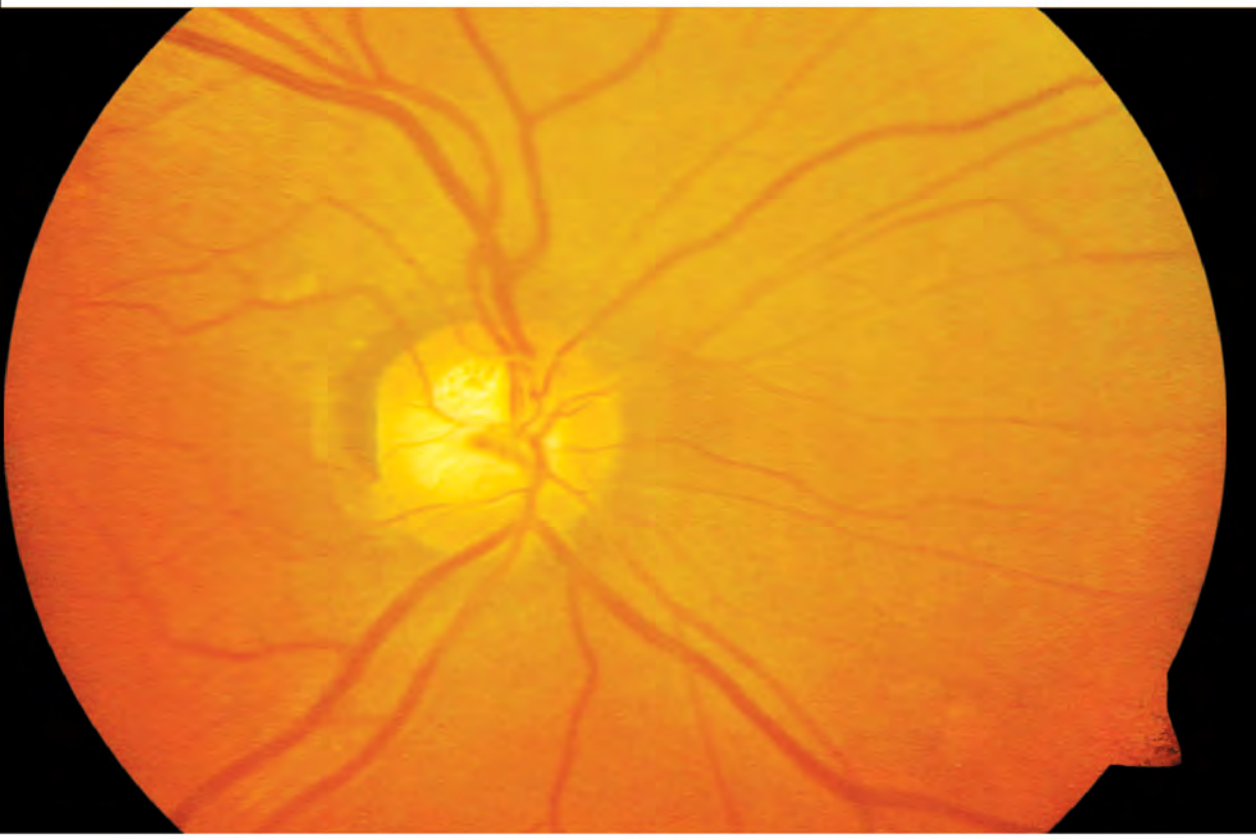
website **www.jaypeebrothers.com,** for detailed information on ophthalmology books, visit our website **www.jaypeebrothers.com**

Manual of GLAUCOMA



Editors
Shibal Bhartiya
Parul Ichhpujani

Foreword
George L Spaeth

JAYPEE

Contents

Section 1: Basic Fundamentals

1. Anatomy of Optic Nerve Head **3**

Nishita Beke, Parul Ichhpujani

- Why Must We Know About the Anatomy of Optic Nerve Head? *3*
- What is the Chronology of the Development of an Optic Nerve? *3*
- What is a "Normal" ONH? *4*
- What is the Blood Supply of ONH? *6*
- What is the "Autoregulation" of ONH Blood Supply? *7*
- What Connective Tissue forms the Support Framework of ONH? *7*
- How Does ONH Biomechanics Change in Glaucoma? *8*

