# Brief Contents

Preface xxiii  
Acknowledgments xxviii  
Prologue A Brief History of Eyes I

## PART ONE  
**Ocular Systems** 55

1. Formation of the Human Eye 57  
2. Ocular Geometry and Topography 77  
3. The Orbit 111  
4. The Extraocular Muscles 133  
5. The Nerves of the Eye and Orbit 191  
6. Blood Supply and Drainage 247  
7. The Eyelids and the Lacrimal System 291

## PART TWO  
**Components of the Eye** 323

8. The Cornea and the Sclera 325  
9. The Limbus and the Anterior Chamber 379  
10. The Iris and the Pupil 411  
11. The Ciliary Body and the Choroid 447  
12. The Lens and the Vitreous 491  
13. Retina I: Photoreceptors and Functional Organization 545  
14. Retina II: Editing Photoreceptor Signals 595  
15. Retina III: Regional Variation and Spatial Organization 649  
16. The Retina In Vivo and the Optic Nerve 701

Epilogue Time and Change 753

Glossary G–1  
Historical References and Additional Reading HR–1  
Index I–1
Contents

Preface xxiii
Acknowledgments xxviii

Prologue  A Brief History of Eyes  1

The Antiquity of Eyes and Vision  1

Thinking about the eye gave Charles Darwin “a cold shudder”  1
The history of the eye is embedded in the history of animals and molecules  2
Several of the eye’s critical molecules are ancient  3
Eyes were invented by multicellular animals almost 600 million years ago  5
Eyes arose not once, but numerous times, in different animal groups  6
Eyes are most common in groups of motile animals living in lighted environments  8

The Diversity and Distribution of Eyes  9

The first step in vision is an eye that can sense the direction of incident light  9
At least ten types of eyes can be distinguished by differences in their optical systems 11
Vertebrates always have simple eyes, but invertebrates can have compound eyes, simple eyes, or both 13

Paths and Obstacles to Perfection  16

Simple eyes improve as they become larger  16
Elaborate simple eyes may have evolved rapidly  18
Compound eyes have inherent optical limitations in their performance  19

An Ocular Bestiary: Fourteen Eyes and Their Animals  21

I. Compound eye—focal apposition, terrestrial variety: Honeybee (Apis mellifera)  21
II. Compound eye—focal apposition, aquatic variety: Horseshoe crab (Limulus polyphemus)  23
III. Compound eye—afocal apposition: Monarch butterfly (Danaus plexippus)  26
PART ONE

Ocular Systems

Chapter 1 Formation of the Human Eye 57

Some Developmental Strategies and Operations 57

Embryogenesis begins with cell proliferation, cell movement, and changes in cell shape 57
Specialized tissues are formed by collections of cells that have become specialized themselves 58
Proliferation, movement, and differentiation in a cell group may require communication with other cells 58

Embryonic Events before the Eyes Appear 59

The blastocyst forms during the first week of embryogenesis 59
The inner cell mass becomes the gastrula, which is divided into different germinal tissues 60
Neurulation begins the development of the nervous system 62

Formation of the Primitive Eye 64

Ocular development begins in the primitive forebrain 64
The optic vesicle induces formation of the lens 64

Elaboration of the Primitive Eye 65

The optic cup and the lens form from different germinal tissues by changes in cell shape 65
The optic cup is initially asymmetric, with a deep groove on its inferior surface 67
Closure of the choroidal fissure completes the optic cup 67
The lens vesicle forms in synchrony with the optic cup 67

The primitive lens is the first ocular structure to exhibit cell differentiation 68
All future growth of the lens comes from the early lens cells, some of which are “immortal” stem cells 69
The precursors of the future retina, optic nerve, lens, and cornea are present by the sixth week of gestation 69
In general, the eye develops from inside to outside 70

Failures of Early Development 71

“If anything can go wrong, it will” 71
One or both eyes may fail to develop completely 71
Congenital absence of the lens may be an early developmental failure 71
Incomplete closure of the choroidal fissure can produce segmental defects in the adult eye 74

VIGNETTE 1.1 The Eye of Mann 72

Chapter 2 Ocular Geometry and Topography 77

Elements of Ocular Structure 77

The human eye is a simple eye 77
The outermost of the three coats of the eye consists of cornea, limbus, and sclera 78
The middle coat—the uveal tract—includes the iris, ciliary body, and choroid 78
The eye’s innermost coat—the retina—communicates with the brain via the optic nerve 79
Most of the volume of the eye is fluid or gel 81

Image Quality and Visual Performance 82

Images of point sources are always small discs of light whose size is a measure of optical quality 82
The amount of smear or spread in the image of a point source is related to the range of spatial frequencies transmitted by the optical system 83
The contrast sensitivity function specifies how well different spatial frequencies are seen by the visual system 86
We can see flies when their images subtend about one minute of visual angle 87

The Anatomy of Image Formation 90

The quality of a focused image is affected by pupil size, curvatures of optical surfaces, and homogeneity of the optical media 90
Defocusing produces large changes in the modulation transfer function 92
The major anatomical factors that determine the refractive power of the eye are the curvatures of the cornea and lens and the depth of the anterior chamber 93
Schematic eyes are approximations of the eye’s optically relevant anatomy 95
Eye Shape and Size  97
Vertebrate eyes vary considerably in shape  97
Both the cornea and the sclera are aspheric  97
On average, the adult human eye measures twenty-four millimeters in all dimensions  100
Axial lengths and other anatomical features vary among individuals, but most eyes are emmetropic  101
Most refractive error is related to relatively large or small axial lengths  102

The Eye’s Axes and Planes of Reference  103
The eyes rotate around nearly fixed points  103
Like the head, the eyes have three sets of orthogonal reference planes  104
The pupillary axis is a measure of the eye’s optical axis  106
The line of sight differs from the pupillary axis by the angle kappa  107
The angles kappa in the two eyes should have the same magnitude  107
Eye position is specified by the direction of the line of sight in a coordinate system whose origin lies at the eye’s center of rotation  108

