²¹ The Argyll-Robertson syndrome is bilateral in approximately 80% to 90% of cases, but the two sides may be affected unequally.²¹ Diabetic neuropathy, alcoholic neuropathy, or neurosyphilis is suspected in a complete Argyll-Robertson pupil that involves both sides.

A near response that exceeds the light response is always a sign of a pathologic pupil.²¹

DISRUPTION IN THE EFFERENT PATHWAY

A lesion in the efferent pathway will cause the eye to show poor direct and consensual pupillary responses as well as a poor near response. The pupil appears large on clinical presentation, and other ocular structures are involved. Damage in the oculomotor nucleus or nerve

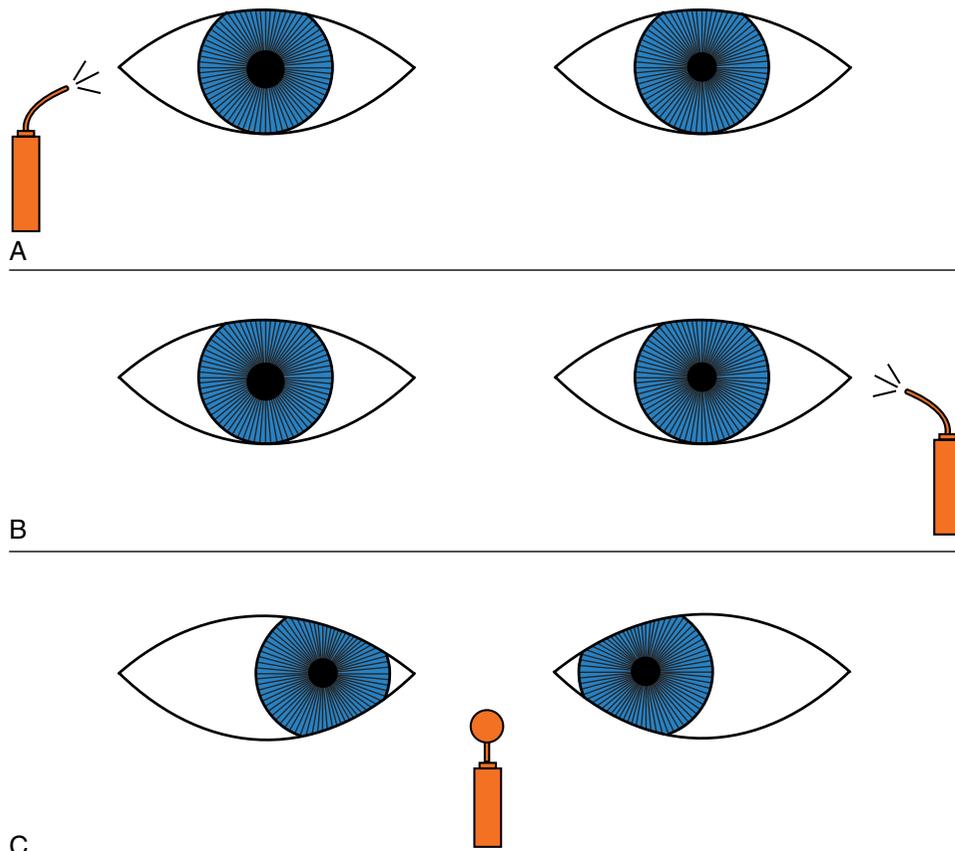


FIGURE 14-12

Argyll-Robertson pupil, right eye (OD). **A**, Poor direct response OD and normal consensual response left eye (OS). **B**, Normal direct response OS and poor consensual response OD. **C**, Normal near response in both eyes.

could involve the superior rectus, medial rectus, inferior rectus, inferior oblique, or levator muscle, and the patient should be examined for related ocular motility impairment. The parasympathetic fibers in the oculomotor nerve are often spared in ischemic lesions, as from diabetes, but are especially vulnerable to compression because the fibers are superficial as the nerve emerges from the midbrain.²¹

Damage to the ciliary ganglion or the short ciliary nerves could be caused by local injury or disease and results in a **tonic pupil**, which is characterized by poor pupillary light response and loss of accommodation. Decreased corneal sensitivity often occurs because some afferent sensory fibers from the cornea pass through the short ciliary nerves and the ganglion.⁴⁴ The affected muscle may exhibit cholinergic denervation supersensitivity, a physiologic phenomenon resulting from injury to the fibers directly innervating muscles.⁴⁵ The near response is retained, but it is delayed and slow, and the pupil redilates sluggishly. One theory postulates that because the density of the innervation to the ciliary muscle is much greater than the density of innervation to the sphincter, some ciliary muscle nerve fibers remain intact. With near stimulation these fibers release acetylcholine, which diffuses into the aqueous humor and then causes the supersensitive sphincter to constrict.⁴⁶ In late stages of this condition the pupil becomes tonic and the miotic near reaction difficult to demonstrate, but the accommodative facility appears to recover, perhaps as a result of regeneration of the fibers.^{17,47}

CLINICAL COMMENT: ADIE'S TONIC PUPIL

If the cause of the tonic pupil is not apparent, the syndrome is called **Adie's tonic pupil**. The typical patient with Adie's pupil is a woman 20 to 40 years of age; 90% of these patients also have diminished tendon reflexes. Because of this systemic manifestation, it is believed that similar degenerative processes are occurring in the ciliary ganglion and in the dorsal column of the spinal cord,⁴⁸ but the etiology is unknown.⁴⁹ If pupillary constriction in early Adie's pupil is examined with the biomicroscope, segmental constriction affecting only a section of the iris may be evident.⁵⁰ An Adie's pupil that has been tonic for years eventually becomes small and does not dilate well in the dark; thus it is the larger pupil in light and the smaller one in darkness.⁴⁷

In the differential diagnosis of Adie's pupil, a very mild, direct-acting cholinergic agonist can be used because the sphincter muscle is supersensitive.^{17,51} A dilute concentration of pilocarpine (0.125%) has minimal effect on a normal sphincter but will cause significant clinical miosis in a supersensitive sphincter. Some investigators believe that a normal pupil can respond to the 0.125% pilocarpine and recommend using a 0.0625% pilocarpine solution.⁵² With 1 drop instilled in each eye, the Adie's pupil should show a much greater constriction than the normal pupil (Figure 14-13).

CLINICAL COMMENT: FIXED, DILATED PUPIL

Recent onset of a fixed, dilated pupil could be caused by accidental drug-induced mydriasis. Investigation of the individual's profession might indicate the handling of drugs (pharmacists, nurses) or chemicals that could exert such an effect (farmers, crop dusters, exterminators). Such a pupil will not respond to 0.125% pilocarpine. Some over-the-counter drops that promise to "get the red out" may also cause a dilated pupil.

DISRUPTION IN THE SYMPATHETIC PATHWAY

An interruption in the sympathetic pathway causes miosis. The usual tone that the dilator muscle normally exerts is not present, and there is no counteracting pull against the sphincter muscle, making the pupil smaller than normal. **Anisocoria** (a difference in pupil size) is present under normal room-light conditions but is more pronounced in dim light, with the normal eye having the larger pupil. The pupil responds briskly to light, but with slow and incomplete dilation in the dark. If the anisocoria decreases in bright lights and the pupils react normally to a light stimulus, the disruption is likely a sympathetic interruption to the dilator muscle or benign anisocoria.⁴⁷

CLINICAL COMMENT: BENIGN ANISOCORIA

Approximately 20% of the population have **benign anisocoria** (also called simple or physiologic anisocoria), which is usually more apparent in dim light than in room light, with the difference between pupils usually less than 1 mm.⁴⁷ Sometimes the anisocoria may switch sides, but both pupils are round and react well to all stimuli and dilate equally with lights off. Benign anisocoria may be caused by asymmetric supranuclear inhibition of the Edinger-Westphal nucleus.⁴⁷

CLINICAL COMMENT: HORNER'S SYNDROME

CLINICAL FEATURES. Damage in the sympathetic pathway to the head can cause **Horner's syndrome**, which consists of ptosis, miosis, and facial anhidrosis (absence of sweat secretion). Loss of innervation to the smooth muscle of the upper eyelid causes ptosis, whereas loss of innervation to the lower eyelid causes it to rise slightly such that the palpebral fissure appears narrow, simulating enophthalmos (Figure 14-14).

The damage can occur anywhere along the sympathetic pathway in the brain, spinal cord, preganglionic path, or postganglionic path. Involvement of the central neuron, which sends its fiber from the hypothalamus through the spinal cord to a synapse with the preganglionic neuron in the cervical dorsal column, can also cause other problems (e.g., vertigo).

Continued

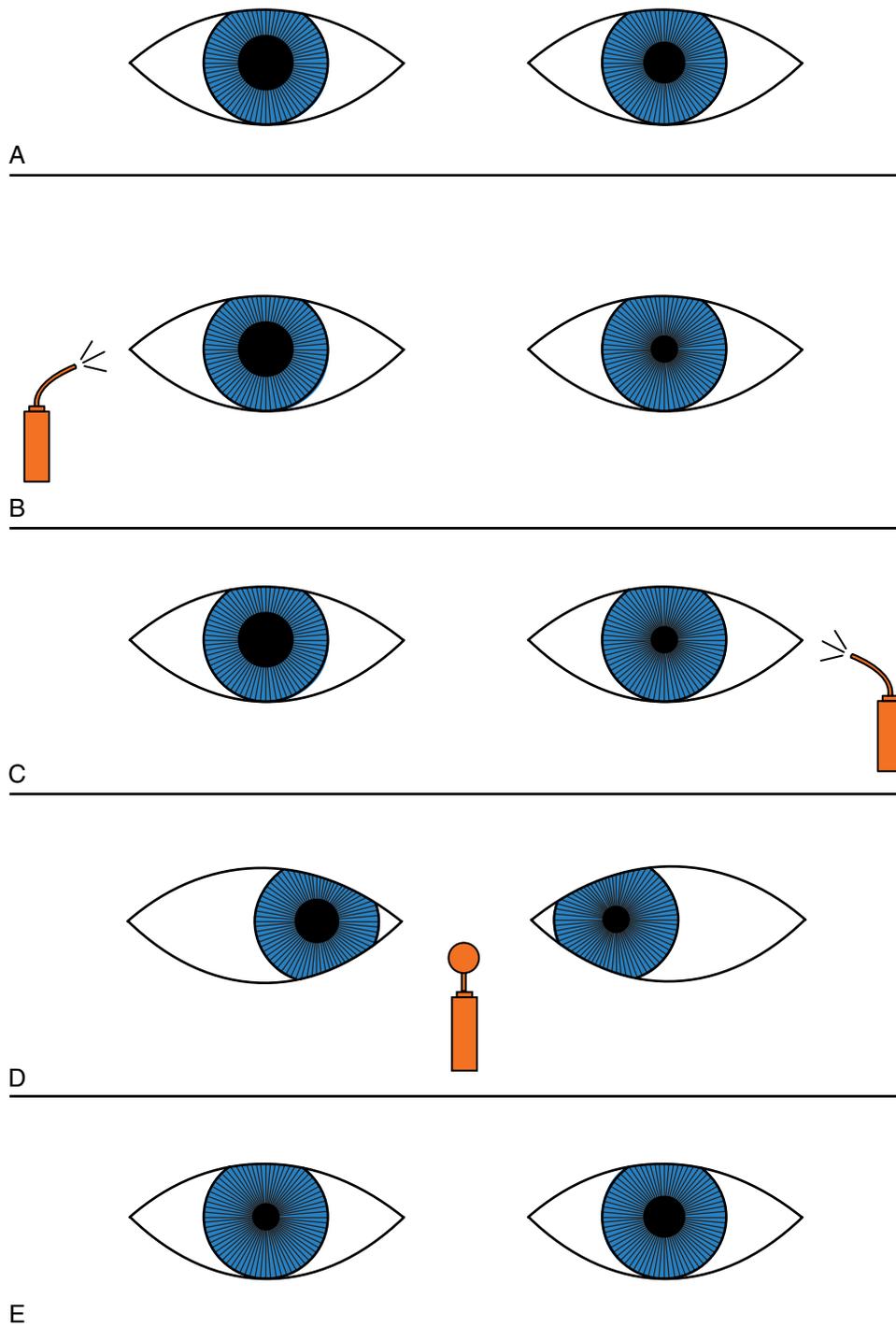
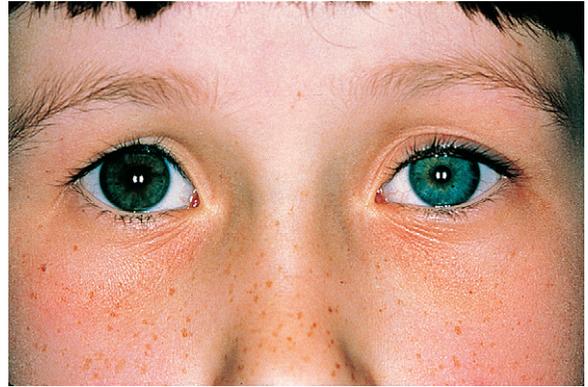


FIGURE 14-13

Adie's pupil OD. **A**, Presenting anisocoria; right pupil is larger than left pupil. **B**, Poor direct response OD and normal consensual response OS. **C**, Normal direct response OS and poor consensual response OD. **D**, Slow and long-lasting near response. **E**, Pilocarpine 0.125% instilled in both eyes. Miosis OD, no response OS.

**FIGURE 14-14**

Ptosis and miosis in Horner's syndrome. (From Kanski JJ, Nischal KK: *Ophthalmology: clinical signs and differential diagnosis*, St Louis, 1999, Mosby.)

**FIGURE 14-16**

Iris heterochromia in congenital Horner's syndrome. (From Kanski JJ, Nischal KK: *Ophthalmology: clinical signs and differential diagnosis*, St Louis, 1999, Mosby.)

Rights were not granted to include this figure in electronic media.
Please refer to the printed publication.

The preganglionic fibers leave the dorsal column of the spinal cord, pass into the chest, course over the apex of the lung, and loop around the subclavian artery en route to the superior cervical ganglion (Figure 14-15). These fibers can be damaged in thoracic injury or surgery or in metastatic disease involving the chest.⁶

The postganglionic fibers that enter the skull through the carotid plexus can be damaged by a fracture of the skull base or an injury to the internal carotid artery. Damage along the rest of the postganglionic neuron can involve the nasociliary or long ciliary nerves.