2. Anatomy of the Anterior Chamber Angle **10**

Ravi Bamotra, Parul Ichhpujani

- What is Anterior Chamber Angle? *10*
- Why do We Need to Know the Anatomy of Anterior Chamber Angle? *10*
- What forms the Boundaries of Anterior Chamber Angle? *10*
- Which Structures form the Angle of Anterior Chamber? *11*
- Surgical Limbus *14*

3. Physiology and Dynamics of Aqueous Humor **16**

M Reza Razeghinejad, M Hossein Nowroozzadeh

- Why Must I Read about Aqueous Humor? *16*
- What is "Normal" Anatomy and Physiology of Aqueous Production and Outflow? *16*
- Aqueous Outflow *19*
- What is the Relation between Aqueous Humor and Intraocular Pressure? *22*
- What Changes in Glaucoma? *22*
- Important Stuff for Clinical Practice: Applied Anatomy and Physiology *25*

4. Pathogenesis of Glaucoma **28**

Monica Gandhi

- Why Must I Read About the Pathogenesis of Glaucoma? *28*
- What Happens in Glaucoma? *28*
- Where Does the Damage Occur? *28*
- How Does the Damage Occur? *28*
- What Important Stuff Must be Known for Clinical Practice? *29*
- What are the Clinical Correlates? *33*

5. Classification of the Glaucomas **35**

Anuj Sharma, Parul Ichhpujani

- Why Must We Know the Classification System? *35*
- What is the "Terminology" for Various forms of Glaucoma? *35*
- What is the Basis of Classification of Glaucomas? *36*

Section 2: Diagnosis Clinchers

6. Tonometry **45**

Paaraj Dave, Nikhil Chaudhary

- What is Tonometry? *45*
- Why do We Need Tonometry? *45*
- Who all need Tonometry? *45*
- What is the Required Instrumentation? *46*
- How to Perform Indentation Tonometry using Schiotz's Tonometer? *46*
- What is the Verdict for Schiotz Tonometer? *48*
- How to Perform Non-Contact Tonometry? *50*
- What is the Verdict for NCT? *51*
- How to Perform Applanation Tonometry using GAT? *51*
- How to Detect Calibration Error of the GAT? *55*
- How to Disinfect GAT Prism? *56*
- What is the Verdict for GAT? *57*
- What is the Verdict for Tonopen? *58*
- How to Perform Contact Tonometry using DCT? *59*
- What is the Verdict for DCT? *59*
- What is the Verdict for ORA? *61*
- What is the Verdict for Rebound Tonometer? *62*

7. Pachymetry in Glaucoma **68**

Oana Stirbu, Oscar Buchacra Castellano

- Principles *68*

- Who all Need the Test? When do We Repeat the Test? *69*
- What is the Required Instrumentation? *69*
- How to Perform the Test? *70*
- What is the Scientific Verdict? *71*
- Clinical Examples *71*

8. Optic Nerve Head Evaluation **75**

Anne Poulsen, Scott Fudemberg

- Test *75*
- Why do We Need to Evaluate the Optic Nerve? *75*
- Who Needs the Test? *75*
- What is the Required Instrumentation for Optic Nerve Head Evaluation? *76*
- How to Perform the Test? *78*
- What is the Scientific Verdict? *88*

9. Gonioscopy **89**

Sushmita Kaushik, Rishi Raj Singh, Neiwete Lomi
Surinder Singh Pandav

- Test *89*
- Principle of Gonioscopy *89*
- Why do We Need Gonioscopy? *89*
- What are the Contraindications for Performing Gonioscopy? *90*
- When to Do Gonioscopy? *91*
- What is the Required Instrumentation for Gonioscopy? *91*
- How to Perform Gonioscopy? *93*
- Indentation Gonioscopy *94*
- Artifacts When Performing Gonioscopy *95*
- What are the Structures of Anterior Chamber Angle Seen Through a Gonioscope? *96*
- How to Grade the Angle? *100*
- Classification of the Angle *101*
- How to Disinfect Goniolenses? *102*