Chapter 3 The Orbit  111
The Bony Orbit  111
The orbits are roughly pyramidal  111
The large bones of the face form the orbital margin and much of the orbit’s roof, floor, and lateral wall  112
The sphenoid bone fills the apex of the orbital pyramid and contributes to the lateral and medial walls  114
The lacrimal and ethmoid bones complete the medial wall between the maxillary bone in front and the sphenoid in back  118
Three major and several minor foramina permit blood vessels and nerves to enter or exit the orbital cavity  118
Blowout fractures of the orbit are a consequence of the relative weakness of the orbital plates  119
Abnormal positioning of the eye relative to the orbital margin may indicate local or systemic pathology  120
Infection and tumors can enter the orbital cavity through the large sinuses that surround the orbit  120
Connections between the Eye and the Orbit  121
Connective tissue lines the interior surface of the orbit  121
Connective tissue surrounds the eye and extraocular muscles  121
Check ligaments connect Tenon’s capsule to the periorbita  124

All structures in the orbital cavity are lined and interconnected with connective tissue  125
Abnormal development of the connective tissue may affect movement of the eyes  125
Fat fills the spaces in the orbital cavity that are not occupied by other structures  126
The septum orbitale prevents herniation of orbital fat into the eyelids  127

Development of the Orbital Bones  127
Many bones form first as cartilage templates  127
Most orbital bones do not have cartilaginous templates  127
The orbital plates begin to form during the sixth week of gestation  130
The capacity of bone for growth, repair, and remodeling lasts many years  130
The eyes and orbits rotate from lateral to frontal positions during development  130
Most developmental anomalies of the orbital bones are associated with anomalies of the facial bones  131

Chapter 4 The Extraocular Muscles  133
Patterns of Eye Movement  133
Our eyes are always moving, and some motion is necessary for vision  133
Large, rapid eye movements are used for looking around, for placing retinal images of interest on the fovea  135
Slow eye movements are used to track or follow movement and to compensate for changes in head and body position  136
Eye movement velocities may vary by a factor of $10^5$  137
Since the eyes have overlapping fields of view, their movements must be coordinated  137
Slow movements of the eyes in opposite directions help keep corresponding images on the foveas in both retinas simultaneously  138
Strabismus is a misalignment of the two visual axes under binocular viewing conditions  139
Control of Eye Position  139
The extraocular muscles are arranged as three reciprocally innervated agonist–antagonist pairs  139
The eyes are stationary when the opposing forces exerted by the extraocular muscles are in balance  141
Imbalanced forces produce eye rotations  142
Muscle force is related to muscle length  143
Most of the force that maintains eye position is passive force  144
Equilibrium muscle lengths and forces for different gaze positions are functions of the innervational command 145
Different patterns of innervation are required for fast and slow eye movements 146
Extraocular motor neurons are located in three interconnected nuclei in the brainstem 146
Motor commands are the result of interactions between visual and nonvisual inputs to the motor control centers 147
A copy of the innervational command is used to verify the system’s operation 148
Extraocular motor neurons receive inputs from premotor areas in the brainstem to generate appropriate signals for saccadic eye movements 148
The pathways for smooth pursuit movements and for vergences go through the cerebellum, but vergences have a separate control center near the oculomotor nucleus 149

Extraocular Muscle Structure and Contractile Properties 153

Muscle fibers are the units from which muscles are constructed 153
Striated muscle fibers have a parallel arrangement of contractile proteins that interleave to cause contraction 154
Striated muscle fibers differ in structural, histochemical, and contractile properties 155
The extraocular muscles contain muscle fiber types not found in skeletal muscles 156
Thick and thin extraocular muscle fibers differ in their contractile properties 156
Different muscle fiber types are not randomly distributed within the muscles 157
Different muscle fiber types may receive different innervational commands 158
Extraocular muscles have very small motor units 159
Acetylcholine at the neuromuscular junctions depolarizes the cell membrane by opening sodium channels 161
The spread of depolarization along the sarcolemma may differ among muscle fiber types, producing different contractile properties 161
Extraocular muscles exhibit high sensitivity to agents that mimic or block the action of acetylcholine 162
Extraocular muscles often exhibit early symptoms of myasthenia gravis 163
Neurotoxins that interfere with acetylcholine action can be used to alleviate strabismus and blepharospasm 163

Sensory Endings in Extraocular Muscles and Tendons 165

Skeletal muscles have two major types of sensory organs 165
Human extraocular muscles have anatomically degenerate sensory organs and exhibit no stretch reflexes 166

Passive extraocular muscle stretch may produce bradycardia 167
Sensory endings in extraocular muscles probably do not convey information about eye position 167
Sensory signals from the extraocular muscles may be involved in motor learning, motor plasticity, and development 168

Actions of the Extraocular Muscles 168

All of the extraocular muscles except the inferior oblique have their anatomical origins at the apex of the orbit 168
The anatomical origin of the inferior oblique and the functional origin of the superior oblique are anterior and medial in the orbit 169
The four rectus muscles are arranged as horizontal and vertical pairs, all inserting onto the anterior portion of the globe 170
The horizontal recti rotate the eye in the horizontal plane around a vertical axis 170
The vertical recti are responsible for upward and downward rotations of the eye 171
The recti define a muscle cone within the orbital cavity that contains most of the ocular blood vessels and nerves 172
The oblique muscles constitute a third functional pair, inserting onto the posterior portion of the eye 172
Extraocular muscle actions cannot be measured directly 174
The classic description of action of the extraocular muscles is based on the geometry of their origins and insertions 174
Boeder diagrams attempt to describe the actions of the extraocular muscles completely 176
The presence of Tenon’s capsule and muscle pulleys invalidates the geometric model of extraocular muscle actions 178
“There is no simple way to describe the action of these muscles on the eye!” 180
A realistic model of the extraocular muscle system is important for the diagnosis and treatment of muscle paresis 182