IRIS HETEROCHROMIA IN HORNER'S PUPIL. Normal sympathetic innervation is necessary for the development and maintenance of iris melanocyte pigmentation. In congenital Horner's syndrome, normal iris pigmentation fails to develop, and heterochromia is present (Figure 14-16). Heterochromia is rarely seen in acquired Horner's syndrome but may develop after long-standing conditions.²¹

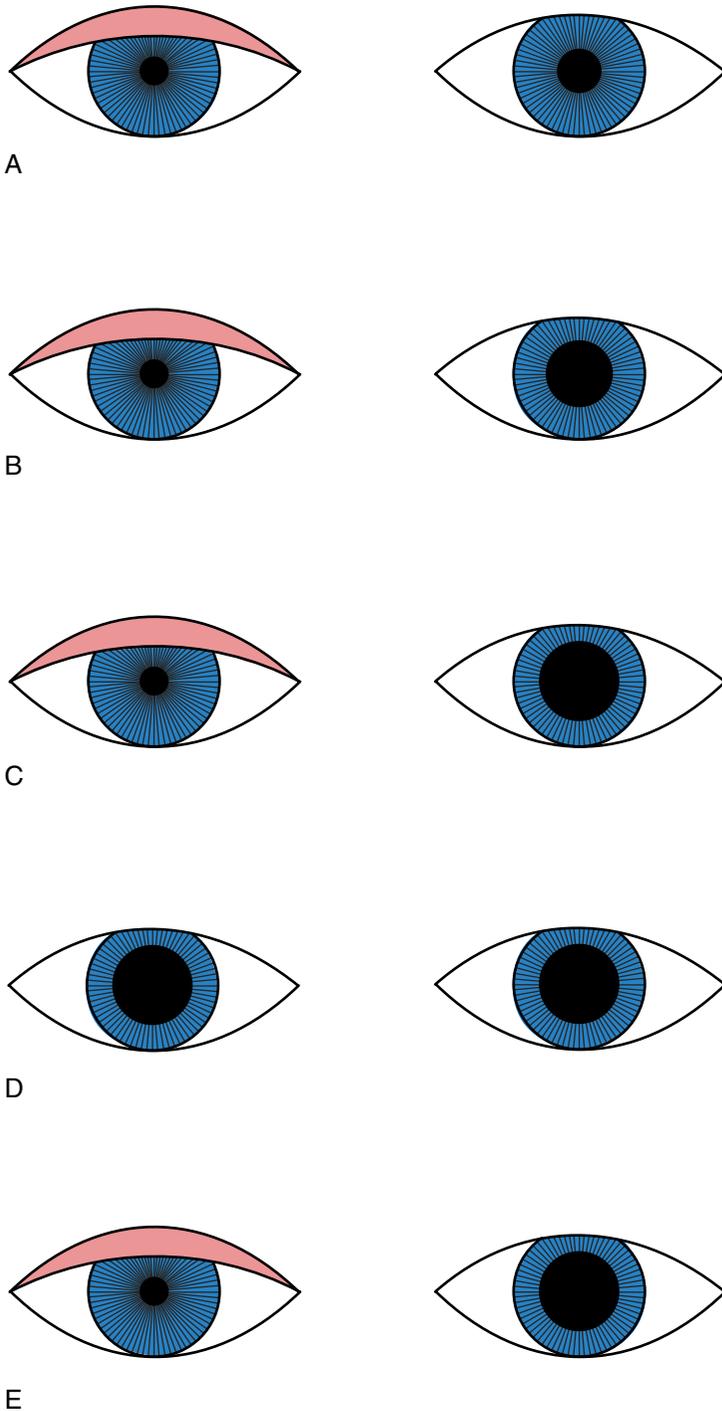
DIFFERENTIAL DIAGNOSIS. In addition to the clinical presentation of ptosis and miosis, dilation lag occurs in dim illumination and this will differentiate Horner's pupil from simple anisocoria. The normal pupil dilates within 5 seconds of lights being off because of the normal sympathetic activity to the dilator and the parasympathetic inactivation of the sphincter. In the Horner pupil there is no sympathetic activity, and the pupil thus dilates only from inactivation of the sphincter muscle and dilates more slowly, taking more than 20 seconds.⁴⁷

The location of the disruption of the sympathetic pathway is useful in determining appropriate care. In the differential diagnosis of Horner's syndrome, diagnostic drugs used to determine the site of interruption include cocaine and hydroxyamphetamine, the effects of which are shown in Figures 14-17 and 14-18. If the sympathetic pathway is intact, instillation of 1 drop of a 5% or 10% ophthalmic cocaine solution, an indirect-acting adrenergic agonist,

FIGURE 14-15

Sympathetic innervation of the eye. Preganglionic pathway courses from the superior cervical ganglion into the thoracic cavity before entering the skull. (From Maloney WF, Younge BR, Moyer NJ: *Am J Ophthalmol* 90:394, 1980. With permission from the Mayo Foundation.)

Continued

**FIGURE 14-17**

Horner's syndrome. **A**, Presenting anisocoria; left pupil is larger than right pupil. Ptosis OD. **B**, Anisocoria greater in dim illumination. **C**, Cocaine 5% instilled in each eye (OU). No response OD, mydriasis OS, interruption in sympathetic pathway OD. **D**, Hydroxyamphetamine 1% instilled OU. Mydriasis OU, interruption in preganglionic pathway OD. **E**, Hydroxyamphetamine 1% instilled OU. No response OD, mydriasis OS, interruption in postganglionic pathway OD.

causes dilation in 30 to 60 minutes.^{47,53,54} In contrast, with a disruption anywhere in the pathway, norepinephrine is lacking in the neuromuscular junction, and therefore cocaine has little or no effect, and the pupil dilates poorly.

Hydroxyamphetamine 1% can be administered to determine whether the damage is in the preganglionic or postganglionic pathway.⁵⁵⁻⁵⁷ A topical administration of this indirect-acting adrenergic agonist acts on the

postganglionic fiber, causing release of norepinephrine. If the lesion is in the preganglionic pathway, the postganglionic fiber still is viable and will contain stores of norepinephrine. Instillation of hydroxyamphetamine will cause release of the neurotransmitter, and dilation will occur. If the disruption is in the postganglionic pathway, norepinephrine will not be stored in the nerve endings, and therefore no dilation will

Continued

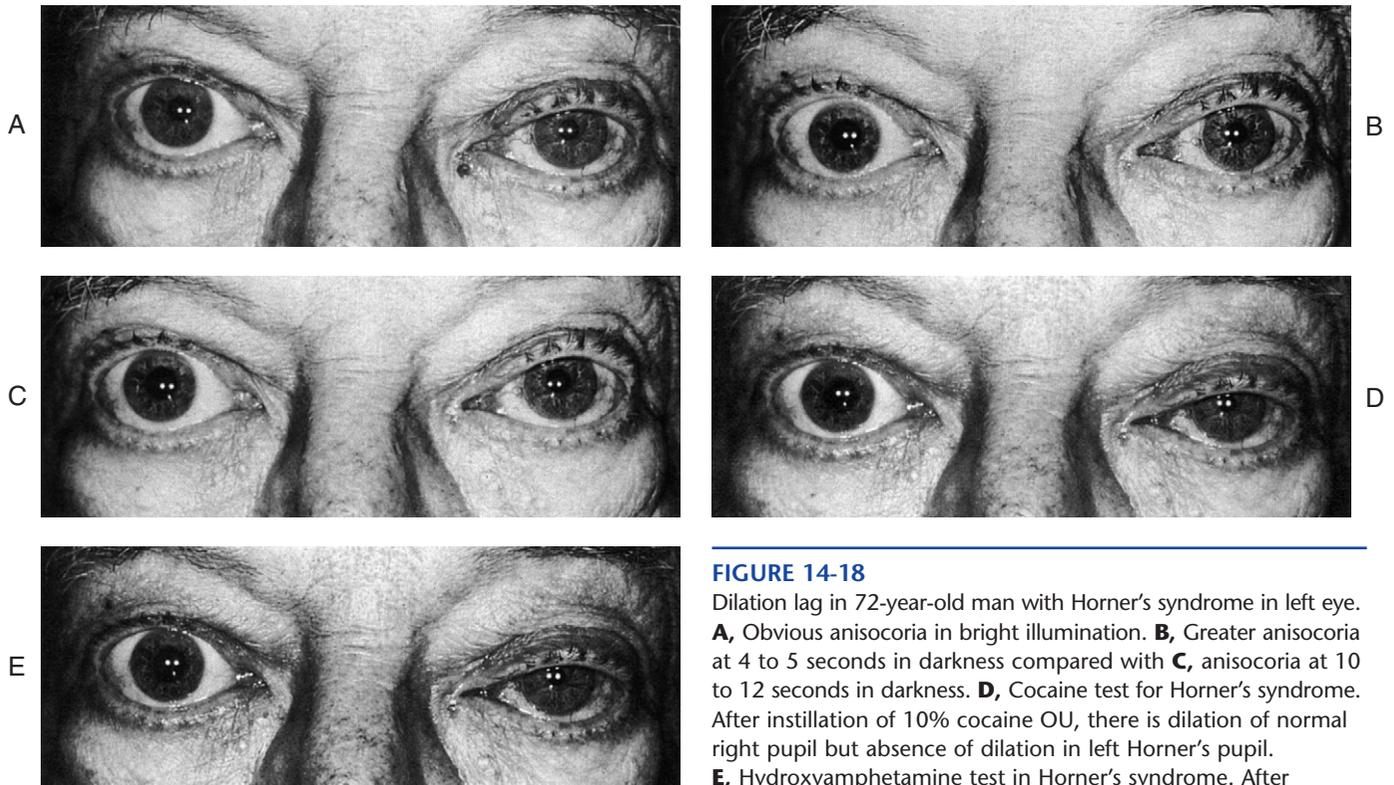


FIGURE 14-18

Dilation lag in 72-year-old man with Horner's syndrome in left eye. **A**, Obvious anisocoria in bright illumination. **B**, Greater anisocoria at 4 to 5 seconds in darkness compared with **C**, anisocoria at 10 to 12 seconds in darkness. **D**, Cocaine test for Horner's syndrome. After instillation of 10% cocaine OU, there is dilation of normal right pupil but absence of dilation in left Horner's pupil. **E**, Hydroxyamphetamine test in Horner's syndrome. After instillation of 1% hydroxyamphetamine OU, there is dilation of normal right pupil but absence of dilation of left Horner's pupil, indicating a postganglionic lesion. (From Bartlett JD, Jaanus SD: *Clinical ocular pharmacology*, ed 2, Boston, 1989, Butterworth-Heinemann.)

occur with instillation of hydroxyamphetamine. The instillation should occur 24 to 48 hours after the cocaine test, and dilation may take up to an hour.^{47,58}

In the presence of preganglionic and central lesions, the pupil on the affected side usually dilates more than the normal eye with hydroxyamphetamine instillation, either because of enhanced receptor sensitivity or because adrenergic nerve endings have accumulated more norepinephrine.^{58,59} In adults, central Horner's syndrome is often related to stroke, preganglionic Horner's often is associated with neoplasm, and postganglionic Horner's syndrome may have a vascular cause.⁴⁷

In evaluating a patient with anisocoria, if the difference between the pupils is greater in dim light, the clinician must differentiate between benign anisocoria and Horner's pupil. With benign anisocoria, the pupil will react well to all stimuli and will redilate well in the dark. The Horner's pupil reacts well to all stimuli but redilates poorly in the dark.

If the anisocoria is more evident in bright light, it occurs because the pupil constricts poorly. This may be caused by drugs, it may be a tonic pupil, or it may be caused by an efferent defect. Associated symptoms will assist in the diagnosis, and such a pupil abnormality, if accompanied by headache, requires a workup for intracranial involvement.

REFERENCES

1. Olmsted JMD, Morgan MW: The influence of the cervical sympathetic nerve on the lens of the eye, *Am J Physiol* 133:720, 1941.
2. Olmsted JMD: The role of the autonomic nervous system in accommodation for near and far vision, *J Nerv Ment Dis* 99:794, 1944.
3. Morgan MW: The nervous control of accommodation, *Am J Optom* 21:87, 1944.
4. Gilmartin B: A review of the role of sympathetic innervation of the ciliary muscle in ocular accommodation, *Ophthalmic Physiol Opt* 6(1):23, 1986.
5. Rosenfield M, Gilmartin B: Oculomotor consequences of beta-adrenoceptor antagonism during sustained near vision, *Ophthalmic Physiol Opt* 7(2):127, 1987.
6. Maloney WF, Younge BR, Moyer NJ: Evaluation of the causes and accuracy of pharmacologic localization in Horner's syndrome, *Am J Ophthalmol* 90:394, 1980.
7. Doxanas MT, Anderson RL: *Clinical orbital anatomy*, Baltimore, 1984, Williams & Wilkins, pp 93, 131.
8. Pick TP, Howden R, editors: *Gray's anatomy*, ed 15, New York, 1977, Crown, p 799.
9. Warwick R: Eugene Wolff's anatomy of the eye and orbit, ed 7, Philadelphia, 1976, Saunders, p 306.