10. Ultrasound Biomicroscopy **104**

Marc Andre Bagnoud, Shibal Bhartiya

- Test *104*
- Why do We Need the Test? *104*
- How to Perform the Test? *104*
- What is the Required/Available Instrumentation? *104*
- Points of Importance During the Evaluation *106*

11. Automated Perimetry: A Synopsis **118**

Murali Ariga

- What is Visual Field *118*
- What are the Basic Perimetry Techniques? *118*
- History of Automation and Statistical Analysis *120*
- What is the Basic Terminology in Relation to Perimetry? *120*
- What is the Required Instrumentation? *122*
- How to do a Visual Field Test? *123*
- What Instructions should be given to the Patient? *124*
- Which Program to Select? *124*
- Which Testing Strategies to Use? *124*
- What are the Characteristics of a Typical Glaucomatous Visual Field? *128*
- Severity of Field Changes (HODAPP, Anderson and Parrish Classification) *130*
- Short Wavelength Automated Perimetry and Frequency Doubling Perimetry *130*
- How to Detect Progression of Visual Field Changes in Glaucoma? *130*
- What is the Difference Between Fluctuation and Progression? *131*
- How Frequently should Visual Fields be done to Assess Glaucoma Progression? *132*
- What are Event and Trend-Based Analyses? *133*
- Progression Analysis using Octopus Eyesuite Perimetry *135*

12. Frequency Doubling Technology Perimetry **139**

Mona Khurana, Aditya Neog

- What is Frequency Doubling Technique Perimetry? *139*
- What is Frequency Doubling? *139*
- Who Need the FDT Perimetry? *140*
- What is the Required Instrumentation? *140*
- What is the Stimulus? *141*
- What are the Test Patterns? *142*
- How to Calibrate the FDT Perimeter? *143*
- How is the FDT Perimetry Test Performed? *144*
- How to Interpret a FDT Perimetry Printout? *146*
- Zone 1: General Information *147*
- When to Label a FDT Test as "Abnormal"? *149*
- FDT Matrix: Updated FDT Perimeter *150*
- Software Upgrades in FDT Matrix Perimeter *151*
- What is the Scientific Verdict for FDT Perimetry? *153*

13. Optical Coherence Tomography for Glaucoma 156
Shibal Bhartiya, Parul Ichhpujani
- Test *156*
- Why the Shift from time Domain OCT and Spectral Domain OCT? *156*
- Why do We Need the Test? *157*
- Who all Need the Test? When do We Repeat the Test? *157*
- What are the Limitations of the TDOCT When used for RNFL Thickness Analysis? *158*
- What is the Required Instrumentation? *158*
- How to Perform the Test? *159*
- Retinal Nerve Fiber Layer *159*
- Optic Nerve Head *160*
- Ganglion Cell Analysis *160*
- Guided Progression Analysis *160*
- Spectralis Posterior Pole Asymmetry Analysis *162*
- What is the Scientific Verdict? *162*

14. Anterior Segment Optical Coherence Tomography in Glaucoma 165
Oscar Albis-Donado, Giovanna Casale-Vargas
- What is Anterior Segment Optical Coherence Tomography? *165*
- How does ASOCT Work? *165*
- Why do We Need ASOCT? *166*
- ASOCT and Glaucoma *166*
- Other Uses *168*
- What is the Required Instrumentation? *169*
- How to Perform the Test? *170*
- What is the Scientific Verdict? *171*
- Clinical Examples *171*

15. Confocal Scanning Laser Tomography: Heidelberg Retina Tomograph 180
Vinay Nangia
- What is the Principle of Confocal Scanning Laser Tomography? *180*
- How is the Optic Disc Imged? *181*
- Which Parameters are Assessed by HRT? *182*
- Progression Analysis *184*
- Clinical Cases *185*
- What is the Scientific Evidence/Verdict? *191*