Development of the Extraocular Muscles 183

Each muscle develops from several foci in the mesoderm surrounding the optic cup 183
The extraocular muscles appear after the optic cup, but before the orbital bones 185
Different muscle fiber types form late in gestation and continue to develop postnatally 185
Most developmental anomalies are associated with the connective tissue of the muscles or with their innervation 186
The oculomotor system is not fully operational at birth 186

BOX 4.1 Detecting Ocular Misalignment 140
Contents

BOX 4.2 Changing the Effects of Extraocular Muscle Contraction 152

VIGNETTE 4.1 Locating the Extraocular Muscles 164

VIGNETTE 4.2 In the Service of the Eye 184

Chapter 5  The Nerves of the Eye and Orbit 191

Elements of Neural Organization 191

The brain deals with information about the external world and the body 191

Neurons are the anatomical elements of neural systems 191

Neural circuits consist of neurons linked mostly by unidirectional chemical synapses 193

The direction of neural information flow distinguishes between sensory and motor nerves 194

Motor outputs are divided anatomically and functionally into somatic and autonomic systems 194

The autonomic system is subdivided into the sympathetic and parasympathetic systems 194

The Optic Nerve and the Flow of Visual Information 195

In the optic nerve, the location of axons from retinal ganglion cells corresponds to their location on the retina 195

Axons from the two optic nerves are redistributed in the optic chiasm 198

The decussation of axons in the chiasm is imperfect 199

Spatial ordering of axons changes in the optic tracts 200

In the lateral geniculate nuclei, which are primary targets of axons in the optic tracts, inputs from the two eyes are separated into different layers 200

Axons terminating in the lateral geniculate nuclei are spatially ordered 201

Some axons leave the optic tracts for other destinations 203

Axons terminating in the superior colliculi form discontinuous retinotopic maps 204

Axons forming the afferent part of the pupillary light reflex pathway terminate in the pretectal nuclear complex 204

Retinal inputs to the accessory optic system may help coordinate eye and head movement 205

Retinal axons may provide inputs to a biological clock 205

Lesions of the optic nerves and tracts produce defects in the visual fields 207

Lesions in the secondary visual pathways can be observed only as motor deficits 212

The Trigeminal Nerve: Signals for Touch and Pain 212

Two of the three trigeminal divisions carry signals from the eye and surrounding tissues 212

All somatosensory information from the eye is conveyed by the nasociliary nerve to the ophthalmic division of the trigeminal 213

Sensory nerve fibers from the cornea, conjunctiva, limbus, and anterior sclera join to form the long ciliary nerves 213

Stimulation of corneal or conjunctival nerve endings elicits sensations of touch or pain, a blink reflex, and reflex lacrimation 215

Other sensory fibers from the eye are conveyed by the short ciliary nerves and the sensory root of the ciliary ganglion 215

Most other branches of the ophthalmic nerve carry somatosensory fibers from the skin of the eyelids and face 215

A few branches of the maxillary nerve pass through the orbit from the facial skin and the maxillary sinus 217

Lesions in the branching hierarchy of the ophthalmic nerve produce anesthesia that helps identify the lesion site 218

Viral infection of the trigeminal system can produce severe corneal damage 219

The Extraocular Motor Nerves 219

The three cranial nerves that innervate the extraocular muscles contain axons from clusters of cells in the brainstem 219

Cells in different parts of the oculomotor nerve nucleus innervate the levator, the superior and inferior recti, the medial rectus, and the inferior oblique 219

Axons destined for different muscles run together in the oculomotor nerve until it exits the cavernous sinus just behind the orbit 221

The oculomotor nerve contains parasympathetic fibers bound for the ciliary ganglion 224

Cells in the trochlear nerve nucleus innervate the contralateral superior oblique 224

Abducent nerve cells innervate the ipsilateral lateral rectus 225

All of the oculomotor nerves pass through the cavernous sinus on their way to the orbit 225

The extraocular motor nerves probably contain sensory axons from muscle spindles and tendon organs 226

Innervation of the Muscles of the Eyelids 226

Three sets of muscles are associated with the eyelids 226

The orbicularis is innervated by the facial nerve 227

The superior and inferior tarsal muscles are innervated by the sympathetic system 227

Ptosis may result from either oculomotor or sympathetic lesions 228

Autonomic Innervation of Smooth Muscle within the Eye 228

The superior cervical ganglion is the source of most sympathetic innervation to the eye 228
Sympathetic fibers enter the eye in the short ciliary nerves 230.

Sympathetic innervation of the dilator muscle acts at alpha-adrenergic receptors to dilate the pupils 230.

The arterioles in the uveal tract receive sympathetic innervation that produces vasoconstriction 231.

Horner’s syndrome is the result of a central lesion in the sympathetic pathway 231.

Parasympathetic fibers entering the eye originate in the ciliary or the pterygopalatine ganglion 231.

Axons from cells in the ciliary ganglion innervate the sphincter and the ciliary muscle 232.

Axons from the pterygopalatine ganglion cells innervate vascular smooth muscle in the choroid 233.

Accommodation and pupillary light reflexes share efferent pathways from the Edinger–Westphal nuclei to the eyes; pupillary reflexes are mediated by retinal signals reaching the Edinger–Westphal nuclei through the pretectal complex 233.

Deficient pupillary reflexes may be associated with midbrain lesions 234.

Innervation of the Lacrimal Gland 235.

Axons from cells in the pterygopalatine ganglion reach the lacrimal gland via the zygomatic and lacrimal nerves 235.

The efferent pathway for lacrimal innervation begins in the facial nerve nucleus 235.

Basal tear production may require tonic innervation of the lacrimal gland 236.

Some Issues in Neural Development 236.

Specialized growth cones guide the extension of axons and dendrites 236.

Pathfinding by growth cones depends on recognition of local direction signs 237.