10. Mohney JB, Morgan MW, Olmsted JMD et al: The pathway of sympathetic nerves to the ciliary muscles in the eye, *Am J Physiol* 135:759, 1942.
11. Ruskell GL: Sympathetic innervation of the ciliary muscle in monkeys, *Exp Eye Res* 16:183, 1973.
12. Gilmartin B, Hogan RE: The relationship between tonic accommodation and ciliary muscle innervation, *Invest Ophthalmol Vis Sci* 26:1024, 1985.
13. Gilmartin B, Bullimore MA, Rosenfield M et al: Pharmacological effects on accommodative adaptation, *Optom Vis Sci* 69(4):276, 1992.
14. Winn B, Culhane HM, Gilmartin B et al: Effect of β -adrenoceptor antagonists on autonomic control of ciliary smooth muscle, *Ophthalmic Physiol Opt* 22(5):359, 2002.
15. Gilmartin B, Mallen EAH, Wolffsohn JS: Sympathetic control of accommodation: evidence for inter-subject variation, *Ophthalmic Physiol Opt* 22(5):366, 2002.
16. Warwick R: The ocular parasympathetic nerve supply and its mesencephalic sources, *J Anat* 88:71, 1954.
17. Ruskell GL: Accommodation and the nerve pathway to the ciliary muscle: a review, *Ophthalmic Physiol Opt* 10(3):239, 1990.
18. Burde RM: Direct parasympathetic pathway to the eye: revisited. *Brain Res* 463:158, 1988.
19. Reiner A, Erichsen JI, Cabot JB et al: Neurotransmitter organization of the nucleus of Edinger-Westphal and its projection to the avian ciliary ganglion, *Vis Neurosci* 6(5):451, 1991.
20. Duke-Elder W: *The anatomy of the visual system*, vol 2, System of ophthalmology, St Louis, 1961, Mosby, p 497.
21. Loewenfeld IE: *The pupil: anatomy, physiology, and clinical applications*, Boston, 1999, Butterworth-Heinemann.
22. Tornqvist G: The relative importance of the parasympathetic and sympathetic nervous systems for accommodation in monkeys, *Invest Ophthalmol Vis Sci* 6:612, 1967.
23. Hurwitz BS, Dacidowitz J, Chin NB et al: The effects of the sympathetic nervous system on accommodation. I. Beta sympathetic nervous system, *Arch Ophthalmol* 87:668, 1972.
24. Tornqvist G: Effect of cervical sympathetic stimulation on accommodation in monkeys, *Acta Physiol Scand* 67:363, 1967.
25. Van Alphen GW: The adrenergic receptors of the intraocular muscles of the human eye, *Invest Ophthalmol Vis Sci* 15:502, 1976.
26. Wax MB, Molinoff PB: Distribution and properties of beta-adrenergic receptors in human iris/ciliary body, *Invest Ophthalmol Vis Sci* 25(suppl):305, 1984 (ARVO abstract).
27. Stephens KG: Effect of the sympathetic nervous system on accommodation, *Am J Optom Physiol Optics* 62(6):402, 1985.
28. Miller RJ, Takahama M: Arousal-related changes in dark focus accommodation and dark vergence, *Invest Ophthalmol Vis Sci* 29(7):1168, 1988.
29. Monkhouse WS: The anatomy of the facial nerve, *Ear Nose Throat J* 69:677, 1990.
30. Ruskell GL: An ocular parasympathetic nerve pathway of facial nerve origin and its influence on intraocular pressure, *Exp Eye Res* 106:323, 1970.
31. Rodriguez-Vazquez JE, Merida-Velasco JR, Jimenez-Collado J: Orbital muscle of Müller: observations on human fetuses measuring 35-150 mm, *Acta Anat (Basel)* 139(4):300, 1990.
32. Ruskell GL: Facial nerve distribution to the eye, *Am J Optom Physiol Optics* 62(11):793, 1985.
33. Stjernschantz J, Bill A: Vasomotor effects of facial nerve stimulation: non-cholinergic vasodilation in the eye, *Acta Physiol Scand* 109:45, 1980.
34. Wobig JL: The lacrimal apparatus. In Reeh MJ, Wobig JL, Wirtschafter JD, editors: *Ophthalmic anatomy*, San Francisco, 1981, American Academy of Ophthalmology, p 55.
35. Jaanus SD, Pagano VT, Bartlett JD: Drugs affecting the autonomic nervous system. In Bartlett JD, Jaanus SD, editors: *Clinical ocular pharmacology*, ed 3, Boston, 1995, Butterworth-Heinemann, p 168.
36. Thompson HS: The pupil. In Hart WM Jr, editor: *Adler's physiology of the eye*, ed 9, St Louis, 1992, Mosby, p 412.
37. Newman SA, Miller NR: The optic tract syndrome: neuro-ophthalmologic considerations, *Arch Ophthalmol* 101:1241, 1983.
38. Johnson LN: The effect of light intensity on measurement of the relative afferent pupillary defect, *Am J Ophthalmol* 109(4):481, 1990.
39. Lam BL, Thompson HS: Brightness sense and the relative afferent pupillary defect, *Am J Ophthalmol* 108(4):462, 1989.
40. Sadun AA, Bassi CJ, Lessell S: Why cataracts do not produce afferent pupillary defects, *Am J Ophthalmol* 110(6):712, 1990.
41. Lam BL, Thompson HS: A unilateral cataract produces a relative afferent pupillary defect in the contralateral eye, *Ophthalmology* 97(3):334, 1990.
42. Loewenfeld IE: The Argyll Robertson pupil, 1869-1969: a critical survey of the literature, *Surv Ophthalmol* 14:199, 1969.
43. Thompson HS: Light-near dissociation of the pupil, *Ophthalmologica* 189:21, 1984.
44. Purcell JJ, Krachmer JH, Thompson HS: Corneal sensation in Adie's syndrome, *Am J Ophthalmol* 84:496, 1977.
45. Scheie HG: Site of disturbance in Adie's syndrome, *Arch Ophthalmol* 24:225, 1940.
46. Wirtschafter JD, Volk CR, Sawchuk RJ: Transaqueous diffusion of acetylcholine to denervated iris sphincter muscle: a mechanism for the tonic pupil syndrome, *Ann Neurol* 4:1, 1978.
47. Kawasaki A, Kardon R: Disorders of the pupil, *Ophthalmol Clin North Am* 14(1):149, 2001.
48. Selhorst JB, Madge G, Ghatak N: The neuropathology of the Holmes-Adie syndrome, *Ann Neurol* 16:138, 1984.
49. Harriman DG, Garland H: The pathology of Adie's syndrome, *Brain* 91:401, 1968.
50. Thompson HS: Segmental palsy of the iris sphincter in Adie's syndrome, *Arch Ophthalmol* 96:1615, 1978.
51. Bourgon P, Pilley FJ, Thompson HS: Cholinergic supersensitivity of the iris sphincter in Adie's tonic pupil, *Am J Ophthalmol* 85:373, 1978.
52. Leavitt JA, Wayman LL, Hodge DO et al: Pupillary response to four concentrations of pilocarpine in normal subjects: application to testing for Adie tonic pupil, *Am J Ophthalmol* 133:333, 2002.
53. Kardon RH, Denison CE, Brown CK et al: Critical evaluation of the cocaine test in the diagnosis of Horner's syndrome, *Arch Ophthalmol* 108(3):384, 1990.
54. Thompson HS, Mensher JH: Horner's syndrome, *Am J Ophthalmol* 72:472, 1974.
55. Cremer SA, Thompson HS, Digre KB, Kardon RH: Hydroxyamphetamine mydriasis in normal subjects, *Am J Ophthalmol* 110(1):66, 1990.
56. Thompson HS, Mensher JH: Adrenergic mydriasis in Horner's syndrome: hydroxyamphetamine test for diagnosis of post-ganglionic defects, *Am J Ophthalmol* 72:472, 1971.
57. Salvesen R, di-Souza CD, Sjaastad O: Horner's syndrome: sweat gland and pupillary responsiveness in two cases with a probable 3rd neurone dysfunction, *Cephalalgia* 9(1):63, 1989.
58. Patel S, Ilsen PF: Acquired Horner's syndrome: clinical review, *Optometry* 74(4):245, 2003.
59. Cremer SA, Thompson HS, Digre KB et al: Hydroxyamphetamine mydriasis in Horner's syndrome, *Am J Ophthalmol* 110(1):71, 1990.

Index

A

- A (anisotropic) band, 177, 178f
- Abducens nerve (cranial nerve VI), 217t, 226-227, 226f
- blood vessel relations of, 225f
 - in cavernous sinus, 222f
 - damage to, 230-231, 230f
 - paralysis of, 227
- Abducens nucleus, 224f, 226-227
- Abduction, 179, 180f, 181t
- Accessory lacrimal glands, 165, 166f, 167f
- of Krause, 161, 161f
 - of Wolfring, 161, 161f, 165
- Accommodation, 49, 97
- ciliary muscle contraction in, 97, 257, 259f
- Accommodation-convergence reaction, 262-263, 264f
- Acetylcholine, 261, 261f, 263f
- Actin, 177, 178f
- Adduction, 179, 180f, 181t
- paired antagonist model of, 194
- Adie's tonic pupil, 269, 270f
- Adipose tissue, 8
- Adrenergic antagonist agents, 261, 262, 263f
- Adrenergic fibers, 261, 261f
- Adult nucleus, 91, 93f
- Afferent (sensory) pathway, 216-223
- pupillary light, 265, 266f
 - disruption in, 265-268
 - trigeminal nerve in, 216-221. *See also* Trigeminal nerve.
- Against-the-rule astigmatism, 9
- Age-related macular degeneration (AMD), 51-52, 52f
- Aging changes
- in anterior chamber, 110
 - in choroid, 53
 - in ciliary body, 53
 - in cornea, 30-31
 - in crystalline lens, 100-101
 - in extraocular muscles, 196
 - in eyebrows, 174
 - in eyelids, 174
 - in iris, 52-53
 - in lacrimal system, 174
 - in ocular circulation, 214
 - in orbit, 152
 - in orbital adnexa, 174
 - in retina, 83-84
 - in sclera, 30-31
 - in uvea, 52-53
 - in visual pathway, 252
 - in vitreous chamber, 113
- Agonist, 261
- Agonist agents. *See also* specific agents.
- adrenergic, 261-262, 262f
 - cholinergic, 261-262, 263f
- Agonist muscles, in isolated agonist model, 191-193
- AII cell, 64, 66f
- Albinism, ocular, 125
- Alzheimer's disease, retinal changes in, 84
- Amacrine cells, 64-65, 66f, 67f
- development of, 124, 127f
- AMD (age-related macular degeneration), 51-52, 52f
- Amsler grid, for metamorphopsia detection, 79
- Anatomic directions, 3, 3f
- Anatomic planes, 3, 4f
- Anatomy, surface, 154, 155f
- Anesthesia, 227
- Angular artery, 207, 209f
- Angular vein, 210, 210f
- Anisocoria, 269
- in Adie's pupil, 269, 270f
 - benign (simple, physiologic), 269
 - in Horner's syndrome, 271-273, 272f
- Anisotropic (A) band, 177, 178f
- Annular muscle, 44, 45f
- development of, 129
- Annular vessel, development of, 122, 123f
- Annulus of Zinn, 147, 147f, 180, 182f
- Antagonist, 261
- Antagonist agents. *See also* specific agents.
- adrenergic, 261, 262, 263f
 - cholinergic, 262, 263f
- Antagonist muscles, in isolated agonist model, 191-193
- Anterior border layer, 34, 35f, 37f
- development of, 130
- Anterior chamber, 1, 2f, 11f, 103-108, 104f. *See also* Anterior chamber angle.
- aging changes in, 110
 - development of, 116, 131
 - filtration apparatus function in, 105, 107
- Anterior chamber angle, 103-108, 104-108f
- canal of Schlemm in, 104-106f, 105, 108f, 110f
 - in aqueous dynamics, 109, 109f, 110f
 - function of, 105, 108
 - giant vacuoles in, 109, 109f, 110f
 - gonioscopy of, 105, 108f
 - scleral spur in, 26, 27f, 103, 104-106f
 - trabecular meshwork in, 103, 104-107f
 - function of, 105, 108
- Anterior ciliary arteries, 203f, 206, 206f
- Anterior ciliary veins, 211
- Anterior ethmoid artery, 199f, 204
- Anterior ethmoid nerve, 216, 218f
- Anterior iris epithelium, 39, 40f, 41f
- Anterior ischemic optic neuropathy (AION), 204
- Anterior lacrimal crest, 141

Page numbers followed by f indicate figures; t, tables.

- Anterior lens epithelium, 89, 89f
 Anterior suture, 91, 93f
 Anterior temporal artery, 207, 209f
 Anterior vascular tunic of the lens (anterior tunica vasculosa lentis),
 development of, 123, 123f
 Apical surface, of epithelial cell, 6
 Apocrine glands, 6
 Aponeurosis
 levator, 157-158, 158f, 159f
 lower eyelid, 159
 Aquaporins, 23
 Aqueous humor
 dynamics of, 108-110, 109f, 110f
 production of, 51, 108
 Argyll-Robertson pupil (syndrome), 268, 268f
 Arteriovenous nicking, 83
 Arteritis, temporal (giant cell), 207
 Artery(ies)
 angular, 207, 209f
 basilar, aneurysm of, 230
 carotid. *See* Carotid artery.
 central retinal, 82, 198-200, 199f, 201f
 development of, 125
 ciliary
 anterior, 203f, 206, 206f
 posterior, 199f, 200-204, 203f
 posterior, long, 199f, 203f, 204, 205f
 posterior, short, 199f, 200-202, 203f, 204, 205f
 cilioretinal, 83, 83f, 204, 204f
 dorsonasal (dorsal nasal), 202f, 207
 ethmoid, 199f, 204
 anterior, 199f, 204
 posterior, 199f, 204
 facial, 207, 209f
 transverse, 207, 209f
 hyaloid arterial system in, 122-123, 123f
 infraorbital, 209, 209f
 iris, major circle of, 203f, 204, 206f
 lacrimal, 199f, 200
 maxillary, 209-210, 209f
 muscular, 204-206, 205t
 ophthalmic, 198, 199f, 203f
 origin of branches of, 200t
 palpebral, 199f, 200, 202f
 lateral, 199f, 200, 202f
 medial, 202f, 207
 recurrent meningeal, 199f, 200
 superior cerebellar, aneurysm of, 228
 superior cerebral, aneurysm of, 228
 supraorbital, 199f, 202f, 204
 supratrochlear, 202f, 207
 temporal, 207, 209f
 anterior, 207, 209f
 superficial, 207, 209f
 in visual pathway, 240-241, 240f
 zygomatic, 207, 209f
 zygomaticofacial, 199f, 200
 zygomaticotemporal, 199f, 200
 Astigmatism, 9
 Astrocytes, 8
 in optic nerve, 234f, 235, 235f
 retinal, 69
 Atropine, 262
 Autonomic innervation. *See* Innervation, autonomic.
 Autonomic pathway, 254-259. *See also* Innervation, autonomic.
 Autonomic pathway (*Continued*)
 efferent, 254
 parasympathetic, 255-257, 256f, 259f
 sympathetic, 254-256, 255f, 258f
 Axons, 8
- B**
 Barkan's membrane, persistence of, 131
 Basal lamina, 6
 of choroid, 49, 50f, 51f
 of cornea, 12, 13f
 Basal surface, of epithelial cell, 6
 Basement membrane. *See* specific structures.
 Basilar artery aneurysm, 230
 Bergmeister's papilla, 124, 124f
 Binasal visual field loss, 248, 249f
 Binocular movements, yoke muscles in, 194, 194f
 Biomicroscope, 5
 Bipolar cells, 62, 63f, 64f, 67f
 development of, 124, 127f
 number and distribution of, 75
 Bitemporal field defect, 248, 249f
 Bitemporal hemianopia, 250f
 Blepharospasm, reflex, 157
 Blind spot, physiologic, 80, 248
 Blindsight, 250
 Blinking. *See also* Orbicularis.
 reflex, 157
 spontaneous involuntary, 157
 Blood-aqueous barriers, 51
 development of, 133
 Blood-retinal barriers, development of, 133
 Blood supply
 to choroid, 50f
 to cornea, 23-24
 to extraocular muscles, 195
 to eyelids, 167, 169f
 to limbus, 29
 to orbit. *See* Orbital blood supply.
 to retina, 81f, 82-83
 to sclera, 26, 28f
 to uveal tract, 52
 to visual pathway, 240-241, 240f
 Blood vessel(s). *See also* Artery(ies); Vein(s); specific vessels.
 conjunctival, 170
 development of barriers in, 133
 development of permeability of, 133
 uveal, 203f
 Blow-out fracture, of orbit, 141, 144f
 Blue cone bipolar cells, 62
 Bones. *See also* specific bones.
 of cranium, 136-139, 137-139f. *See also* Skull bones.
 of face, 138f, 140
 of orbit, 140-148. *See also* Orbit.
 Border tissue of Jacoby, 232, 234f
 Bowman's layer, 12-14, 13f, 14f
 development of, 128, 129f
 Brachium, 216
 Brodmann area 17, 238, 239f
 Brodmann area 18, 239, 239f
 Brodmann area 19, 239, 239f
 Brown's superior oblique sheath syndrome, 193, 193f
 Bruch's membrane, 49, 50f, 51f
 age-related changes in, 84
 development of, 128
 lipid accumulation in, 52, 52f