Section 3: Open Angle Glaucomas

16. Glaucoma Suspects **195**

Sally Ameen, Laura Crawley

- What is a Glaucoma Suspect? *195*
- When should you Suspect Glaucoma in a Patient? *196*
- Who is at Risk of Developing Glaucoma? *197*
- How do Glaucoma Suspects Present? *197*
- What is the Natural History of Glaucoma? *197*
- What to do with a Patient Referred as a Glaucoma Suspect? *198*
- How to Follow up Glaucoma Suspects? *201*
- What are the Indications to Commence Treatment in Glaucoma Suspects? *202*

17. Ocular Hypertension **204**

Anjum Koreishi, Leonard K Seibold

- What is Ocular Hypertension? *204*
- Who is at Risk? *204*
- What Causes Ocular Hypertension? *204*
- How Does it Present? *204*
- What is the Natural Course of the Disease? *205*
- How Do I Manage Ocular Hypertension? *205*
- Follow-Up: When and How? *206*

18. Primary Open-Angle Glaucoma **208**

Anne Lee, Ivan Goldberg

- What is Primary Open-Angle Glaucoma? *208*
- Who is at Risk? *208*
- What Causes POAG? *210*
- How Does it Present? *211*
- What are the Symptoms of Glaucomatous Scotomata? *211*
- What is the Natural Course of the Disease? *212*
- How to Manage POAG? *212*
- What if Cataract and POAG Coexist? *227*
- How to Follow-Up a Patient of POAG? *229*

19. Normal Tension Glaucoma **234**

Dexter Yl Leung, Jennifer WH Shum, Jonathan Ch Ho, WL Ho, Clement CY Tham, Jimmy SM Lai

- What is Normal Tension Glaucoma? *234*
- Who is at Risk? *234*
- What Causes NTG? *236*

- What is the Natural Course of NTG? *240*
- How to Diagnose, Manage, and Follow Up NTG Patients? *241*

20. Pseudoexfoliation Glaucoma **250**

Jed Lusthaus, Colin Clement

- What is Pseudoexfoliation Glaucoma? *250*
- Who is at Risk? *250*
- What Causes PXF and PXFG? *250*
- How Does it Present? *251*
- What is the Natural Course of the Disease? *252*
- How to Manage PXFG? *252*
- Follow-Up: When and How? *254*

21. Pigmentary Glaucoma **255**

Parul Ichhpujani

- What is Pigmentary Glaucoma? *255*
- Who is at Risk? *255*
- What Causes PG? *255*
- How Does it Present? *256*
- What is the Natural Course of the Disease? *258*
- How to Manage PG? *258*
- Follow-Up: When and How? *259*

22. Traumatic Glaucoma **260**

Parul Ichhpujani

- What is Traumatic Glaucoma? *260*
- Who is at Risk? *260*
- What is the Pathogenesis of Traumatic Glaucoma? *260*
- How Does it Present? *263*
- What is the Natural Course of the Disease? *264*
- How to Manage Traumatic Glaucoma? *264*
- Follow-Up: When and How? *265*

23. Steroid-Induced Glaucoma **267**

Rita Dhamankar

- What is Steroid-Induced Glaucoma? *267*
- Who is at a Greater Risk? *267*
- What Causes Steroid-Induced Glaucoma? *268*
- How Steroids Alter TM Function? *268*
- How Does it Present? *269*
- What is the Natural Course of the Disease? *270*
- How to Manage? *271*

- Perspective *272*
- Follow-Up: When and How? *273*

24. Glaucoma in Systemic Affections **275**

Vinita Gupta

- Why Must We Know About any Systemic Disease a Patient with Glaucoma may Have? *275*
- Which Systemic Inflammatory and Infectious Conditions are Associated with Raised Intraocular Pressure? *275*
- What is the Association between Glaucoma and Elevated Episcleral Venous Pressure? *278*
- What is the Association between Glaucoma and Vascular and Hematologic Disorders? *278*
- What is the Association between Glaucoma and Neoplasia? *278*
- Is there any Syndromal Association between Glaucoma and Systemic Disorders? *279*
- Are there any Forms of Glaucoma Having an Uncertain Relationship and Systemic Diseases? *281*