Target recognition and acquisition may require specific markers produced by the target cells 238.

Many early neurons are eliminated as mature patterns of connectivity are established 238.

Adult connectivity patterns are not always complete at birth, and postnatal development is subject to modification 239.

Ocular albinism is associated with a pathfinding error in the development of optic nerve axons 239.

Anomalous innervation of the extraocular muscles may be the result of pathfinding or target recognition errors 240.

Some forms of amblyopia may be related to problems with postnatal establishment and maintenance of synaptic connections 240.

Innervation of the extraocular muscles begins early in gestation, sensory innervation much later 241.

Postnatal Neuron Growth and Regeneration 241.

Most postnatal neuron growth is interstitial growth 241.

Neurons do not undergo mitosis postnatally 242.

Spinal neurons in peripheral nerves can regenerate after being damaged 242.

Central nervous system neurons do not regenerate following major damage 242.

Corneal nerve endings will regenerate following local damage 243.

Neuronal degeneration can affect other, undamaged neurons 243.

VIGNETTE 5.1 The Integrative Action of the Nervous System 196.

BOX 5.1 Tracing Neural Pathways: Degeneration and Myelin Staining 206.

VIGNETTE 5.2 Seeing One World with Two Eyes: The Problem of Decussation 210.

BOX 5.2 Tracing Neuronal Connections: Axonal Transport Methods 222.

Chapter 6 Blood Supply and Drainage 247.

Distributing Blood to Tissues 247.

Arteries control blood flow through capillary beds, and veins regulate blood volume 247.

Blood flow through capillary beds can be controlled locally or systemically 248.

Capillary beds in a tissue may be independent or interconnected 251.

The interchange between blood and cells depends partly on the structure of the vascular endothelium 252.

Capillary endothelium is renewable, and capillary beds can change 253.

Neovascularization is a response to altered functional demands 253.

Structurally weakened capillaries may be prone to excessive neovascularization 254.

The Ophthalmic Artery and Ophthalmic Veins 255.

The ophthalmic artery distributes blood to the eye and its surroundings 255.

Blood supplied to tissues by the ophthalmic artery is drained to the cavernous sinus by the ophthalmic veins 257.

Supply and Drainage of the Eye 260.

Muscular arteries supply both the extraocular muscles and the anterior segment of the eye 260.

The anterior ciliary arteries contribute to the episcleral and intramuscular arterial circles 261.

The conjunctiva and corneal arcades are supplied by branches from the episcleral arterial circle and drained by the episcleral and anterior ciliary veins 262.

The system of episcleral veins drains the conjunctiva, corneal arcades, and limbus 263.
Chapter 7  The Eyelids and the Lacrimal System  291

Structure and Function of the Eyelids  291

Structural rigidity of the lids is provided by the tarsal plates 291
The tarsal plates are made of dense connective tissue in which glands are embedded 292
The palpebral fissure is opened by muscles inserting onto or near the edges of the tarsal plates 294
The palpebral fissure is closed by contraction of the orbicularis  296
Blinking may be initiated as a reflex response or as a regular, spontaneous action 298
Lid movements during spontaneous blinks move tears across the cornea  299
Overaction of the orbicularis may appear as blepharospasm or as entropion  299
Paresis of the orbicularis produces ectropion and epiphora 300
Other glands in the lids are associated with the eyelashes 301
The skin on the lids is continuous with the conjunctiva lining the posterior surface of the lids and covering the anterior surface of the sclera  302
The orbital septum is a connective tissue sheet extending from the orbital rim to the tarsal plates 303
The shape and size of the palpebral fissure vary 304
The overall structure of the lids consists of well-defined planes or layers of tissue 306

Tear Supply and Drainage  307

Most of the tear fluid is supplied by the main lacrimal gland 307
Secretion by the lacrimal gland is regulated by autonomic inputs operating through a second-messenger system 308
The composition of the lacrimal gland secretion varies with the secretion rate 309
Dry eye may result from a decreased amount of tears, abnormal tear composition, or both 310
Tears are drained off at the medial canthus and deposited in the nasal cavity 311
Pressure gradients created by contraction of the orbicularis during blinks move tears through the canaliculi into the lacrimal sac 312

Formation of the Eyelids and the Lacrimal System 315

The eyelids first appear as folds in the surface ectoderm, which gives rise to the lid glands 315
The lacrimal gland and the lacrimal drainage system derive from surface ectoderm 316
Most developmental anomalies in the eyelids and lacrimal system are problems in lid position or blockage of the drainage channels 318
Anomalous innervation can produce eyelid movements linked to contraction of muscles in the jaw 318
PART TWO

Components of the Eye

Chapter 8 The Cornea and the Sclera 325

Components and Organization of the Cornea and Sclera 325

The cornea, sclera, and limbus are made primarily of collagen fibrils 325
Collagen is embedded in a polysaccharide gel that forms the extracellular matrix 326
The fibroblasts in the corneal and scleral stroma constitute a small fraction of the stroma's volume 327
Collagen fibrils in the cornea are highly organized; those in the sclera are not 328
The structure of the corneal stroma is altered in Bowman's layer 331
Corneal transparency is a function of its regular structure 332
Collagen organization in the stroma and corneal transparency depend on intact epithelium and endothelium 334
The corneal epithelium is a multilayered, renewable barrier to water movement into the cornea 335
The corneal endothelium is a single layer of metabolically active cells 339
The endothelial cell tiling changes with time because cells that die cannot be replaced 340
Descemet's membrane separates the endothelium from the stroma 345
Nerve endings in the cornea give rise to sensations of touch or pain, a blink reflex, and reflex lacrimation 347
The epithelium contains a dense array of free terminals of nerve fibers from the long ciliary nerves 347
Corneal sensitivity can be measured quantitatively 349
The dense innervation of the cornea makes it subject to viral infection 349