- Brush bipolars, 62
 Bulbar conjunctiva, 168, 170f
 Bulbar fascia, 150, 151f
- C**
- Calcarine fissure, 238, 239f
 maps of, 251f
- Canal of Hannover, 108, 109f
 Canal of Petit, 108, 109f
 Canal of Schlemm, 104-106f, 105, 108f, 110f
 in aqueous dynamics, 109, 109f, 110f
 development of, 116, 131
 function of, 105, 108
 giant vacuoles in, 109, 109f, 110f
- Canaliculi, 173-174, 173f
- Canthus, lateral and medial, 153
- Capillary networks, retinal, 82
- Capsule, lens, 87-88, 88f
 development of, 122
- Capsulopalpebral fascia, 159
- Carotid artery and its branches, external, 207-210
 facial artery in, 207, 209f
 flow chart of, 208f
 maxillary artery in, 209-210, 209f
 superficial temporal artery in, 207, 209f
 temporal arteritis and, 207
- Carotid artery and its branches, internal, 198-207
 aneurysm of, 231
 anterior ciliary arteries in, 203f, 206, 206f
 anterior ischemic optic neuropathy (AION) and, 204
 central retinal artery in, 198-200, 199f, 201f
 cilioretinal artery in, 204, 204f
 dorsonasal (dorsal nasal) artery in, 202f, 207
 ethmoid arteries in, 199f, 204
 lacrimal artery in, 199f, 200
 medial palpebral arteries in, 202f, 207
 muscular arteries in, 204-206, 205t
 ophthalmic artery in, 198, 199f, 203f
 origin of branches of, 200t
 in optic chiasm, 236, 236f
 posterior ciliary arteries in, 199f, 200-204, 203f
 "red eye" and, 207
 sclerosis of, 198
 supraorbital artery in, 199f, 202f, 204
 supratrochlear artery in, 202f, 207
 in visual pathway, 240, 240f
- Carotid artery aneurysm, 230, 231
- Carotid-cavernous sinus fistula, 211
- Carotid plexus, sympathetic fibers from, 254, 255f, 258f
- Caruncle, 155f, 170
- Cataract, 98, 100f
 afferent pupillary defect in, 265
 congenital, 122
 cortical, 98, 100f
 diabetic, 98
 grading system for, 99f
 nuclear, 98, 100f
 posterior subcapsular, 98, 100f
 surgery for, 100
- Cavernous sinus, 211, 212f, 213f
 coronal section through, 212f
- Cavernous sinus thrombosis, 211
- Cell body, of rods and cones, 59f, 60
- Cellulitis
 orbital, 148
 preseptal, 150
- Central foveal reflex, 79, 80f
- Central nervous system, 216
- Central retina, 76-79
- Central retinal artery, 82, 198-200, 199f, 201f
 development of, 125
- Central retinal vein, 210-211, 210f
 development of, 125
- Central supporting connective tissue strand, 234f
- Chalazion, 167, 167f
- Chambers. *See also* Anterior chamber; Posterior chamber.
 of eye, 1, 2f
- Check ligaments, 186
- Chemical synapses, 75
- Chemosis, 171
- Cholinergic agonist agents, 261-262, 263f
- Cholinergic antagonist agents, 262, 263f
- Cholinergic fibers, 261, 261f
- Choriocapillaris, 48-49, 48f, 50f
 development of, 128
- Chorioretinal atrophy, peripapillary, 84
- Choroid, 1, 2f, 48-49, 48-51f
 aging changes in, 53
 development of, 128
 functions of, 51
- Choroidal blood vessels, autonomic innervation of, 254, 255, 258f
- "Choroidal fissure," 117-119, 118f, 120f
- Choroidal stroma, 48, 50f
- Cilia, 154, 155f
 abnormalities of, 156
- Ciliary arteries
 anterior, 203f, 206, 206f
 posterior, 199f, 200-204, 203f
- Ciliary body, 1, 2f, 35f, 42-47
 aging changes in, 53
 ciliary epithelium in, 46-47, 46f, 47f
 ciliary muscle in, 44-45, 45f
 ciliary processes in, 43, 44f
 ciliary stroma in, 42f, 45-46
 development of, 129
 functions of, 49-51
 inner aspect of, 43, 43f
 partitions and layers of, 42, 42f
 structure and parts of, 41f, 42-43, 42-43f
 supraciliaris (supraciliary lamina) in, 42f, 43-44, 45f
- Ciliary epithelium, 46-47, 46f, 47f
 nonpigmented, 42f, 45f, 46, 47f
 pigmented, 42f, 45f, 46
- Ciliary ganglion, 256-257, 256f
 autonomic innervation of, 255f, 259f
 damage to, 269
- Ciliary muscle, 44-45, 45f
 in accommodation, 97, 257, 259f
 cholinergic agonists on, 261-262, 262f
 cholinergic antagonists on, 262, 263f
 contraction of, from parasympathetic stimulation, 257
 development of, 129
 paralysis of, 229
 parasympathetic innervation of, 255f, 256, 257, 259f
- Ciliary nerves
 fibers in, 255f
 long, 217, 218f, 219f
 short, damage to, 269
- Ciliary processes, development of, 129
- Ciliary veins, anterior, 211
- Ciliary zone, 34, 35f
- Cilioretinal artery, 83, 83f, 204, 204f

- Cilium, 58, 59f, 60f
- Circle of Willis, 236, 236f
- Circle of Zinn (Zinn-Haller), 201f, 202, 203f, 240
- Circular contraction folds, 39, 41f
- Circular vessel, 35
- Clivus, 76
- Cloquet's canal, 112-113, 112f
development of, 131
- Clump cells, 34, 37f
- Cocaine, 261, 262f
on Horner's syndrome pupil, 271-272, 272f
- Collagen, in vitreous, 113
- Collagen fibers, 8
- Collagen fibrils, corneal, 15, 16f, 17f
- Collarette, 34, 35f, 39, 41f
- Coloboma, 119, 121f
- Color
of iris, 39, 42
of sclera, 26
- Common styte, 167, 167f
- Common tendinous ring, 147, 147f, 180, 182f
- Concretions, conjunctival, 164
- Cone pedicle, 62, 63f
development of, 124
- Cones
composition of, 58-60, 59f, 60f
morphology of, 61-62, 61f
number and distribution of, 74-75, 75f
in photopic vision, 72-74
- Congenital cataract, 122
- Congruency, 250
- Conjunctiva, 167-171
biomicroscopic examination of, 170
blood vessels of, 170
bulbar, 168, 170f
caruncle in, 155f, 170
chemosis in, 171
edema of, 171
fornix of, 167, 170f
histologic features of
epithelium in, 168
submucosa in, 168-169
infection of, 171
innervation of, 170
limbal, 27f
lymphatics of, 170, 214
palpebral, 167-168, 170f
pingueculae in, 171, 171f
plica semilunaris in, 155f, 170
pterygia in, 171, 171f
- Conjunctival concretions, 164
- Conjunctival cysts, 164
- Conjunctival injection, 171
- Conjunctivitis, 171
- Connective tissue, 7-8
of eye, 7-8
of orbit, 148-151, 185-186, 186f. *See also* Orbit, connective tissue of.
- Connexins, 7
- Contact lenses
on cornea, 22
fitting of, 30
- Contraction folds, circular, 39, 41f
- Contralateral hemifield, 248
- Contralateral homonymous field defect, 249, 249f
- Convergence, 180, 180t
in accommodation-convergence reaction, 262-263, 264f
in yoke muscle innervation, 194
- Cornea, 1, 2f, 9-24
aging changes in, 30-31
blood supply to, 23-24
central optical area of, assessment of, 9
contact lenses on, 22
definition of, 9
development of, 116, 125-128, 129f
dimensions of, 9, 10f
edema of, 23
erosion of, recurrent, 12, 14f
function of, 22
guttata in, 20, 22f
Hassall-Henle bodies in, 20
histologic features of, 9-22, 11f, 13-22f. *See also* specific features.
Bowman's layer in, 12-14, 13f, 14f
Descemet's membrane in, 11f, 18-19, 18f, 19f
endothelium in, 19-20, 19-22f
epithelial replacement in, 12
epithelium in, 9-12, 11f, 13f, 14f
light micrograph of, 11f, 14f
scanning electron micrograph of, 11f
stroma or substantia propria in, 11f, 14f, 15-18, 16f, 17f
hydration of, 22-23
innervation of, 11f, 24, 219f
keratoconus of, 14, 15f
neovascularization of, 24, 25f
physiologic properties of, 23
puncture of, 14f
UV light radiation on, 22
wound healing in, 23
- Corneal arcus, 30, 30f
- Corneal endothelium, development of, 125
- Corneal epithelium, development of, 125
- Corneal guttata, 20, 22f
- Corneal reflex, 259, 260f
- Corneal refractive power, 5
- Corneoscleral meshwork, 103, 104f, 106f, 108f
- Corrugator muscle, 153, 154f
- Cortical cataract, 98, 100f
- Corticonuclear tract, 227
- Cranial nerve(s)
damage to, 227-228, 228f
relationships among, 225f
- Cranial nerve II. *See* Optic nerve.
- Cranial nerve III (oculomotor nerve), 217t, 223-226, 224-226f
aberrant regeneration of, 229
blood vessel relations of, 225f
damage to, 228-229, 229f, 268-269
oculomotor nucleus of, 223-225, 224f
pathway of, 225-226, 225f, 226f
- Cranial nerve innervation, 216-231, 217t. *See also* specific cranial nerves.
of afferent (sensory) pathway, 216-223
trigeminal nerve in, 216-221. *See also* Trigeminal nerve.
of efferent (motor) pathway, 223-227
abducens nerve in, 222f, 225f, 226-227, 226f
abducens nerve in, damage to, 230-231, 231f
cranial nerve damage in, 227-228
eye movement control in, 227
facial nerve in, 227, 228f
oculomotor nerve in, 217t, 223-226, 224-226f. *See also* Oculomotor nerve.
Oculomotor nerve.
oculomotor nerve in, damage to, 228-229, 229f
superior orbital fissure in, 147f, 227

- Cranial nerve innervation (*Continued*)
 trochlear nerve in, 222f, 225f, 226, 226f
 trochlear nerve in, damage to, 230, 230f
 nervous system and, 216
 oculo-cardiac reflex and, 223
 trigeminal nerve formation in, 221-223, 222f, 223f
- Cranial nerve IV. *See* Trochlear nerve.
- Cranial nerve V, 223f
- Cranial nerve VI (abducens nerve), 217t, 226-227, 226f
 blood vessel relations of, 225f
 in cavernous sinus, 222f
 damage to, 230-231, 230f
 paralysis of, 227
- Cranial nerve VII (facial nerve), 217t, 227, 228f
- Cranial nerve VII pathway, 227, 228f
- Cranium
 bones of, 136-139, 137-139f. *See also* Skull bones.
 venous sinus drainage of, 213f
- Cribriform layer, 105
- Crypts, 39
 Fuchs', 39, 41f
- Crypts of Henle, 163-164
- Crystalline lens. *See* Lens, crystalline.
- Crystallins, 89
- Cuneus gyrus, 238, 239f
- Cup-to-disc ratios, 80, 81f
 assessment of, 82
- Cyclopentolate, 262, 263f
- Cyclosporin A, for dry eye, 173
- Cysts, conjunctival, 164
- D**
- Dapiprazole, 262, 263f
- Deep petrosal nerve, 256f, 257
- Déjà vu phenomenon, 250
- Dendrites, 8
- Dentate processes, 43, 43f
- Deorsumduction, 181t
- Depression, 179, 180f, 181t
 paired antagonist model of, 194
- Descemet's membrane, 11f, 18-19, 18f, 19f, 103, 106f
 development of, 125, 128, 129f
 in limbus, 29
 in sclera, 27f
- Desmosome (macula adherens), 6, 7f
 of cornea, 12
 of iris, 39, 40f
- Dextroversion, 180, 180t
 in yoke muscle innervation, 194
- Diabetic cataract, 98
- Diabetic ophthalmoplegia, 229
- Diameter, lens, 87
- Diffuse cone bipolar cells, 62
- Dilated fundus examination, drugs in, 262
- Dilator muscle
 development of, 130
 drug activation of, 262
 of iris, 38f, 39, 41f
- Diplopia, 227, 228, 228f
 from abducens nerve damage, 230
- Direct-acting agonist, 261
- Directions, anatomic, 3, 3f
- Divergence, 180, 180t
- Dorsonasal (dorsal nasal) artery, 202f, 207
- Drusen, 51
- Dry eye, 173
- Dry-eye syndrome, 173
- Ductions, 179, 180f
- E**
- Ectoderm, neural, 116
- Ectoderm, surface, 116
- Ectropion, 156, 157f
- Edema
 of conjunctiva, 171
 of cornea, 23
 in eyelid, 162
- Edinger-Westphal nucleus, 224f, 225
 autonomic innervation of, 256, 256f, 259f
 in benign anisocoria, 269
 lesion in, 268, 268f
 in pupillary light pathway, 265, 266f
- Efferent (motor) pathway
 autonomic, 254
 cranial nerve innervation in, 223-227. *See also under* Cranial nerve innervation.
 pupillary light, 265, 266f
 disruptions in, 268-269
- EFI (epithelium-fiber interface), 94
- Elevation, 179, 180f, 181t
 paired antagonist model of, 194
- Ellipsoid, 59f, 60
- Embryology, ocular, 116-134
 Bergmeister's papilla in, 124, 124f
 blood vessel permeability and barriers in, 133
 development of adnexa in, 132-134
 extraocular muscles in, 133-134, 134f
 eyelids in, 132-133, 133f
 nasolacrimal system in, 134
 orbit in, 133, 133f
 development of structures in, 116-132
 anterior chamber in, 116, 131
 choroid in, 128
 ciliary body in, 129
 cornea in, 116, 125-128, 129f
 embryologic derivation in, 116-117, 117f
 hyaloid arterial system in, 122-123, 123f
 induction in, 119
 iris coloboma in, 119, 121f
 iris in, 130
 lens in, 119-122, 121f, 122f
 neural retina in, 124-125, 126-128f
 optic cup in, 118f, 119
 optic nerve in, 131-132, 132f
 optic pits in, 117-119, 118f, 120f
 pupillary membrane in, 130-131, 130f
 retinal pigment epithelium in, 122f, 124
 retinal vessels in, 125
 sclera in, 128
 uvea in, 128-130
 vitreous in, 123f, 131
 emmetropization in, 132
 Mittendorf's dot in, 124
 ocular albinism in, 125
 Pax-6 gene in, 116
 persistent pupillary membrane in, 131
 retinopathy of prematurity in, 125
- Embryonic fissure, 117-119, 118f, 120f
- Embryonic nucleus, 91, 93f
 of lens, 119
- Emmetropia, 3, 5f
- Emmetropization, 132