Section 4: Angle Closure Glaucoma

25. Angle Closure Glaucoma **285**

Victor T Koh, Chelvin CA Sng, Maria Cecilia Aquino Joel Aduan, Paul TK Chew

- What is Angle Closure? *285*
- Who is at Risk of Angle Closure Glaucoma? *286*
- What are the Mechanisms of Angle Closure? *286*
- How do We Assess the Anterior Chamber Angle? *288*
- How does Angle Closure Present? *289*
- What is the Natural Course of the Disease? *292*
- How do I Manage Angle Closure? *292*
- Follow-Up: When and How? *297*

26. Uveitic/Inflammatory Glaucoma **302**

Parul Ichhpujani

- What is Uveitic/Inflammatory Glaucoma? *302*
- Who is at Risk? *302*
- What Causes Uveitic/Inflammatory Glaucoma? *302*
- How Does it Present? What is the Natural Course of the Disease? *303*

- How to Manage Uveitic/Inflammatory Glaucoma? *306*
- Follow-Up: When and How? *306*

27. Neovascular Glaucoma **308**

Parul Ichhpujani

- What is Neovascular Glaucoma? *308*
- Who is at Risk? *308*
- What Causes NVG? *310*
- How does it Present? *310*
- What is the Natural Course of the Disease? *311*
- How to Manage NVG? *312*
- Follow-Up: When and How? *313*

28. Lens-Induced Glaucoma **315**

Barun K Nayak, Sachin Dharwadkar

- What are Lens-Induced Glaucomas? *315*

29. Malignant Glaucoma **327**

Elena Milla

- What is Malignant Glaucoma? *327*
- Who is at Risk? *327*
- What Causes Malignant Glaucoma? *327*
- How does it Present? *328*
- What is the Natural Course of the Disease? *328*
- How to Manage Malignant Glaucoma? *328*
- Follow-Up: When and How? *329*

30. Postoperative Glaucoma **334**

Wanda D Hu, Marlene R Moster

- Uveitic-Glaucoma-Hyphema Syndrome *334*
- Steroid-Induced Glaucoma *336*
- Silicone Oil-Induced Glaucoma *339*
- Glaucoma after Scleral Buckling Surgeries *341*
- Glaucoma after Intravitreal Gas *342*
- Aqueous Misdirection *343*
- Suprachoroidal Hemorrhage *347*

Section 5: Childhood Glaucoma

31. Congenital and Developmental Glaucomas **353**

Oscar Albis-Donado, Giovanna Casale-Vargas

- What are Congenital and Developmental Glaucomas? *353*

- Who is at Risk? *354*
- What Causes Congenital Glaucoma? *355*
- How does it Present? *356*
- Glaucomas Associated with Nonacquired Ocular Anomalies *359*
- What is the Natural Course of the Disease? *366*
- How to Manage Glaucoma in Children? *367*
- Management *370*
- Follow-Up: When and How? *372*

Section 6: Battling Glaucoma

32. Glaucoma Progression **379**

Colin Clement

- What is Glaucoma Progression? *379*
- In Whom do We Monitor for Progression? *379*
- How to Assess for Progression? *379*
- What is the Scientific Verdict? *382*

33. Medical Management of Glaucoma **384**

Shibal Bhartiya, Parul Ichhpujani

- Who is "Fit" for Medical Therapy? *384*
- Who is "Not" Fit for Medical Therapy? *385*
- How to Choose the Medication? *386*
- Special Considerations *386*
- What can Go Wrong? *389*
- How Frequently to Follow Up? *390*

34. Selective Laser Trabeculoplasty **393**

Shibal Bhartiya, Parul Ichhpujani

- Who is "Fit" for this Procedure? *394*
- Who is "Not" Fit for this Procedure? *394*
- How to Perform the Procedure? *394*
- What can Go Wrong? *396*
- What is the Scientific Verdict? *396*
- How Frequently to Follow Up Postprocedure? *397*

35. Laser Iridotomy and Iridoplasty **399**

Tin Wai Andrea Liu, Nafees Begum Baig

- Iridotomy (Laser Peripheral Iridotomy) *399*
- Iridoplasty (Argon Laser Peripheral Iridoplasty) *404*