The Cornea as a Refractive Surface 349

The optical surface of the cornea is the precorneal film covering the surface of the epithelium 349
The cornea's outline is not circular, its thickness is not uniform, and its radius of curvature is not constant 351
The shape of the cornea is determined by comparison to a sphere 353
The cornea does not have a single, specifiable shape 354
Contact lenses can affect corneal shape and structure directly or indirectly 356
The shape and optical properties of the cornea can be permanently altered 358
Surgically reshaped corneas may change with time 359
Corneal shape can be changed by removing tissue 360
Stromal reshaping leaves the epithelium intact 361
Corneal grafts are used to repair optically damaged corneas 361

Corneal Healing and Repair 365

The epithelium heals quickly and completely 365
Corneal healing may require limbal transplants 368
Repair of damage to the stroma produces translucent scar tissue 368
The endothelium repairs itself by cell expansion and migration 369
Corneal graft incisions are repaired by the normal healing processes 369
Radial keratotomy incisions are repaired by epithelial hyperplasia and collagen formation 370
Photorefractive keratectomy ablations are healed mostly by the epithelium 371

Growth and Development of the Cornea 371

The epithelium and endothelium are the first parts of the cornea to appear 371
The stroma is derived from neural crest cells associated with the mesoderm 372
The regular arrangement of the stromal collagen appears soon after collagen production begins 372
Corneal growth continues for a few years postnataally 374
Anomalous corneal development can produce misshapen or opaque corneas 375

BOX 8.1 Biomicroscopy of the Cornea 342
VIGNETTE 8.1 The Invisible Made Visible 350
BOX 8.2 Some Reservations about Corneal Refractive Surgery 362
VIGNETTE 8.2 The Art of William Bowman 366

Chapter 9 The Limbus and the Anterior Chamber 379

The Anterior Chamber and Aqueous Flow 379

The anterior chamber is the fluid-filled space between the cornea and the iris 379
The angle of the anterior chamber varies in magnitude 380
Aqueous is formed by the ciliary processes and enters the anterior chamber through the pupil 381
Aqueous drains from the eye at the angle of the anterior chamber 383
Intraocular pressure depends on the rate of aqueous production and the resistance to aqueous outflow 385

The Anatomy of Aqueous Drainage 390

The scleral spur is an anchoring structure for parts of the limbus and the ciliary body 390
The trabecular meshwork is made of interlaced cords of tissue extending from the apex of the angle to the margin of the cornea 392
Schwalbe's ring separates the trabecular meshwork from the cornea 393
The trabecular cords have a collagen core wrapped with endothelial cells 393

The major source of outflow resistance is the juxta-canalaricular tissue separating the canal of Schlemm from the trabecular spaces 395

The canal of Schlemm encircles the anterior chamber angle 395

Aqueous enters the canal of Schlemm by way of large vacuoles in the endothelial lining of the canal 397

Aqueous drains out of the canal into venous plexuses in the limbal stroma 399

Pilocarpine reduces intraocular pressure, probably by an effect of ciliary muscle contraction on the structure of the trabecular meshwork 400

An effective way to reduce intraocular pressure seems to be to increase the uveoscleral outflow 402

Surgery for glaucoma aims to increase aqueous outflow 402

The outer surface of the limbus is covered with episcleral tissue and a heavily vascularized conjunctiva 403

Development of the Limbus 405

The anterior chamber is defined by the iris growing between the developing cornea and lens 405

The angle of the anterior chamber opens during development as the root of the iris shifts posteriorly 406

The trabecular meshwork develops between the fourth and eighth months 408

Most developmental anomalies in the limbus are associated with structural anomalies that affect other parts of the anterior chamber 408

BOX 9.1 Through the Looking Glass: Gonioscopy 382

BOX 9.2 Estimating the Pressure Within: Tonometry 388

Chapter 10 The Iris and the Pupil 411

Functions of the Iris and Pupil 411

The iris is an aperture stop for the optical system of the eye 411

The entrance pupil is a magnified image of the real pupil 412

Variation of pupil size changes the amount of light entering the eye, the depth of focus, and the quality of the retinal image 413

Pupil size varies with illumination level, thereby helping the retina cope with large changes in illumination 414

Pupil size varies with accommodation and accommodative convergence 416

The pupillary near response is smaller in children than in adults 417

The pupil is in constant motion, and it reacts quickly to changes in retinal illumination 418

Decreased iris pigmentation in ocular albinism affects the optical function of the iris 419

Structure of the Iris 420

The pupils in the two eyes are normally the same size and are decentered toward the nose 420

The iris is constructed in layers and regional differences in the iris are related to the different muscles within them 421

The anterior border layer is an irregular layer of melanocytes and fibroblasts interrupted by large holes 422

The iris stroma has the same cellular components as the anterior border layer, but loosely arranged 423

Small blood vessels run radially through the stroma, anastomosing to form the minor arterial circle and supply the iris muscles 425

The sphincter and dilator occupy different parts of the iris and have antagonistic actions 426

The sphincter is activated by the parasympathetic system, the dilator by the sympathetic system 427

The anterior pigmented epithelium is a myoepithelium, forming both the epithelial layer and the dilator muscle 428

The posterior epithelial cells contact the anterior surface of the lens 430

Surgery for closed-angle glaucoma often involves the iris rather than the limbus 432

Some Clinically Significant Anomalies of the Iris and Pupil 432

Changes in iris color after maturity are potentially pathological 432

Differences between the two eyes in pupil size or pupillary responses to light are commonly associated with neurological problems 433

Anisocoria and unresponsive pupils are often associated with defects in the efferent part of the innervational pathways 435

Clinically useful drugs affecting pupil size fall into four functional groups 437

Development of the Iris 440

The iris stroma forms first by migration of undifferentiated neural crest cells 440

The epithelial layers and the iris muscles develop from the rim of the optic cup and are therefore of neuroectodermal origin 440