- Endfoot, 69
- Endocrine glands, 6
- Endomysium, 177, 178f
- Endothelial mosaic, 19, 20f
- Endothelium, corneal, 19-20, 19-22f
- Enophthalmos, 181t
in Horner's syndrome, 269, 271f
- Entropion, 157, 157f
- Epicanthus, 156, 156f
- Epimysium, 177, 178f
- Epinephrine, 261, 262f
- Episclera, 24
- Epithelial replacement, corneal, 12
- Epithelial tissue (epithelium), 6-7f
ciliary, 46-47, 46f, 47f
nonpigmented, 45f, 46, 47f
pigmented, 42f, 45f, 46
of conjunctiva, 168
of cornea, 9-12, 11f, 13f, 14f
development of, 125
of crystalline lens, 88-90f, 89
of eye, 6-7, 7f
glandular, 6
of iris
anterior, 39, 40f, 41f
posterior, 37f, 39
leaky, 6, 7f
stratified, 6
- Epithelium-fiber interface (EFI), 94
- Equator, of lens, 87
- Erosion, recurrent corneal, 12, 14f
- Esotropia, from epicanthal fold, 156
- Ethmoid arteries, 199f, 204
- Ethmoid bone
in medial orbital wall, 141, 141f, 142f, 144-145, 144f
in skull, 138f, 139
- Ethmoid nerve, 216, 218f
posterior, 218f
- Ethmoid sinus, 147-148, 148f, 148t
- Eversion, eyelid, 160
- Excyclorotation, 179, 180f, 181t
- Exocrine glands, 6
- Exophthalmos, 151, 151f, 181t
- External carotid artery and its branches. *See* Carotid artery and its branches, external.
- External hordeolum, 167, 167f
- External limiting membrane, 69f, 70
- Extorsion, 179, 180f, 181t
paired antagonist model of, 194
- Extraocular muscles, 177-196
aging changes in, 196
agonist and antagonist, 191-193
assessment of, 192, 192f
blood supply to, 195, 204-206, 206t
in Brown's superior oblique sheath syndrome, 193
Brown's superior oblique sheath syndrome and, 193f
cranial nerve damage on, 227-228
development of, 133-134, 134f
forced duction test of, 194
in hyperthyroidism (Graves' disease), 193
innervation of, 183f, 185t, 195
isolated agonist model of, 186-194. *See also* Isolated agonist model.
in long-standing immobility, 193
macroscopic anatomy of, 180-186, 181f
inferior oblique muscle in, 181f, 184f, 185, 185t
inferior rectus muscle in, 181f, 183t, 184-185, 184f, 185t
- Extraocular muscles (*Continued*)
lateral rectus muscle in, 181f, 183t, 184, 184f, 185t
medial rectus muscle in, 181f, 183, 183t, 184f, 185t
orbital connective tissue structure and, 185-186, 186f, 187f
rectus muscle in, innervation of, 185t
rectus muscle in, insertions of, 182-183, 183f, 184f
rectus muscle in, origin of, 180-182, 182f
rectus muscle in, tendon measurements of, 183t
retrobulbar optic neuritis and, 182
superior oblique muscle in, 181f, 184f, 185, 185t
superior rectus muscle in, 181f, 183t, 184, 184f, 185t
microscopic anatomy of, 177-180, 178f
eye movements in, 179-180, 179f, 180f, 181t
sliding ratchet model in, 177-178
structure in, 178-179
oblique muscle complexity in, 194-195
origin, insertion, and action of, 189t
paired antagonist model of, 194, 195f, 196f
in strabismus, 193
yoke muscles in, 194, 194f
- Extrinsic muscles, of globe, 177
- Eye(s). *See also* specific structures and disorders.
anatomic directions of, 3, 3f
anatomic features of, 1-3, 2f
anatomic planes of, 3, 4f
chambers of, 1, 2f
connective tissue of, 7-8
epithelial tissue of, 6-7, 7f
glandular epithelium of, 6
histologic features of, 6-8
intercellular junctions of, 6-7, 7f
muscle tissue of, 8
nerve tissue of, 8
refractive conditions of, 3, 5f
- Eye movements, 179-180, 179f, 180f, 181t
cranial nerve control of, 227
direction of, on muscle contraction, 192, 192f
- Eyebrows, 153, 154f
aging changes in, 174
- Eyelashes, 154
- Eyelid(s), 153-167
aging changes in, 174
blood supply to, 167, 169f
cilia of, 154, 155f
abnormalities of, 156
conjunctival concretions in, 164
conjunctival cysts in, 164
development of, 132-133, 133f
ectropion of, 156, 157f
entropion of, 157, 157f
epicanthus of, 156, 156f
eversion of, 160
fluid accumulation in, 162
histological features of, 161-166
glands in, 164-166, 164-166f
muscles in, 161f, 162
palpebral conjunctiva in, 162f, 163-164, 163f
skin in, 161-162, 162f
tarsal plates in, 163
hordeolum of, 167, 167f
innervation of, 167, 168f
margin of, 154-156, 155f
Meibomian glands in, 155f, 156, 160, 161f, 162f, 164-165, 164f, 166f
palpebrae fissure in, 153, 155f

- Eyelid(s) (*Continued*)
 ptosis in, 160, 160f
 structures of, 156-161
 capsulopalpebral fascia in, 159
 glands in, 160-161, 161f
 orbicularis oculi muscle in, 154f, 156-157
 palpebral ligaments in, 150f, 159f, 160
 retractor of lower eyelid in, 159
 superior palpebral levator muscle in, 157-159, 158f, 159f
 tarsal muscle (of Müller), 158f, 159, 159f
 tarsal plate in, 158f, 159f, 160
 topography of, 154, 155f
 vitamin A deficiency on, 164
 Eyelid margin, 154-156, 155f
- F**
- Face
 bones of, 138f, 140
 infections of, 211
 Facial artery, 207, 209f
 Facial nerve (cranial nerve VII), 217t, 227, 228f
 Facial nerve pathway, 227, 228f
 Facial nucleus, 227
 Farsightedness, 3, 5f
 Fascia bulb, 172
 Fasciculus, 216
 Fat cells, connective tissue, 8
 Fetal fissure, 117-119, 118f, 120f
 Fetal nucleus, 91, 93f, 122
 Fiber baskets (of Schultze), 67, 68f
 Fiber orientation, and visual fields, 241-253
 Fibers, crystalline lens, 89-91, 91f, 92f
 Fibroblasts
 of connective tissue, 9
 of cornea. *See* Keratocytes, corneal.
- Fick's axes, 179, 179f
 globe movement around, on rectus muscle contraction, 188, 188f
 muscle movement and, with eye in secondary position, 190f, 191f
- Fifth nerve (cranial nerve V), 223f
- Filtration apparatus, 103
 function of, 105, 107
- Fissure(s)
 calcarine, 238, 239f
 maps of, 251f
 "choroidal," 117-119, 118f, 120f
 embryonic, 117-119, 118f, 120f
 fetal, 117-119, 118f, 120f
 optic, 117-119, 118f, 120f
 orbital, 142f, 146-147, 146f
 inferior, 142f, 147, 147f
 superior, 142f, 147, 147f, 227
 palpebral, 153, 155f
 sympathetic innervation in widening of, 254, 258f
- Flat bipolars, 62
 Flat junctions, 75
 Flat midjet bipolar cell, 62
 Floaters, 113
 Fluid accumulation, in eyelid, 162
- Foramen (foramina)
 infraorbital, 141, 142f, 146
 oculomotor, 182, 182f
 optic, 142f, 146
 orbital, 142f, 146-147, 146f
 scleral, 26, 28f
- Foramen ovale, 138f, 139, 139f
 Foramen rotundum, 139, 139f
 Foramen spinosum, 138f, 139, 139f
 Forced duction test, 194
 Forehead muscles, in eyebrow control, 153, 154f
 Fornix, of conjunctiva, 167, 170f
 Fourth nerve. *See* Trochlear nerve (cranial nerve IV).
 Fovea (fovea centralis), 76, 77-79f
 development of, 125, 128f
 Foveal reflex, 79, 80f
 Foveola, 76, 77f, 79
 development of, 125
 Freckle, 42
 Frontal bone, 136, 137f, 138f, 140, 142f, 143f, 145f, 158f
 Frontal sinus, 147, 148f, 148t
 Frontalis muscle, 153, 154f
 Fuchs' crypts, 39, 41f
 Fuchs' endothelial dystrophy, guttata in, 22f
- Fundus
 age on, 84
 normal, 83f
 Fundus examination, 5
 dilated, drugs in, 262
 Fundus view
 of internal limiting membrane, 72
 of retinal vessels, 83
- G**
- GAG. *See* Glycosaminoglycan (GAG).
 Ganglion cell(s), 62-64, 65f, 67f
 number and distribution of, 75
 Ganglion cell layer, 69f, 72
 development of, 125, 126f, 127f
 Gap junctions, 7, 75
 of cornea, 12
 Gasserian ganglion, 221
 Gaze positions, 180
 agonist and antagonist muscles in, 191-193
 Geniculocalcarine tract, 238, 238f
 fiber orientation fields in, 245, 246f, 250-252
 macular sparing in, 252
 maps of, 250-252, 251f
 German measles, on lens development, 122
 Germinal zone, 89, 90f
 Germinating zone, 124, 127f
 Giant cell arteritis, 207
 Giant cone bipolar cells, 62
 Girdle of Vogt, limbal, 30
 Glands, 6. *See also* specific glands.
 in eyelids, 160-161, 161f, 164-166, 164-166f
 Glands of Moll, 160, 161f, 165, 166f
 infected, 167, 167f
 Glandular epithelium, 6
 Glaucoma, 110
 arcuate scotoma and nasal step in, 248, 248f
 optic nerve cupping in, 26
 pachometry in diagnosis of, 30
 Global layer, of extraocular muscles, 185
 Globe
 extrinsic muscles of, 177
 intrinsic muscles of, 177
 in orbit, from lateral side, 181f
 Glutamate
 in cones, 62
 in rods, 61
 Glutathione, 98

Glycosaminoglycan (GAG)
 of cornea, 15, 18
 of sclera, 26

Goblet cells, 163, 163f
 reduced populations of, 173

Gonioscopy, 105, 108f

Gradient, lens, 87

Gradient refractive index, 87

Graves' disease
 on extraocular muscles, 193
 ophthalmic, 151, 151f

Gray line, 156

Greater petrosal nerve, 256f, 257, 259f

Greater wing of sphenoid bone, 145, 145f

Ground substance, 7, 8
 of cornea, 15, 18

Guidance molecules, 125

Guttata, 20, 22f

H

H zone, 177, 178f

HA (hyaluronic acid), in vitreous, 113

Haller's layer, 48

Hallucinations, olfactory and visual, 250

Hassall-Henle bodies, 20, 30

Headache, ice cream, 220

Hemianopia, 250f

Hemidesmosomes, 7
 corneal, 12

Hemifield, contralateral, 248

Hemorrhage, retinal-shaped, 72, 74f

Henle's fiber layer, 76, 77f
 development of, 125

Henle's fibers, 76, 77f

Hering's law of equal innervation, 194

Heterochromia, 42
 iris, in congenital Horner's syndrome, 271, 271f

HI cells, 64, 66f

HII cells, 64, 66f

HIIL cells, 64, 66f

Hippus, 257

Histology, of eye, 6-8. *See also* specific structures.

Holmes map, 250, 251f

Holocrine glands, 6

Homonymous, 248

Homonymous field defect, 248, 250f

Homonymous hemianopia, 250f

Hordeolum, 167, 167f

Horizontal axis, 179, 179f

Horizontal cells, 64, 66f, 67f
 development of, 124, 127f

Horizontal raphe, 125

Horizontal rotation, extraocular muscle length in, 194, 196f

Horner's muscle, 156

Horner's syndrome, 231, 269-273, 271f
 anisocoria in, 271-273, 272f
 differential diagnosis of, 271-273, 272f
 iris heterochromia in, 271, 271f
 ptosis and miosis in, 269, 271f
 sympathetic innervation in, 269, 271f

Horns, of levator aponeurosis, 158

Hudson-Stähli line, 30, 30f

Hutchinson's sign, 217

Hyalocytes, in vitreous, 113

Hyaloid arterial system, development of, 122-123, 123f

Hyaloid artery, development of, 122, 123f

Hyaloid capsular ligament, 87

Hyaloid channel, 112-113, 112f

Hyaloid surface, 112, 112f

Hyaloidcapsular ligament (of Weiger), 111, 111f

Hyaluronic acid (HA), in vitreous, 113

Hydration, corneal, 22-23

Hydroxyamphetamine, 261, 262f
 on Horner's syndrome pupil, 272-273, 272f

Hyperemia, 207

Hyperopia (farsightedness), 3, 5f

Hyperthyroidism (Graves' disease)
 on extraocular muscles, 193
 ophthalmic, 151, 151f

Hypophyseal fossa, 139

I

I (isotropic) band, 177, 178f

Ice cream headache, 220

Immobility, on extraocular muscles, 193

Incyclorotation, 179, 180f, 181t

Indirect-acting agonist, 261

Induction, 119

Infections. *See also* specific infections.
 of face or orbit, 211

Inferior conchae, 140

Inferior oblique muscles, 181f, 185
 blood supply to, 204-205, 205t
 innervation of, 185t
 insertions of, 184f

Inferior ophthalmic vein, 210f, 211

Inferior orbital fissure, 142f, 147, 147f

Inferior palpebral sulcus, 154, 155f

Inferior petrosal sinus, 211, 213f

Inferior rectus muscles, 181f, 184-185
 blood supply to, 204-205, 205t
 innervation of, 185t
 insertions of, 184f
 movements of, 188, 188f
 in spiral of Tillaux, 182, 183f
 tendon measurements in, 183t

Inferior tarsal muscle, 159

Infraduction, 179, 180f, 181t

Infraorbital artery, 209, 209f

Infraorbital foramen, 141, 142f, 146

Infraorbital vein, 211

Infratrochlear nerve, 216, 218f

Infraversion, 180, 180t

Inion, 136

Injection, conjunctival, 171

INL, 70-71, 71f

Inner fiber, of rods and cones, 59f, 60

Inner neuroblastic layer, 124, 127f

Inner nuclear layer (INL), 70-71, 71f

Inner plexiform layer (IPL), 69f, 71-72, 73f

Inner segment, of rods and cones, 59f, 60, 60f

Inner synaptic layer, 69f, 71-72, 73f

Innervation
 of choroid, 50f
 of conjunctiva, 170
 of cornea, 11f, 24, 219f
 by cranial nerves. *See* Cranial nerve innervation.
 of extraocular muscles, 183f, 185t, 195
 of eyelids, 167, 168f
 of limbus, 219f
 of sclera, 28, 28f
 of uvea, 52

- Innervation, autonomic, 254-273
 in accommodation-convergence reaction, 262-263, 264f
 pathway of, 254-259
 ciliary muscle inhibition and, 257, 259f
 corneal reflex in, 259, 260f
 efferent, 254
 iris equilibrium and, 257
 to lacrimal gland, 256f, 257, 259f
 parasympathetic, 255-257, 256f, 259f
 sympathetic, 254-256, 255f, 258f
 in pharmacologic intrinsic muscle responses, 259-262
 agonist agents in, 261-262, 262f, 263f
 antagonist agents in, 261, 262, 262f, 263f
 drug-induced mydriasis and, 262, 269
 neurotransmitters in, 261, 261f
 pupillary light pathway in, 263-273, 266f. *See also* Pupillary light pathway.
- Intercellular junctions, 6-7, 7f
 Intermediary tissue of Kuhnt, 232, 234f
 Intermediate zone, of vitreous, 112, 112f
 Internal carotid artery and its branches. *See* Carotid artery and its branches, internal.
 Internal carotid artery aneurysm, 248, 249f
 Internal carotid artery sclerosis, 198
 Internal hordeolum, 167, 167f
 Internal jugular vein, 211, 213f
 Internal limiting membrane, 69f, 72
 fundus view of, 72
 Internal scleral sulcus, 103
 Interphotoreceptor matrix (IPM), 58
 Interplexiform neurons, 66, 67f
 Intorsion, 179, 180f, 181t
 paired antagonist model of, 194
 Intraocular pressure (IOP), 110
 glaucoma and, 110
 Intrinsic muscles, of globe, 177
 Invagination midjet bipolar cell, 62
 Inverted-Y suture, 122
 IPL, 69f, 71-72, 73f
 IPM, 58
 Iridectomy, 35
 Iridodialysis, 34
 Iridotomy, 35
 Iris, 1, 2f, 34-42
 aging changes in, 52-53
 anterior surface of, 39, 41f
 blunt trauma to, 34
 color of, 39, 42
 development of, 130
 functions of, 49
 heterochromia in, 42
 histologic features of, 34-39
 anterior border layer in, 34, 35f, 37f
 anterior epithelium in, 39, 40f, 41f
 dilator muscle in, 38f, 39, 41f
 iris stroma in, 34-35, 37f
 light micrographs of, 34, 35f, 36f
 posterior epithelium in, 37f, 39
 sphincter muscle in, 35, 35f, 37f, 38f
 iridectomy of, 35
 major arterial circle of, 203f, 204, 206f
 pigmentary dispersion syndrome in, 42
 posterior surface of, 39
 pupillary portion of, 35, 38f
 Iris coloboma, 119, 121f
 Iris dilator muscle, 38f, 39, 41f
 sympathetic innervation of, 254-256, 255f, 257, 258f
 Iris epithelium
 anterior, 39, 40f, 41f
 posterior, 37f, 39
 Iris equilibrium, 257
 Iris heterochromia, in congenital Horner's syndrome, 271, 271f
 Iris root, 34, 35f, 36f
 Iris sphincter, 35, 35f, 37f, 38f
 cholinergic agonists on, 261-262, 262f
 cholinergic antagonists on, 262, 263f
 development of, 130
 paralysis of, 229
 parasympathetic innervation of, 255f, 257, 259f
 Iris stroma, 34-35, 37f
 development of, 130
 Iris synechia, 39
 Iron deposits, in cornea, 30
 Isolated agonist model, 186-194
 agonist and antagonist muscles in, 191-193
 movements from primary position in, 187-190
 of horizontal rectus muscles, 187, 187f
 of oblique muscles, 189-190, 189f, 189t
 of vertical rectus muscles, 188, 188f
 movements from secondary position in, 190-191, 190f, 191f
 yoke muscles in, 194, 194f
 Isotropic (I) band, 177, 178f
- J**
 Juxtacanalicular tissue, 105
- K**
 Keratin, 6
 Keratoconus, 14, 15f
 Keratocytes, corneal, 14f, 15, 16f, 17f
 Keratometer, 5
 Keratoplasty, photorefractive, 30
 Keratotomy, radial, 30
 Krukenberg's spindle, 30
- L**
 Lacrimal artery, 199f, 200
 Lacrimal bone, 140, 141, 142f, 144, 144f
 Lacrimal canaliculus, 173-174, 173f
 Lacrimal crest
 anterior, 141
 posterior, 144, 144f
 Lacrimal gland, 159f, 172
 accessory, 165, 166f, 167f
 autonomic innervation to, 256f, 257, 259f
 in corneal reflex, 259, 260f
 Lacrimal lake, 153
 Lacrimal papilla, 173
 Lacrimal punctum, 173
 Lacrimal sac, 174
 Lacrimal secretory system, 172-174. *See also* Lacrimal gland.
 aging changes in, 174
 dry eye and, 173
 nasolacrimal drainage system in, 173-174, 173f
 secretory, 172
 tear drainage in, 174
 tear film in, 172
 assessment of, 173
 distribution of, 173
 Lacrimation, autonomic innervation in, 256f, 257, 259f
 Lagophthalmos, 153, 154f, 230