36. Diode Laser Cyclophotocoagulation **407**
Shibal Bhartiya, Parul Ichhpujani
- What is the Principle of Cyclophotocoagulation? *407*
- Who is "Fit" for this Procedure? *408*
- Who is "Not" Fit for this Procedure? *408*
- How to Perform the Procedure? *408*
- How Frequently to Follow Up Post-Procedure? *409*
- What can Go Wrong? *411*
- What is the Scientific Verdict Versus other Similar Options? *411*

37. Endoscopic Cyclophotocoagulation **413**
Steven Schendel, Colin Clement
- What is Endoscopic Cyclophotocoagulation? *413*
- Who is "Fit" for this Procedure? *413*
- Who is "Not" Fit for this Procedure? *413*
- What is the Instrumentation Required? *414*
- How to Perform the Procedure? *414*
- What can Go Wrong? *416*
- What is the Scientific Verdict? *416*
- How to Follow Up Post-ECP? *416*

38. Nonpenetrating Deep Sclerectomy **418**
Sangtam Tiakumzuk, Mermoud André
- Who is "Fit" for this Procedure? *418*
- Who is "Not" Fit for this Procedure? *418*
- How to Perform the Procedure? *418*
- What can Go Wrong? *427*
- What is the Scientific Verdict Versus other Similar Options? *428*
- How Frequently to Follow-Up Post-Procedure? *428*

39. Modern Trabeculectomy **429**
Parul Ichhpujani, Shibal Bhartiya
- Who is "Fit" for this Procedure? *429*
- Who is "Not" Fit for this Procedure? *429*
- How to Perform the Procedure? *430*
- What can Go Wrong? *434*
- How Frequently to Follow Up Post-Procedure? *434*
- What is the Scientific Verdict? *437*

40. Glaucoma Drainage Devices **439**

Shibal Bhartiya, Oscar Albis Donado, Parul Ichhpujani

- What are Glaucoma Drainage Devices? *439*
- Who are "Fit" for GDDs? *439*
- Does "One Size" Fit all? *439*
- Who are "Unfit" for GDDs? *440*
- What are the Types of GDDs? *440*
- What are the Criteria for Choosing a GDD? *443*
- How to Perform a GDD Surgery? *443*
- Who can have Complications with Glaucoma Implants? *447*
- What are the Most Frequent Complications with all Glaucoma Implants? *447*
- How to Manage the Most Common Intraoperative Complications? *447*
- How to Manage the Most Common Early Postoperative Complications? *450*
- How to Manage the Most Common Late Postoperative Complications? *451*
- What is the Scientific Verdict? *453*

41. Newer Surgical Procedures **457**

Parul Ichhpujani, Shibal Bhartiya

- Who all are "Fit" and "Unfit" for the Newer Procedure? *457*
- What are the Anatomical Principles for these Procedures? *457*
- What can Go Wrong? *464*
- What is the Scientific Verdict Versus other Similar Options? *464*

42. Wound Healing **467**

Sonia Corredor-Casas, Nadia Rios-Acosta

- What is the Basic Physiology of Wound Healing? *468*
- Highlights of Pharmacological Modulation of Wound Healing *470*
- Future Perspectives *483*

43. Postoperative Management after Trabeculectomy **487**

Prakashchand Agarwal, Mary Jenifa Tigga

- What forms the Standard Post-Trabeculectomy Regimen? *487*
- What are the Early Postoperative Complications Following Trabeculectomy? *490*
- What are the Late Postoperative Complications? *495*

- Blebitis *496*
- Bleb Related Endophthalmitis *497*

44. Complementary and Alternate Therapies **498**

Shibal Bhartiya, Parul Ichhpujani

- What are the Current Concepts of Holistic Healing for Glaucoma? *498*
- Who is "Fit" for CAM? *498*
- Who is "Not" Fit for CAM? *499*
- What are the Available Options? *499*
- What can Go Wrong? *500*
- What is the Scientific Verdict Versus other Similar Options? *500*

Index *503*

Physiology and Dynamics of Aqueous Humor

3

M Reza Razeghinejad, M Hossein Nowroozzadeh

WHY MUST I READ ABOUT AQUEOUS HUMOR?