The pupil is the last feature of the iris to appear 442

Most postnatal development of the iris is an addition of melanin pigment 443

Segmental defects and holes in the iris result from unsynchronized or failed growth of the optic cup rim 443

An ectopic pupil is improperly centered in an otherwise normal iris 445

A persistent pupillary membrane may be the result of either insufficient tissue atrophy or tissue hyperplasia 445
Chapter 11  The Ciliary Body and the Choroid  447

Anatomical Divisions of the Ciliary Body  447

The ciliary processes characterize the pars plicata  447
The ciliary muscle extends through both pars plicata and pars plana  449

The Ciliary Processes and Aqueous Formation  449

The ciliary processes are mostly filled with blood vessels  449
The capillaries in the ciliary processes are highly permeable  451
Two layers of epithelium lie between the capillaries and the posterior chamber  452
Aqueous formation involves metabolically driven transport systems  452
The ciliary epithelium is anatomically specialized as a blood–aqueous barrier  454
Ions are transported around the band of tight junctions to produce an osmotic gradient in the basal folds of the unpigmented epithelium  455
Aqueous production varies during the day and declines with age  456
The major classes of drugs used to reduce aqueous production interact either with adrenergic membrane receptors or with the intracellular formation of bicarbonate ions  458
The pars plana is covered by epithelial layers that are continuous with the epithelial layers of the pars plicata  459

The Ciliary Muscle and Accommodation  461

The ciliary muscle has three parts with a complex geometry  461
Contraction of the ciliary muscle produces movement inward toward the lens so that the muscle behaves like a sphincter  463
The zonule provides a mechanical linkage between ciliary muscle and lens  465
Accommodation is a result of ciliary muscle contraction  468
The primary stimulus to accommodation is retinal image blur  469
Accommodative amplitude decreases progressively with age  472
Presbyopia is not a consequence of reduced innervation to the ciliary muscle  473
Aging of the ciliary muscle is unlikely to be a significant factor in presbyopia  474

The Choroid  477

The choroidal stroma consists of loose connective tissue and dense melanin pigment  477
Blood vessels that supply and drain the capillary bed supplying retinal photoreceptors make up the main part of the choroid  478

The choriocapillaris is heavily anastomotic but has local functional units  479
The choriocapillaris varies in capillary density and in the ratio of arterioles to venules  480
Capillaries in the choriocapillaris are specialized for ease of fluid movement across the capillary endothelium  481
Bruch’s membrane lies between capillaries and pigmented epithelium in both the choroid and the pars plana of the ciliary body  481

Development of the Ciliary Body and Choroid  482

The ciliary epithelium arises from the optic cup, the ciliary muscle from neural crest cells  482
Formation of the ciliary epithelium may be induced by the lens  483
Formation of the ciliary muscle may be induced by the ciliary epithelium  484
The ciliary muscle begins to form during the fourth month and continues to develop until term  485
The muscles associated with the eye originate from different germinal tissues  486
The ciliary processes form in synchrony with the vascular system in the ciliary body  486
The zonule is produced by the ciliary epithelium  486
The choroidal vasculature has two developmental gradients: center to periphery and inside to outside  488

VIGNETTE 11.1 The Source  470

Chapter 12  The Lens and the Vitreous  491

Structure of the Lens  492

Some unusual proteins, the crystallins, are the dominant structural elements in the lens  492
Dense, uniform packing of the crystallins within lens cells is responsible for lens transparency  494
Crystallins are highly stable molecules, making them some of the oldest proteins in the body, but they can be changed by light absorption and altered chemical environments  494
a-Crystallins may play a special role in maintaining native crystallin structure over time  496
The lens is formed of long, thin lens fibers arranged in concentric shells to form a flattened spheroid  497
Lens fibers in each shell meet anteriorly and posteriorly along irregular lines  498
Lens shells are bound together with miniature locks and keys, a kind of biological Velcro  499
The anterior epithelium is the source of new cells for the lens  501
Elongating epithelial cells at the equator become long lens fibers that form new shells in the lens  503
The size of the lens and the number of lens fibers increase throughout life  503
Each new lens shell has one more fiber than the previous shell and about five new shells are added each year after the age of five  504
An aged lens has about 2500 shells and 3.6 million lens fibers 505
The lens capsule encloses the lens shells and epithelium 507
The locations at which the zonule inserts onto the lens change with age 510

The Lens as an Optical Element 513
The refractive index of the ocular lens varies from one part of the lens to another 513
Lens transparency is related not only to protein regularity but also to water content, which is maintained by ion pumping in the epithelium 514
The lens contains several different optical zones 515
The lens surfaces are parabolic and therefore flatten gradually from the poles to the equator 516
Both anterior and posterior lens surfaces become more curved with accommodation, but the anterior surface change is larger 519
The lens thickens with age and its curvatures increase, but unaccommodated lens power does not increase with age 520
The increased lens surface curvatures in accommodation are primarily a consequence of tissue elasticity 522
Presbyopia is largely, if not solely, associated with age-related changes in the lens 525
Cataracts, most of which are age-related, take different forms and can affect any part of the lens 526

The Vitreous 530
The vitreous is the largest component of the eye 530
The primary structural components of the vitreous are collagen and hyaluronic acid 530
The external layer of the vitreous—the vitreous cortex—attaches the vitreous to surrounding structures 532
Inhomogeneity of the vitreous structure produces internal subdivisions in the vitreous 533
The vitreous changes with age 533
Shrinkage of the vitreous gel may break attachments to the retina 536
Altered activity of cells normally present in the vitreous or the introduction of cells from outside the vitreous may produce abnormal collagen production and scar formation 537
Vitrectomy removes abnormal portions of the vitreous 538

Development of the Lens and Vitreous 539
The lens forms from a single cell line 539
Most failures of lens development are manifest as congenital cataracts 540
The primary vitreous forms around the embryonic hyaloid artery 541
The secondary vitreous, initially acellular, forms outside the vasa hyaloidea propria 541
Most developmental anomalies in the vitreous represent incomplete regression of the hyaloid artery system 541