- Lamellae, corneal, 15, 16f, 17f, 19f
- Lamina
- basal, 6
 - of choroid, 49, 50f, 51f
 - of cornea, 12, 13f
 - reticular, 6
 - suprachoroid, 48, 51f
 - supraciliary, 42f, 43-44, 45f
- Lamina cribrosa, 26, 233-234, 234f, 235f
- development of, 128, 131
- Lamina fusca, 48, 48f, 49f, 51f
- Laser-assisted in situ keratomileusis (LASIK), 30
- Lateral canthus, 153
- Lateral geniculate nucleus (LGN, lateral geniculate body), 233f
- anatomy of, 237-238, 237f
 - fiber orientation in, 242-245, 245f
 - lesions in, 249
- Lateral orbital tubercle, 145
- Lateral palpebral arteries, 199f, 200, 202f
- Lateral rectus muscles, 181f, 184
- blood supply to, 204-205, 205t
 - innervation of, 185t
 - insertions of, 184f
 - movements of, 187, 187f
 - palsy of, 231
 - paralysis of, 230
 - in spiral of Tillaux, 182, 183f
 - tendon measurements in, 183t
- Left homonymous hemianopia, 250f
- Left macular homonymous hemianopia, 250f
- Left temporal crescent loss, 250f
- Lens, crystalline, 1-3, 2f, 87-101
- accommodation in, 97
 - aging changes in, 100-101
 - cataract of, 98, 99f, 100f
 - surgery for, 100
 - development of
 - embryologic, 87, 88f
 - embryonic, 119-122, 121f, 122f
 - fetal *vs.* adult, 91, 93f
 - histology of, 87-97
 - capsule in, 87-88, 88f
 - divisions in, 91, 93-94f
 - epithelium-fiber interface in, 94
 - epithelium in, 88-90f, 89
 - fibers in, 89-91, 91f, 92f
 - sutures in, 91, 93-94f
 - zones of discontinuity in, 94, 95t
 - zonules (of Zinn) in, 95-97, 96f
 - lens paradox in, 95
 - opacity of. *See* Cataract.
 - optical section of, 94, 95f
 - physiology of, 97-98
 - presbyopia in, 97
 - relationship to other structures of, 87, 88f
 - slit-lamp appearance of, 94, 95f, 95t
 - UV radiation on, 98
- Lens bow, 88f, 89
- Lens brunescence, 98
- Lens capsule, 87-88, 88f
- development of, 122
- Lens cortex, 91, 93f
- Lens fibers, 89-91, 91f, 92f
- primary, 87, 88f
 - development of, 119, 122f
 - secondary, 89
- Lens paradox, 95
- Lens pit, 119
- Lens placode, 119, 121f, 122f
- Lens plate, 119, 121f, 122f
- Lens shagreen, 94, 95f
- Lens sutures, 91, 93-94f
- Lens vesicle, 87, 88f, 119, 122f
- Lenses, contact
- on cornea, 22
 - fitting of, 30
- Lesser wing of sphenoid bone, 140, 142f, 144f
- Levator aponeurosis, 157-158, 158f, 159f, 161f, 162
- Levator muscle paralysis, 229, 229f
- Levoversion, 180, 180t
- LGN. *See* Lateral geniculate nucleus (LGN, lateral geniculate body).
- Light-near dissociation, 268, 268f
- Limbs, upper and lower, 180-182, 182f
- Limbus, 27f, 28-29, 29f, 104f
- innervation of, 219f
- Line of fixation of muscle pairs, in gaze positions, 194, 195f
- Line of projection, 245
- Lingual gyrus, 238, 239f
- Lipofuscin granules
- aging and, 83
 - in retinal pigment epithelium, 55
- Long ciliary nerves, 217, 218f, 219f
- Long posterior ciliary arteries, 199f, 203f, 204, 205f
- Long-standing immobility, on extraocular muscles, 193
- Longitudinal muscle fibers (of Brücke), 44, 45f
- Lower eyelid aponeurosis, 159
- Lutein, in macula lutea, 76
- Lymphatic drainage, of ocular adnexa, 214, 214f
- Lymphatics, of conjunctiva, 170, 214
- M**
- Macrophages, in connective tissue, 8
- Macula, 55, 76
- Macula adherens (desmosome), 6, 7f
- of cornea, 12
 - of iris, 39, 40f
- Macula lutea, 76, 77f
- Macula occludens, 6, 7f
- of cornea, 19
- Macular degeneration, age-related, 51-52, 52f
- Macular fibers, mapping of, 251f
- Macular sparing, 252
- Madarosis, 156
- Major arterial circle of the iris, 203f, 204, 206f
- Major circle of the iris, 35
- Mandible, 137f, 138f, 140
- Marginal arcade, 202f, 207
- Marginal orbital tubercle, 145
- Marginal zone (of His), 124, 127f
- Margins, orbital, 145-146, 146f
- Mast cells, connective tissue, 8
- Matrix, 7
- Maxillae, 137f, 138f, 140, 141, 142f, 144f
- Maxillary artery, 209-210, 209f
- Maxillary bones, 137f, 138f, 140, 142f, 144f
- Maxillary nerve, 221
- Maxillary sinus, 147, 148f, 148t
- Medial canthus, 153
- Medial longitudinal fasciculus, 224f, 227
- Medial palpebral arteries, 202f, 207
- Medial palpebral ligament, 150f, 159f, 160

- Medial rectus muscles, 181f, 183
 in accommodation-convergence response, 263, 264f
 blood supply to, 204-205, 205t
 innervation of, 185t
 insertions of, 184f
 movements of, 187, 187f
 in spiral of Tillaux, 182, 183f
 tendon measurements in, 183t
- Meibomian glands, 160, 161f, 162f, 164-165, 164f, 166f
 infection of, 167, 167f
 pores of, 155f, 156, 161f, 164f
 swelling of, 167, 167f
 tear film from, 172
- Meibomianitis, 173
- Melanocytes, development of, 125
- Melanosomes, in retinal pigment epithelium, 55
- Merocrine glands, 6
- Metoderm, 116-117
- Metamorphopsia, 79
- Meyer's loops, 245, 246f
 interruption in left optic radiations of, 250f
 lesion in, 250
 maps of, 251f
- Microglia, 8
 retinal, 69
- Microplacae, corneal, 11, 11f
- Microvilli
 in cornea, 11, 11f, 13f, 19f
 in retinal pigment epithelium, 55, 57f
- Midget bipolar cells, 62, 64f
- Midget ganglion cell, 63, 65f
- Minor circle of the iris, 35, 41f
- Miosis, 35
 in accommodation-convergence reaction, 262-263, 264f
 cholinergic antagonists in, 262, 263f
 in corneal reflex, 259, 260f
 in Horner's syndrome, 269, 271f
 parasympathetic innervation in, 259f
- Miotic pupil, 34
- Mittendorf's dot, 124
- Moll gland, 160, 161f, 165, 166f
 infected, 167, 167f
- Motor (efferent) pathway
 autonomic, 254
 cranial nerve innervation in, 223-227. *See also under* Cranial nerve innervation.
 pupillary light, 265, 267f
 disruptions in, 268-269
- Movements, eye, 179-180, 179f, 180f, 181t
 cranial nerve control of, 227
 direction of, on muscle contraction, 192, 192f
- M-type ganglion cell, 63, 65f
- Mucocutaneous junction, 163
- Müller cells, 66-69, 68f, 70
 age on, 84
 development of, 124, 127f
- Müller's annular muscle, 44, 45f
- Müller's muscle, 149f, 151, 161f
 sympathetic innervation of, 255f, 256f, 257
 weakness of (ptosis), 149f, 151
- Muscle(s). *See also* specific muscles.
 extraocular, 177-196. *See also* Extraocular muscles.
 sliding ratchet model of contraction of, 177-178
- Muscle of Horner, 156
- Muscle of Müller, 149f, 151, 161f
 weakness of (ptosis), 149f, 151
- Muscle of Riolan, 156, 161f, 162, 164f
- Muscle tissue, in eye, 8
- Muscular arteries, 204-206, 205t
- Mydriasis
 drug-induced, 262
 sympathetic innervation in, 258f
- Mydriatic pupil, 34
- Myelin, 8
- Myelinated neurons, 8
- Myofibrils, 177, 178f
- Myoid, 59f, 60
- Myopia (nearsightedness), 3, 5f
 PRK and LASIK for, 30
 sclera in development of, 26
- Myosin, 177, 178f
- N**
- Nasal bones, 137f, 138f, 140, 142f, 144f
- Nasal field, 246, 247f, 248
- Nasal step, 248, 248f
- Nasolacrimal canal, 143f, 144
- Nasolacrimal drainage system, 173-174, 173f
 development of, 134
- Nasolacrimal duct, 174
- Near-point reaction (near response), 262-263, 264f
- Nearsightedness. *See* Myopia (nearsightedness).
- Neovascularization, of cornea, 24, 25f
- Nerve fiber layer (NFL), 69f, 72
 in Alzheimer's disease, 84
- Nerve fiber orientation, and visual fields, 241-253
- Nerve of the pterygoid canal, 256f, 257
- Nerve tissue. *See also* specific nerves.
 of eye, 8
- Nervous system, 216. *See also* specific nerves and structures.
- Neural cells. *See also* specific cells.
 number and distribution of, 74-75, 75f
- Neural crest cells, 116
- Neural ectoderm, 116
- Neural folds, 116
- Neural plate, 116
- Neural retina, development of, 124-125, 126-128f
- Neural signals, in retina, 74
- Neural tube, 116, 117f
- Neuroblastic layers, 124, 127f
- Neuroglia, 8
- Neuroglial cells, retinal, 66-69, 68f
 astrocytes as, 69
 microglial cells as, 69
 Müller cells as, 66-69, 68f
- Neurons, 8
- Neurotransmitters, 8. *See also* specific neurotransmitters.
 on intrinsic muscles, 261, 261f
- Nevus, 42
- Nonpigmented ciliary epithelium, 42f, 45f, 46, 47f
- Norepinephrine, 261, 261f, 262f
- Nuclear cataract, 98, 100f
- O**
- Oblique muscles
 aging of, 196
 blood supply to, 195, 204-205, 205t
 complexity of, 194-195
 connective tissues for, 185-186, 186f, 187f
 in horizontal rotation, 194-195, 196f
 inferior, 181f, 184f, 185, 185t
 innervation of, 185t, 195

- Oblique muscles (*Continued*)
 insertions of, 184f
 movements of
 from primary position, 189-190, 189f
 from secondary position, 190-191, 191f
 origin, insertion, and action of, 189t
 primary action of, 189-190, 189t, 194-195
 superior, 181f, 184f, 185, 185t
- Occipital bones, 136, 137f
- Occipital lobe defect, 250
- Occipitotemporal cortex injury, 250
- Occluding (tight) junctions, 6
 of cornea, 11, 13f
 development of, 125
 of iris, 39, 40f
- Ocular adnexa. *See also* Conjunctiva; Eyebrows; Eyelid(s); Tenon's capsule.
 lymphatic drainage of, 214, 214f
- Ocular albinism, 125
- Ocular embryology. *See* Embryology, ocular.
- Ocular pain. *See also* specific disorders.
 in optic neuritis, 233
 from tooth abscess, 220
- Oculocardiac reflex, 223
- Oculomotor foramen, 182, 182f
- Oculomotor nerve (cranial nerve III), 217t, 223-226, 224-226f
 aberrant regeneration of, 229
 blood vessel relations of, 225f
 damage to, 228-229, 229f, 268-269
 oculomotor nucleus of, 223-225, 224f
 pathway of, 225-226, 225f, 226f
- Oculomotor nucleus, 223-225, 224f
 damage to, 268-269
- Oligodendrocytes, in optic nerve, 233, 234f, 235f
- Olfactory hallucination, 250
- Oligodendrocytes, 8
- ONL, 69f, 70
- Opacity, scleral, 26
- Ophthalmic artery, 198, 199f, 203f
 origin of branches of, 200t
- Ophthalmic instrumentation, 5-6
- Ophthalmic nerve, 218f, 220
- Ophthalmic vein
 inferior, 210f, 211
 superior, 210, 210f
- Ophthalmoplegia, 229
- Ophthalmoscope, 5
- Optic canal, 142f, 146
- Optic chiasm, 233f
 anatomy of, 235-236, 236f
 fiber orientation in, 242, 243f
 interruption of midline of, 250f
 lesions of, 248, 249f
 prefixed and postfixed positions of, 236
- Optic cup, development of, 118f, 119
- Optic disc, 80-82, 81f
 assessment of, 82
 fiber orientation in, 242, 242f
 papilledema of, 82, 82f
- Optic fissure, 117-119, 118f, 120f
- Optic foramen, 142f, 146
- Optic nerve (cranial nerve II), 217t, 218f, 219f
 anatomy of, 232-235, 233f
 intraocular and orbital sections in, 232-233, 234f
 prelaminar, laminar, and postlaminar sections in, 233-235, 235f
 damage to
- Optic nerve (cranial nerve II) (*Continued*)
 orbital, 147
 visual field defect with, 248
 development of, 131-132, 132f
 fiber orientation in, 242, 242f
 formation of, 119, 120f
 interruption of, 250f
 longitudinal section of, 201f
- Optic nerve cupping, 26
- Optic nerve head. *See* Optic disc.
- Optic neuritis
 pain with eye movements in, 233
 relative afferent pupillary defect in, 268
 retrobulbar, 182
- Optic neuropathy, anterior ischemic, 204
- Optic pits, 117-119, 118f, 120f
- Optic radiations, 238, 238f, 240f, 241
 damage to, 249-250, 249f
 fiber orientation in, 245-246, 246f
 interruption in, 250f
- Optic stalk, 117, 118f, 120f
 development of, 131
- Optic tract, 233f, 237
 fiber orientation in, 242, 244f
 lesion in, 248, 250f
- Optic vesicles, 117, 118f
- Optokinetic nystagmus, abnormal, 250
- Ora serrata, 43, 43f, 47f, 79
- Oral bays, 43, 43f
- Orbicularis oculi muscle, 153, 154f, 156-157, 158f, 161f, 162
 ciliary part of, 156, 161f, 162
 in corneal reflex, 259, 260f
 lacrimal part of, 156
- Orbit, 140-148
 aging changes in, 152
 anterior view of, 142f
 blood supply to. *See* Orbital blood supply.
 blow-out fracture of, 141, 144f
 cellulitis of, 148
 preseptal, 150
 connective tissue of, 148-151
 fat in, 151, 151f
 muscle of Müller in, 149f, 151
 periorbita in, 148-149, 149f, 151f
 septal system in, 151, 151f
 septum in, 144f, 149-150, 149f, 151f
 suspensory ligament (of Lockwood) in, 149f, 151
 Tenon's capsule, 150, 151f
 development of, 133, 133f
 exophthalmos in, 151, 151f
 fascial system of
 in horizontal section, 150f
 in vertical section, 149f
 foramina and fissures in, 142f, 146-147, 146f
 horizontal section through, 146f
 infections in, 211
 margins in, 145-146, 146f
 optic nerve damage in, 147
 paranasal sinuses in, 147-148, 148f, 148t
 walls in, 140-145
 floor of, 140-141, 143f
 lateral, 140, 141f, 145, 145f
 medial, 140, 141, 144-145, 144f
 roof of, 140, 143f
- Orbital adnexa. *See* Conjunctiva; Eyebrows; Eyelid(s); Tenon's capsule.
- Orbital apex, with globe removed, 226f