Knowledge about physiology and dynamics of aqueous humor is fundamental to in-depth understanding of glaucoma pathophysiology and its management.

The aqueous humor has several important functions in the human eye, which are as follows:

- It provides nutrients (e.g. glucose and amino acids) and removes metabolic waste products for most avascular surrounding tissues such as cornea, trabecular meshwork (TM), and crystalline lens.
- Normal aqueous humor dynamics is also essential to maintain appropriate intraocular pressure (IOP), which is necessary for the proper shape and optical properties of the eye.
- The optically clear aqueous humor (devoid of blood cells and >99% of the plasma proteins) helps for optimal light transmission. With a refractive index of 1.33332, the aqueous humor constitutes an important component of the eye's optical system.

WHAT IS "NORMAL" ANATOMY AND PHYSIOLOGY OF AQUEOUS PRODUCTION AND OUTFLOW?

Aqueous Production

Anatomy

- Ciliary processes are composed of a double layer of epithelium overlying a core of stroma and a large number of fenestrated capillaries, which are derived from major arterial circle of the iris.
- Ciliary epithelium is constituted from two layers (Fig. 3.1): the non-pigmented ciliary epithelium (NPE), which faces the aqueous, and the underlying pigmented ciliary epithelium (PE).
- The apical surfaces of NPE and PE face each other and are connected through gap junctions.
- Blood aqueous barrier in the ciliary epithelium is established by the tight junctions proximal to apical plasma membrane of the NPE.

JAYPEE BROTHERS

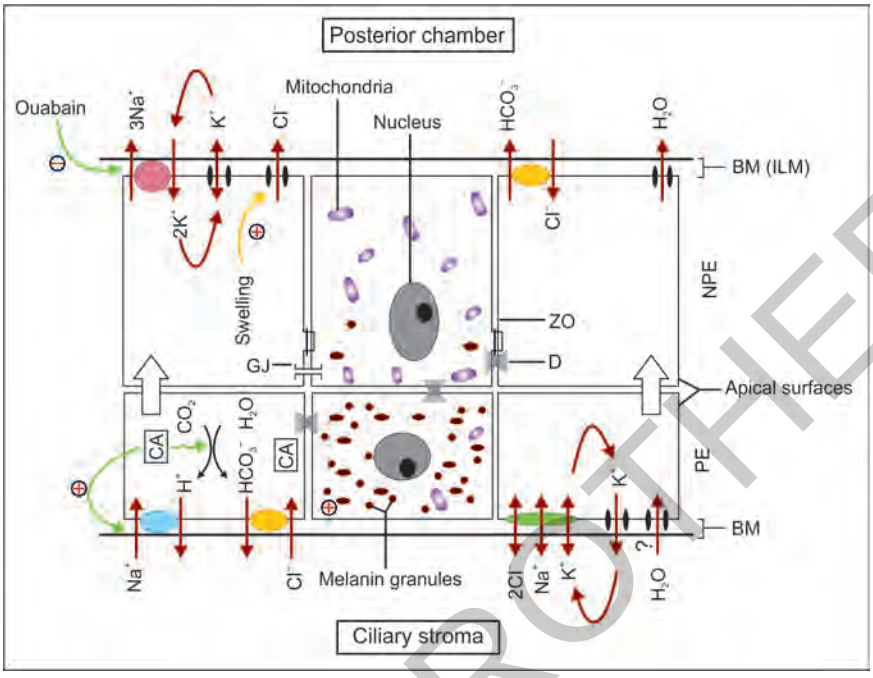


Fig. 3.1: Unidirectional secretion of aqueous humor by the ciliary epithelium bilayer. (BM: Basement membrane; CA: Carbonic anhydrase enzyme; D: Desmosomes; GJ: Gap junctions; ILM: Internal limiting membrane; NPE: Nonpigmented epithelium; PE: Pigmented epithelium; ZO: Zonula occludens).