VIGNETTE 12.1 Putting the Lens in Its Proper Place 512
BOX 12.1 Cataract Surgery 528

Chapter 13 Retina I: Photoreceptors and Functional Organization 545
The Retina's Role in Vision 545
The retina detects light and tells the brain about aspects of light that are related to objects in the world 545
Objects are defined visually by light and by variations in light reflected from their surfaces 546
The retina makes sketches of the retinal image from which the brain can paint pictures 547

Functional Organization of the Retina 549
Photoreceptors catch photons and produce chemical signals to report photon capture 549
Photoreceptor signals are conveyed to the brain by bipolar and ganglion cells 551
Lateral pathways connect neighboring parts of the retina 552
Reciprocal pathways may assist in adjusting the sensitivity of the retina 554
The retina has anatomical and functional layers 555

Catching Photons: Photoreceptors and Their Environment 560
Each photoreceptor contains one of four photopigments, each of which differs in its spectral absorption 560
Color vision requires more than one photopigment 562
The photopigments are stacked in layers within the outer segments of the photoreceptor 564
Light absorption produces a structural change in the photopigments 565
Structural change in the photopigment activates an intracellular second-messenger system using cGMP as the messenger 566
A decrease in cGMP concentration closes cation channels, decreases the photocurrent, and hyperpolarizes the photoreceptor 568
Absorption of one photon can produce a detectable rod signal 570
Photocurrent in the outer segment decreases in proportion to the number of absorbed photons 572
Photopigments activated by photon absorption are inactivated, broken down, and then regenerated 573
Photoreceptor sensitivity is modulated by intracellular Ca²⁺ 575
Changes in photoreceptor sensitivity account for less than half of the retina's sensitivity increase in the dark and sensitivity decrease in the light 578
The tips of photoreceptor outer segments are surrounded by pigment epithelial cell processes. The pigment epithelium and the interphotoreceptor matrix are necessary for photopigment regeneration. Both rods and cones undergo a continual cycle of breakdown and renewal. The inner segments of photoreceptors assemble the proteins to construct the outer segment membranes. The inner segments form tight junctions with Müller’s cells; these junctions are the external limiting membrane. Photoreceptors signal light absorption by decreasing the rate of glutamate release from their terminals. Glutamate release from a photoreceptor is subject to modification by activity in other photoreceptors.

Chapter 14 Retina II: Editing Photoreceptor Signals

The Editing Process

Interactions among Photoreceptors, Horizontal Cells, and Bipolar Cells

Horizontal cells integrate photoreceptor signals. Horizontal cells receive inputs from photoreceptors and send signals of opposite sign back to the photoreceptor terminals, using GABA as the neurotransmitter. Horizontal cell connections emphasize differences in illumination between different photoreceptors. Different glutamate receptors on cone bipolar cells cause increases and decreases in light intensity to be reported by ON and OFF bipolar cells, respectively. Signals from both red and green cones go to midget bipolar cells, which are specific for cone type, and to diffuse bipolar cells, which are not cone specific. Blue cones have their own bipolar cells. Rods have sign-inverting synapses to rod bipolar cells, which do not contact ganglion cells but send signals to the cone pathways through an amacrine cell.

Interactions among Bipolar Cells, Amacrine Cells, and Ganglion Cells

Bipolar cell terminals in the inner plexiform layer release glutamate at synapses to amacrine or ganglion cells and receive inputs from amacrine cells. Bipolar cells terminate at different levels within the inner plexiform layer, thereby creating functional sublayers. Amacrine cells vary in the extent over which they promote lateral interactions among vertical pathways and in the levels of the inner plexiform layer in which they operate. Amacrine cells exert their effects mainly at glycine and GABA synapses, while several other neurotransmitters or neuromodulators play subsidiary roles.

Ganglion Cell Signals to the Brain: Dots for the Retinal Sketches

Most ganglion cells are midget or parasol cells. The small region of the world seen by a ganglion cell is its receptive field. The concentric organization of excitation and inhibition makes ganglion cells sensitive to contrast rather than to average light intensity. Ganglion cell receptive fields can be thought of as filters that modify the retinal image. Sensitivity functions of ganglion cell receptive fields differ in size and in the strength of their inhibitory components. Ganglion cell signals differ in their reports on stimulus duration and on the rate of intensity change. Midget ganglion cells have wavelength information embedded in their signals, but only small bistratified cells are known to convey specific wavelength information. Axons from midget and parasol ganglion cells go to different layers in the lateral geniculate nucleus. Ganglion cell responses are the elements of retinal sketches.

Chapter 15 Retina III: Regional Variation and Spatial Organization

Making Retinal Sketches out of Dots: Limits and Strategies

The detail in a sketch is limited by dot size and spacing, and cones set the dot size in the central retina. The entire retinal image cannot be sketched in great detail. Most retinas are organized around points or lines. Retinal sketches should be continuous, with no unnecessary blank spots. Tilings do not need to be regular, and tiles do not have to be the same size. Tilings formed by axonal or dendritic arbors at different levels of the retina need not match precisely. The fovea is a depression in the retina where the inner retinal layers are absent.
The spatial distribution of a pigment in and around the fovea is responsible for entoptic images associated with the fovea.

Photoreceptor densities vary with respect to the center of the fovea, where cones have their maximum density and rods are absent.

The human retina varies from center to periphery in terms of the spatial detail in the retinal sketch.

Maximum cone densities vary among different retinas by a factor of three.

The human retina has about 4.5 million cones and 91 million rods.

Blue cones have a different distribution than red and green cones: the center of the fovea is dichromatic.

There are more red cones than green cones, and more green cones than blue cones.

The distribution of different types of cones is neither regular nor random.

Cone pedicles probably tile the retina in and near the fovea, but rod spherules probably never form a single-layered tiling.