- Orbital blood supply, 198-214
aging on, 214
external carotid artery and its branches in, 207-210
 facial artery in, 207, 209f
 flow chart of, 208f
 maxillary artery in, 209-210, 209f
 superficial temporal artery in, 207, 209f
 temporal arteritis and, 207
internal carotid artery and its branches in, 198-207. *See also*
 Carotid artery and its branches, internal.
lymphatic drainage in, 214, 214f
veins in, 210-213
 anterior ciliary veins in, 211
 cavernous sinus in, 211, 212f, 213f
 cavernous sinus thrombosis of, 211
 central retinal vein in, 210-211, 210f
 inferior ophthalmic vein in, 210f, 211
 infraorbital vein in, 211
 papilledema and, 211
 superior ophthalmic vein in, 210, 210f
 vortex veins in, 203f, 211
- Orbital cellulitis, 148
Orbital connective tissue structure, 185-186, 186f
Orbital fascia, 148-149, 149f, 151f
Orbital layer, of extraocular muscles, 185
Orbital periosteum, 148-149, 149f, 151f
Orbital portion, of eyelid, 154, 155f
Orbital tubercles, 145
Orthokeratology, 30
Outer fiber, of rods and cones, 59f, 60
Outer neuroblastic layer, 124, 127f
Outer nuclear layer (ONL), 69f, 70
Outer plexiform layer, 63f, 69f, 70, 71f
Outer segment, of rods and cones, 58, 59f, 60f
Outer synaptic layer, 63f, 69f, 70, 71f
- P**
- P1 ganglion cell, 63, 65f
P2 ganglion cell, 63, 65f
Pachometry, 30
Pain. *See also* specific disorders.
 with eye movements, in optic neuritis, 233
 ocular. *See also* specific disorders.
 from tooth abscess, 220
 referred, 220
Paired antagonist model, 194, 195f, 196f
Palatine bones, 140, 144f
Palisades of Vogt, 29
Palpebrae, 153
Palpebrae fissure, 153, 155f
Palpebral arcades, 200, 202f, 207
Palpebral arteries, 199f, 200, 202f
 medial, 202f, 207
Palpebral conjunctiva, 162f, 163-164, 163f, 167-168, 170f
Palpebral fissure widening, sympathetic innervation in,
 256, 258f
Palpebral ligaments, 150f, 159f, 160
Palpebral orbicularis, 156
Palsy(ies)
 of abducens nerve, 227, 230-231, 230f
 of lateral rectus muscle, 231
 of oculomotor nerve, 228-229, 229f
 of trochlear nerve, 230, 230f
Papilla, lacrimal, 155f, 156
Papilledema, 82, 82f, 211
Papillomacular bundle, 241
Paralysis, 227, 228
 of abducens nerve (CN VI), 227
 of ciliary muscle, 229
 of iris sphincter, 229
 of lateral rectus muscle, 230
 of levator muscle, 229, 229f
Paranasal sinuses, 147-148, 148f, 148t
Parasympathetic accessory third-nerve nucleus. *See* Edinger-Westphal
 nucleus.
Paresis, 227, 228
Parietal bones, 136, 137f
Parietal lobe lesions, 250
Pars ciliaris, 156
Pars lacrimalis, 156
Pars plana, 42f, 43, 43f
Pars plicata, 42f, 43, 43f
 aqueous humor from, 108
Patellar fossa, 111
Pax-6 gene, 116
Pedicle, 59f, 61-62
Peduncle, 216
Pericytes, 49, 83
Perikaryon, 8
Perimeters, computerized, 5-6
Perimysium, 177, 178f
Periorbita, 148-149, 149f, 151f
Peripapillary chorioretinal atrophy, 84
Peripheral anterior synechia (PAS), 39
Peripheral arcade, 202f, 207
Peripheral retina, 75, 79
 degeneration of, 80
Peripheral retinal traction, 113
Peripheral vision, 76
Persistent pupillary membrane, 131
Petrosal nerves, 256f, 257, 259f
Petrosal sinuses, 211, 213f
Phenylephrine, 261, 262f
 in dilated fundus examination, 262
Photokeratitis, 55
 from UV radiation, 22
Photopic vision, 72-74
Photoreceptor cell(s), 58-62, 59-61f, 67f
 retinal pigment epithelium—neuroretinal interface in, 58
 rod and cone composition in, 58-60, 59f, 60f
 rod and cone morphology in, 59f, 60-62, 61f
Photoreceptor cell layer, 69f, 70
Photorefractive keratoplasty (PRK), 30
Physiologic blind spot, 80
Physiologic cup, 80, 81f
Physostigmine, 262, 263f
Pigment ruff, 41f
Pigmentary dispersion syndrome, 42
Pigmented ciliary epithelium, 42f, 45f, 46
Pilocarpine, 261-262, 263f
Pingueculae, 171, 171f
Pituitary gland tumor, bitemporal field effect with,
 248, 249f
Planes, anatomic, 3, 4f
Plasmalemma
 of cones, 61
 of rods, 59f, 60
Pleomorphism, corneal endothelial cell, 20, 21f
Plica semilunaris, 153, 155f, 170
Point of fixation, 246
Poles, lens, 87
Polymegathism, corneal endothelial cell, 20, 21f

- Positions of gaze, 180
 agonist and antagonist muscles in, 191-193
 line of fixation of muscle pairs in, 194, 195f
- Posterior chamber, 1, 2f, 108, 109f
- Posterior ciliary arteries, 199f, 200-204, 203f
- Posterior commissure, 265, 266f
- Posterior epithelium, iris, 37f, 39
- Posterior ethmoid artery, 199f, 204
- Posterior ethmoid nerve, 216, 218f
- Posterior lacrimal crest, 144, 144f
- Posterior pole, 76
- Posterior sclera, 219f
- Posterior subcapsular cataract, 98, 100f
- Posterior vascular tunic of the lens (posterior tunica vasculosa lentis),
 development of, 122, 123f
- Posterior vitreal detachment, 114
- Postfixed optic chiasm, 236
- Postganglionic fiber, 254
 parasympathetic, 257, 259f
 sympathetic, 254, 258f
- Postganglionic neuron, 254
- Prefixed optic chiasm, 236
- Preganglionic fiber, 254
 in Horner's syndrome, 271, 271f
 parasympathetic, 256, 259f
 sympathetic, 258f
- Preganglionic neuron, 254
 parasympathetic, 259f
 sympathetic, 258f
- Prematurity, retinopathy of, 125
- Presbyopia, 49, 97
 age-related, 101
- Preseptal cellulitis, 150
- Pretectal nucleus, 265
 lesion in, 268, 268f
- Primary lens fibers, 87, 88f
 development of, 119, 122f
- Primary visual cortex, 238-240, 239f
- Primary vitreous, development of, 123f, 131
- Primary zonules, 97
- PRK, 30
- Procerus muscle, 153, 154f
- Projection, line of, 245
- Proliferative zone, 124, 127f
- Proptosis, 151, 151f
- Protrusion, 181t
- Pseudoesotropia, from epicanthal fold, 156, 156f
- Pterygia, 171, 171f
- Pterygoid venous plexus, 210f, 211
- Pterygopalatine ganglion, 256f, 257, 258f
- Ptosis, 160, 160f, 229, 229f
 in Horner's syndrome, 269, 271f
- Puncta, 173
- Punctum, lacrimal, 155f, 156
- Pupil, 34, 35f
 fixed, dilated pupil, 269
 in sleep, 257
 tonic, 269
 Adie's, 269, 270f
- Pupillary constriction, 263. *See also* Pupillary light pathway.
 from parasympathetic stimulation, 257
- Pupillary fibers, 263
- Pupillary frill, 35f, 38f, 39
- Pupillary light pathway, 263-273, 266f
 Adie's tonic pupil and, 269, 270f
 afferent, 265, 266f
- Pupillary light pathway (*Continued*)
 afferent, disruption in, 265-268
 in cataract, 265
 in optic neuritis, 268
 swinging-flashlight test of, 265, 267f
- Argyll-Robertson pupil (syndrome) and, 268, 268f
- CNS disruption on, 268, 268f
- efferent, 265, 266f
- efferent, disruptions in, 268-269
- fixed, dilated pupil and, 269
- pupillary light response of, 265
- sympathetic, disruption in, 269-273, 271f, 272f. *See also*
 Sympathetic pathway, disruption in.
 tonic pupil and, 269
- Pupillary light response, 265
- Pupillary membrane
 development of, 130-131, 130f
 persistent, 131
- Pupillary ruff, 35f, 38f, 39
- Pupillary zone, 34, 36f
- R**
- Radial contraction furrows (of Schwalbe), 39, 41f
- Radial fibers, 44, 45f
- Radial keratotomy, 30
- Radiation, UV. *See* Ultraviolet (UV) light radiation.
- RAPD, 265, 267f
 in optic neuritis, 268
- Rectus muscles
 action of, 189t
 aging of, 196
 blood supply to, 195, 204-205, 205t
 connective tissues for, 185-186, 186f, 187f
 in horizontal rotation, 194, 196f
 inferior. *See* Inferior rectus muscles.
 innervation of, 185t, 195
 insertions of, 182-183, 184f, 189t
 spiral of Tillaux from, 182-183, 183f
 lateral. *See* Lateral rectus muscles.
 medial. *See* Medial rectus muscles.
 movements of
 from primary position, 187-188, 187f, 188f
 from secondary position, 190, 190f
 origin of, 180-182, 182f, 189t
 superior. *See* Superior rectus muscles.
 tendon measurements of, 183t
- Recurrent corneal erosion, 12, 14f
- Recurrent meningeal artery, 199f, 200
- "Red eye," 207
- Referred pain, 220
- Reflex blepharospasm, 157
- Refractive conditions, 3, 5f
- Refractive index, of lens, 87
- Refractive power
 corneal, 5
 of unaccommodated lens, 87
- Relative afferent pupillary defect (RAPD), 265, 267f
 in optic neuritis, 268
- Reticular lamina, 6
- Retina, 1, 2f, 55-84
 aging changes in, 83-84
 in Alzheimer's disease, 84
 blood supply to, 81f, 82-83
 central, 76-79
 development of, 124-125, 126-128f
 fiber orientation in, 241-242, 241f

- Retina (*Continued*)
 function of, 72-75
 histologic features of, 55-69
 amacrine cells in, 64-65, 66f, 67f
 bipolar cells in, 62, 63f, 64f, 67f
 ganglion cells in, 62-64, 65f, 67f, 263-265
 horizontal cells in, 64, 66f, 67f
 interplexiform neurons in, 66, 67f
 layers in, 55, 56f
 neuroglial cells in, 66-69, 68f. *See also* Neuroglial cells.
 photoreceptor cells in, 58-62, 59-61f. *See also* Photoreceptor cell(s).
 retinal pigment epithelium in, 55-57, 56f, 57f, 67f
 layers of, 69-72, 69f
 external limiting membrane in, 69f, 70
 ganglion cell layer in, 69f, 72
 inner nuclear layer in, 70-71, 71f
 inner plexiform layer in, 69f, 71-72, 73f
 internal limiting membrane in, 69f, 72
 nerve fiber layer in, 69f, 72
 outer nuclear layer in, 69f, 70
 outer plexiform layer in, 63f, 69f, 70, 71f
 photoreceptor cell layer in, 69f, 70
 retinal pigment epithelium in, 69f, 70. *See also* Retinal pigment epithelium (RPE).
 neural cell number and distribution in, 74-75, 75f
 neural signals in, 74
 orientation of image on, 246-248, 247-248f
 peripheral, 75, 79
 photopic vision in, 72-74
 regions of, 75-82, 77f
 fovea (fovea centralis), 76, 77-79f
 foveola, 76, 77f, 79
 macula lutea, 76, 77f
 optic disc, 80-82, 81f, 82f
 peripheral, 79
 scotopic vision in, 72
 synapses in, 75
 synaptic contacts in, 71-72, 71f
 Retinal artery, central, 198-200, 199f, 201f
 development of, 125
 Retinal blur, 97
 Retinal degeneration, peripheral, 80
 Retinal detachment, 58
 Retinal ganglion cells, 62-64, 65f, 67f
 classification of, 263-265
 layer of, 69f, 72
 Retinal pigment epithelium (RPE), 46, 47f, 55-57, 56f, 57f, 67f, 69f, 70
 aging on, 83
 development of, 122f, 124
 Retinal-shaped hemorrhages, 72, 74f
 Retinal sheen, 72
 Retinal traction, peripheral, 113
 Retinal vein, central, 210-211, 210f
 development of, 125
 Retinal venous branch occlusion, 200
 Retinal vessels. *See also* specific vessels.
 development of, 125
 Retinopathy of prematurity, 125
 Retinoscope, 5
 Retinotopic map, 244-245, 245f
 Retraction, 181t
 Retractor of lower eyelid, 159
 Retrobulbar inflammation, 229
 Retrobulbar optic neuritis, 182
 Retrobulbar tumor, 229
 Retrolental fibroplasia, 125
 Retrolental ligament, 111, 111f
 Retrolental space (of Berger), 87
 Retrolental tract, 112-113, 112f
 Ribbon junctions, 75
 Right homonymous half-field map, 251f
 Right homonymous hemianopia, 250f
 Right homonymous superior quadrantanopia, 249f, 250
 Riolan's muscle, 156, 161f, 162, 164f
 Rod bipolar cell, 62
 Rod spherule, 62, 63f
 development of, 124
 Rods
 aging on, 83
 composition of, 58-60, 59f, 60f
 morphology of, 59f, 60-61
 number and distribution of, 74-75, 75f
 in scotopic vision, 72
 Rouget cells, 49
 RPE. *See* Retinal pigment epithelium (RPE).
 Rubella virus, on lens development, 122
- S**
 Sagittal axis, 179, 179f
 Sarcomere, 177-178, 178f
 Sattler's layer, 40f, 48
 Schirmer test, 173
 Schlemm's canal, 104-106f, 105, 108f, 110f
 aging changes in, 110
 in aqueous dynamics, 109, 109f, 110f
 development of, 116, 131
 function of, 105, 108
 giant vacuoles in, 109, 109f, 110f
 Schwalbe's line (ring), 18, 103, 108f
 Schwann cell, 8
 Sclera, 1, 2f, 24-28
 aging changes in, 30-31
 blood supply to, 26, 28f
 ciliary injection of, 24
 color of, 26
 definition of, 9
 development of, 128
 foramina and canals of, 26, 28f
 histologic features of, 24-26
 innervation of, 28, 28f
 in myopic development, 26
 opacity of, 26
 posterior, 219f
 Scleral spur, 26, 27f, 103, 104-106f
 Scleral sulcus, 28
 Sclerosis
 of internal carotid artery, 198
 senile nuclear, 98, 100f
 Scotoma
 arcuate, in field of left eye, 248, 248f
 of physiologic blind spot, 247f, 248
 Scotopic vision, 72
 Sebaceous glands of Zeis, 160, 161f, 164f, 165, 165f
 infected, 167, 167f
 tear film from, 172
 Second nerve. *See* Optic nerve (cranial nerve II).
 Secondary lens fibers, 89
 development of, 119, 122
 Secondary vitreous, development of, 131
 Secondary zonules, 97