The pedicles of cones in and near the fovea are displaced radially outward from the cone inner segments, but spatial order is preserved.

The density of horizontal cells is highest near the fovea and declines in parallel with cone density.

Neither H1 nor H2 horizontal cells form tilings.

All types of cone and rod bipolar cells are distributed like their photoreceptor types.

The different types of bipolar cells provide different amounts of coverage with their dendrites.

All bipolar cell terminals form tilings at different levels in the inner plexiform layer.

All amacrine cells tile the retina, varying in density as ganglion cells do.

Medium- and large-field amacrine cells are low-density populations whose processes generate high coverage factors.

Ganglion cell density declines steadily from the parafovea to the periphery of the retina.

Midget and parasol ganglion cell dendrites tile at different levels in the inner plexiform layer.

Spatial resolution is limited by cone spacing in the fovea and parafovea and by midget ganglion cells elsewhere in the retina.

**A Final Look at Three Small Pieces of Retina: Dots for the Retinal Sketches**

A sampling unit is the smallest retinal region containing at least one representative from each type of ganglion cell.

Sampling units are smallest at the foveal center and are dominated by cone signals.

Rods and blue cones become significant in the parafoveal sampling units.

Rods and rod pathways dominate in peripheral sampling units.

The problem of understanding how the retina works can be reduced to the problem of understanding its sampling units.

The central representation of a sampling unit depends on the number of ganglion cells it contains.

**BOX 15.1 Locating Species of Molecules: Immunohistochemistry**

**Chapter 16 The Retina In Vivo and the Optic Nerve**

**Electrical Signals and Assessment of Retinal Function**

A difference in electrical potential exists between the vitreal and choroidal surfaces of the retina and between the front and back of the eye.

The electroretinogram measures a complex change in voltage in response to retinal illumination.

The a-wave and off effect are generated by the photoreceptors, the c-wave by the pigment epithelium.

The b-wave is either a direct reflection of ON bipolar cell activity or is indirectly related to their activity by a secondary potential arising from Müller’s cells.

The ERG is useful as a gross indicator of photoreceptor function.

Multifocal ERGs provide assessments of retinal function within small areas of the retina.

**The Retinal Vessels and Assessment of Retinal Health**

The retina in vivo is invisible.

Since the choroidal circulation is usually not directly visible, irregularities and nonuniformities on the fundus are commonly indicators of pathology.

The central retinal artery is an end-arterial system.

The capillaries supplied by the central retinal artery ramify in the inner two-thirds of the retina.

Retinal detachment separates photoreceptors from their blood supply.

The foveal center lacks capillaries.

Retinal capillaries are specialized to create a blood–retina barrier.

Retinal blood flow is autoregulated.

The arterial and venous branches on the retinal surface can be distinguished ophthalmoscopically.

Drainage of the inner retina is segmental.

**The Optic Nerve**

All ganglion cell axons and all branches of the central retinal artery and vein converge at the optic nerve head.

The nerve head and the optic nerve consist primarily of axon bundles separated by sheaths of glial cells and connective tissue.

The blood supply and drainage differ between the pre- and postlaminar portions of the nerve head.
Ganglion cell axons form a stereotyped pattern as they cross the retina to the optic nerve head 722
Axons from many widely separated ganglion cells are collected in bundles in the nerve fiber layer 723
Axon bundles have an orderly arrangement in the nerve head 724
Scotomas observed in advanced stages of glaucoma correspond to those produced by lesions along the superior and inferior temporal margin of the nerve head 727
The lamina cribrosa is weaker than the rest of the sclera 727
Field defects in glaucoma may be due to blockage of axonal transport secondary to deformation of the lamina cribrosa 728
Ganglion cell loss in experimental glaucoma does not appear to be selective by cell type or axon diameter 730

Development of the Retina and Optic Nerve 732
The retina develops from the two layers of the optic cup 732
Retinal development proceeds from the site of the future fovea to the periphery 733
Retinal neurons have identifiable birthdays 733
Ganglion cells, horizontal cells, and cones are the first cells in the retina to be born 733
As distance from the fovea increases, the firstborn cells appear at progressively later dates 735
Synapse formation has a center-to-periphery gradient superimposed on a gradient from inner retina to outer retina 736
The location of the future fovea is specified very early; the pit is created by cell migration 737
Foveal cones are incomplete at birth 737
Photoreceptor densities are shaped by cell migration and retinal expansion 739
Ganglion cell density is shaped by migration, retinal expansion, and cell death 740
The spatial organization of the retina may depend on specific cell–cell interactions and modifications of cell morphology during development 741
Retinal blood vessels develop relatively late 743
Developing vessels are inhibited by too much oxygen 744
The optic nerve forms as tissue in the optic stalk is replaced with developing ganglion cell axons and glial cells 745

Fusion of the optic stalks produces the optic chiasm, where pioneering axons must choose the ipsilateral or contralateral path 746
The last stages of development in the optic nerve are axon loss and myelination 746
The inner retina seems relatively immune to congenital anomalies 748
The most common developmental anomalies are failures to complete embryonic structures or eliminate transient structures 748

BOX 16.1 Fluorescein Angiography and the Adequacy of Circulation 710

Epilogue Time and Change 753

Postnatal Growth and Development 753
The newborn eye increases in overall size for the next 15 years 753
Refractive error is quite variable among newborn infants, but the variation decreases with growth 754
Visual functions mature at different rates during the first 6 years of life 756
Changes in the lens and vitreous that begin in infancy continue throughout life 758

Maturation and Senescence 759
The average refractive error is stable from ages 20 to 50, but the eye becomes more hyperopic and then more myopic later in life 759
Although the gross structure of the eye is stable after the age of 20, tissues and membranes are constantly changing 760
Retinal illuminance and visual sensitivity decrease with age 761
Visual acuity declines after age 50, largely because of optical factors 763

Historical References and Additional Reading HR–1

Glossary G–1

Index I–1