- Sella turcica, 139
- Semilunar ganglion, 221
- Senile annular ring, 114
- Senile nuclear sclerosis, 98, 100f. *See also* Cataract.
- Sensory (afferent) pathway, 216-223
trigeminal nerve in, 216-221. *See also* Trigeminal nerve.
- Septal system, orbital, 151, 151f
- Septal tissue, 234f
- Septum, orbital, 144f, 149-150, 149f, 151f
- Seventh nerve (facial nerve, cranial nerve VII), 217t, 227, 228f
- Sherrington's law of reciprocal innervation, 191
- Short posterior ciliary arteries, 199f, 200-202, 203f, 204, 205f
- Sixth nerve. *See* Abducens nerve (cranial nerve VI).
- Skeletal muscle, 8
- Skull bones, 136-139
anterior view of, 138f
disarticulated view of base of, 139f
floor of, 138f
inion in, 136
lateral view of, 137f
posterior view of, 137f
- Sliding ratchet model, 177-178
- Slit-lamp appearance, of crystalline lens, 94, 95f, 95t
- Smooth muscle, 8
- Spaces of Fontana, 103
- Sphenoid bone, 136-139, 137-139f, 141, 145
coronal section through, 212f
greater wing of, 145, 145f
lesser wing of, 140, 142f, 144f
- Sphenoid sinus, 147-148, 148f, 148t
- Sphenopalatine (pterygopalatine) ganglion, 256f, 257
- Sphincter muscle, of iris. *See* Iris sphincter.
- Spiral of Tillaux, 182-183, 183f
- Strabismus, 193
- Stratified epithelium, 6
- Stratum opticum, 69f, 72
- Striate cortex, 238-240, 239f
fiber orientation fields in, 245f, 246, 250-252
interruption of fibers of, 250f
macular sparing in, 252
maps of, 250-252, 251f
projections on, 233f
- Striated muscle, 8
microscopic anatomy of, 177-180, 178f
sliding ratchet model in, 177-178
structure in, 178-179
- Striped fundus, 84
- Stroma
choroidal, 48, 50f
ciliary, 42f, 45-46
corneal, 11f, 14f, 15-18, 16f, 17f
development of, 128
iris, 34-35, 37f
palpebral conjunctival, 164
- Structural furrows (of Schwalbe), 39, 41f
- Stye, common, 167, 167f
- Subarachnoid space, 211
- Submucosa, conjunctival, 168-169
palpebral, 164
- Submuscular areolar layer, 161f, 162
- Subretinal space, 55, 57f
- Substantia propria
corneal, 11f, 14f, 15-18, 16f, 17f
palpebral conjunctival, 164
- Superficial temporal artery, 207, 209f
- Superior cerebellar artery aneurysm, 228
- Superior cerebral artery aneurysm, 228
- Superior cervical ganglion, 255f
- Superior field, 246, 247f, 248
- Superior oblique muscles, 181f, 185
blood supply to, 204-205, 205t
innervation of, 185t
insertions of, 184f
- Superior ophthalmic vein, 210, 210f
- Superior orbital fissure, 142f, 147, 147f, 227
- Superior palpebral levator muscle, 157-159, 158f, 159f
- Superior palpebral sulcus, 154, 155f
- Superior petrosal sinus, 211, 213f
- Superior rectus muscles, 181f, 184
blood supply to, 204-205, 205t
innervation of, 185t
insertions of, 184f
movements of, 188, 188f
in spiral of Tillaux, 182, 183f
tendon measurements in, 183t
- Superior tarsal muscle, 158f, 159, 159f, 161f
- Superior transverse ligament, 157, 158f
- Suprachoroid lamina, 48, 48f, 49f, 51f
- Supraciliary, 42f, 43-44, 45f
- Supraciliary lamina, 42f, 43-44, 45f
- Supraduction, 179, 180f, 181t
- Supraorbital artery, 199f, 202f, 204
- Supraorbital nerve, 218f, 220, 220f
- Supraorbital notch, 142f, 145
- Supraorbital vein, 210, 210f
- Supratrochlear artery, 202f, 207
- Supratrochlear nerve, 217, 218f, 220f
- Supratrochlear notch, 145-146
- Supraversion, 180, 180t
- Surface ectoderm, 116
- Sursumduction, 181t
- Suspensory ligament
of lens, 95, 96f
of Lockwood, 149f, 151
- Sutures, lens, 91, 93-94f
- Swinging-flashlight test, 265, 267f
- Sympathetic pathway, 254-255, 255f, 258f
disruption in, 269-273, 271f, 272f
in anisocoria, 269
in anisocoria, benign, 269
in Horner's syndrome, 269-273, 271f
- Synapse, 8
- Synaptic complexes, development of, 124
- Synaptic contacts
in inner plexiform layer, 71-72, 73f
in vertebrate retinas, 71-72, 71f
- Synechia, iris, 39
- Syneresis, of vitreous, 114
- Synkinesis, 262
- ## T
- T tubules, 177
- Tarsal (Meibomian) glands, 160, 161f, 162f, 164-165, 164f, 166f
infection of, 167, 167f
pores of, 155f, 156, 161f, 164f
swelling of, 167, 167f
tear film from, 172
- Tarsal muscle (of Müller), 158f, 159, 159f
- Tarsal plates, 158f, 159f, 160, 161f, 163, 164f
- Tarsal portion, of eyelid, 154, 155f
- Tear drainage, 174

- Tear film, 9, 172. *See also* Lacrimal secretory system.
 assessment of, 173
 distribution of, 173
- Tear film breakup time (TBUT), 173
- Tectobulbar tract, 227
- Temporal arteries, 207, 209f
- Temporal arteritis, 207
- Temporal bones, 136, 137f, 139f
- Temporal crescent, 248
- Temporal field, 246, 247f, 248
- Temporal lobe lesions, 249f, 250
- Tendons
 measurements of, 183t
 upper and lower, 180-182, 182f
- Tenon's capsule, 150, 151f, 172
- Terminal bars, 6, 7f
 in retinal pigment epithelium, 58
- Tertiary vitreous, development of, 131
- Test(s). *See also* specific tests.
 forced duction, 194
 Schirmer, 173
 swinging-flashlight, 265, 267f
 visual field, 246-247, 247-248f
- Thickness, lens, 87
- Third nerve. *See* Oculomotor nerve (cranial nerve III).
- Third ventricle, optic chiasm and, 236, 236f
- Thrombosis, cavernous sinus, 211
- Tight (occluding) junctions, 6
 of cornea, 11, 13f
 development of, 125
 of iris, 39, 40f
- Tonic pupil, 269
- Tonofilaments, 6
- Tonometer, 110
- Tooth abscess, ocular pain from, 220
- Torsional movements, 179, 180f, 181t
 paired antagonist model of, 194
- Trabecular meshwork, 103, 104-107f
 development of, 116, 131
 function of, 105, 108
- Transient fiber layer of Chievitz, 124, 127f
- Transmembrane linkers, 6
- Transparency, crystalline lens, 97-98
- Transverse axis, 179, 179f
- Transverse facial artery, 207, 209f
- Triads, 62, 75
- Trichiasis, 156
- Trigeminal ganglion, 221
- Trigeminal nerve, 216-221
 branches and paths of, 216, 218f, 221f
 irritation of, 257
 mandibular division of, 221, 221f
 maxillary division of, 220-221, 221f
 infraorbital nerve in, 220, 220f, 221f
 zygomatic nerve in, 218f, 220f, 221
 maxillary nerve formation in, 221
 ophthalmic division of, 216-220
 frontal nerve in, 217-220, 218f
 herpes zoster in, 217
 nasociliary nerve in, 216-217, 218f
 ophthalmic nerve formation in, 218f, 220
- Trigeminal nerve (*Continued*)
 (scleral) nerve loops (of Axenfeld) in, 217
 referred pain and, 220
- Trigeminal nerve formation, 221-223, 222f, 223f
- Tigroid fundus, 84
- Trochlea, 140, 142f
- Trochlear nerve (cranial nerve IV), 217t, 226, 226f
 blood vessel relations of, 225f
 in cavernous sinus, 222f
 damage to, 230, 230f
- Trochlear nucleus, 224f, 226
- Tropicamide, 262, 263f
 in dilated fundus examination, 262
- Tropocollagen, 8
- ## U
- Ultraviolet (UV) light radiation
 on cornea, 22
 on crystalline lens, 98
- Unmyelinated neurons, 8
- Upright-Y suture, 122
- UV radiation. *See* Ultraviolet (UV) light radiation.
- Uvea, 34-53
 aging changes in, 52-53
 blood supply to, 52
 choroid in, 48-49, 48f, 49f
 ciliary body in, 42-47. *See also* Ciliary body.
 development of, 128-130
 functions of, 49-52
 innervation of, 52
 iris in, 34-42. *See also* Iris.
- Uveal meshwork, 103, 106f, 108f
- ## V
- V1, 238, 239f
- V2, 239
- V3, 239
- V4, 239
- V5, 239
- Valleys (of Kuhnt), 43, 43f
- Valve of Hasner, 174
- Vasoconstriction, sympathetic innervation in, 258f
- Vein(s)
 angular, 210, 210f
 central retinal, 210-211, 210f
 development of, 125
 ciliary, anterior, 211
 infraorbital, 211
 jugular, internal, 211, 213f
 ophthalmic
 inferior, 210f, 211
 superior, 210, 210f
 orbital, 210-213. *See also under* Orbital blood supply.
 supraorbital, 210, 210f
 vortex, 203f, 211
- Vergences, 179-180, 180t
- Versions, 179-180, 180t
- Vertigo, in Horner's syndrome, 269
- Vidian nerve, 256f, 257, 258f
- Vision. *See also* specific aspects.
 peripheral, 76
 photopic, 72-74
 scotopic, 72
- Visual cortex, primary, 238-240, 239f
- Visual-evoked response (VER), inion in, 136
- Visual field, 5, 241
- Visual field defects, 248-250, 248-250f. *See also* specific defects.
- Visual field testing, 246-248, 247-248f
- Visual hallucination, 250
- Visual pathway, 232-253, 233f. *See also* specific aspects of.
 aging in, 252

Visual pathway (*Continued*)

- anatomy of structures of, 232-240. *See also* specific structures.
 - lateral geniculate nucleus in, 237-238, 237f
 - optic chiasm in, 235-236, 236f
 - optic nerve in, 232-235, 234f, 235f
 - optic radiations in, 238, 238f
 - optic tract in, 237
 - primary visual cortex in, 238-240, 239f
- blood supply to, 240-241, 240f
- fiber orientation and visual fields in, 241-253
 - of lateral geniculate nucleus, 242-245, 245f
 - of optic chiasm, 242, 243f
 - of optic disc, 242, 242f
 - of optic nerve, 242, 242f
 - of optic radiations, 245-246, 246f
 - of optic tract, 242, 244f
 - of retina, 241-242, 241f
 - of striate cortex, 245f, 246, 250-252, 251f
- visual field defects in, 248-250, 248-250f. *See also* specific defects.
 - visual field testing in, 246-248, 247-248f
- Visual system, 1-8, 2f. *See also* Eye(s).
- Vitamin A
 - deficiency of, on goblet cells, 164
 - for dry-eye disorders, 164
- Vitreous detachment, posterior, 114
- Vitreous
 - composition of, 112-113
 - development of, 123, 123f, 131
 - function of, 113
- Vitreous base, 111, 111f
- Vitreous cells, 113
- Vitreous chamber, 1, 2f, 111-114
 - age-related changes in, 113
 - attachments in, 111-112, 111f
 - Cloquet's canal of, 112-113, 112f
 - cortex of, 112, 112f
 - intermediate zone of, 112, 112f
 - peripheral retinal traction and, 113
 - posterior vitreal detachment and, 114
- Vitreous cortex, 112, 112f
- Vitreous production, 51

- Vomer, 140
- Vortex veins, 203f, 211

W

- W cells, 62, 265
- Weiss' ring, 114
- Whitnall's ligament, 157, 158f
- Whitnall's tubercle, 145
- Willbrand's knees, 242, 243f
- Wing cells, 12, 13f, 14f
- With-the-rule astigmatism, 9
- Wound healing, corneal, 23

X

- X cells, 63, 265-267

Y

- Y cells, 62-63, 265-267
- Y sutures, 91, 93f
 - development of, 122
 - slit-lamp appearance of, 94, 95f, 95t
- Yoke muscles, 194, 194f

Z

- Z line, 177, 178f
- Zeaxanthin, in macula lutea, 76
- Zeis gland, 160, 161f, 164f, 165, 165f
 - infected, 167, 167f
 - tear film from, 172
- Zona occludens (tight junctions), of cornea, 11, 11f
- Zones of discontinuity, in lens, 94, 95t
- Zonula adherens, 6, 7f
- Zonula occludens (tight junctions). *See* Tight (occluding) junctions.
- Zonular lamella, 87
- Zonule fibers, 43, 44f
 - development of, 131
- Zonules (of Zinn), 95-97, 96f
- Zygomatic artery, 207, 209f
- Zygomatic bones, 137f, 139f, 140, 142f, 143f, 145, 145f
- Zygomatic process, 136, 137f
- Zygomaticofacial artery, 199f, 200
- Zygomaticotemporal artery, 199f, 200