- Pigmented ciliary epithelium is a leaky epithelium.
- Tight junctions are also present in the endothelium of the inner wall of Schlemm's canal, preventing retrograde movement of fluid and solutes back into the anterior chamber.
- Iridal vascular endothelium and iris epithelium have tight junctions and do not leak.
- Capillaries of the ciliary processes and choroid are fenestrated and leaky.
- Both sympathetic and parasympathetic nerve terminals are present in the ciliary body.

Physiology

- The NPE contains numerous mitochondria and microvilli and is thought to be the actual site of aqueous production.
- The average flow rate of aqueous secretion is 2.2–3.1 μL/min and gradually decreases with age by approximately 4% per decade of life.
- The rate of aqueous volume turnover is about 1–1.5% of the anterior chamber volume per minute.
- Fluorophotometry is the most common method used to measure the rate of aqueous humor formation.

JAYPEE BROTHERS

- Factors controlling the rate of aqueous humor formation include the following:
  - Integrity of the blood–aqueous barrier
  - Blood flow to the ciliary body
  - Neurohumoral regulation of vascular tissue and the ciliary epithelium
  - Circadian rhythm
- Several factors are associated with reduced aqueous humor secretion including:
  - General or systemic
    - Sleep (50% reduction at night)
    - Aging
    - Exercise
    - Hypothermia
    - Acidosis
    - Carotid occlusive disease
    - Administration of certain drugs (e.g. general anesthetics and some systemic hypotensive agents)
  - Ocular
    - Trauma
    - Intraocular inflammation (especially iridocyclitis)
    - Increased IOP
    - Retinal or choroidal detachment
    - Retrobulbar anesthesia
    - Cyclodialysis, cyclocryotherapy, cyclodiathermy, cyclophotocoagulation
- Aqueous humor formation mechanisms
  - Active transport
    - Performed by ciliary epithelium and consumes energy
    - Accounts for the majority of aqueous humor formation (80–90%)
    - Move substances against an electrochemical gradient
    - Independent to pressure
    - Active secretion involves selective active transport systems (e.g. Na^+, K^+-$2Cl^-$ symport, Cl^- - HCO_3^- and Na^+, H^+ antiports, cation channels, water channels, Na^+, K^+ - ATPase, K^+ channels, Cl^- channels, H^+-ATPase); and at least in part, activity of the enzyme carbonic anhydrase II (Fig. 3.1).
  - Ultrafiltration
    - A pressure-dependent movement along a pressure gradient
    - The hydrostatic pressure difference between capillary pressure of ciliary body and IOP favors fluid flow into the eye, while oncotic gradient between the aqueous and ciliary capillaries resists the flow
    - Decreases with increasing IOP

JAYPEE BROTHERS

- Diffusion
  - Refers to the passive movement of ions through a membrane based on their charge and concentration

AQUEOUS OUTFLOW

Anatomy

Trabecular Meshwork

- Trabecular meshwork is roughly a triangular structure bounded anteriorly by periphery of the cornea and posteriorly by scleral spur and anterior surface of the ciliary body.
- Trabecular meshwork is divided into three parts, which are as follows:
  - *Uveal part*: faces the anterior chamber and is organized into bands that spread from the iris root and the ciliary body to the peripheral cornea
  - *Corneoscleral meshwork*: Composed of sheets of trabeculum that extend from the scleral spur to the lateral wall of the scleral sulcus
  - *Juxtacanalicular meshwork*: faces and forms the inner wall of Schlemm's canal
- Trabecular meshwork is a sieve-like multilayer tissue. Cords of the sieve have a collagenous connective tissue core covered by an endothelial layer.
- There are about 1,200,000–1,300,000 trabecular endothelial cells per eye.
- The population of trabecular endothelial cells diminishes with age, and their basement membrane thickens. A rate of 0.58–0.85% per year cell loss is reported.
- In older eyes, the trabecular cells have a large number of pigment granules giving the TM a brown or muddy appearance.

Schlemm's Canal

- Is completely lined with a continuous endothelial layer with tight junctions between neighboring cells, but the underlying basement membrane is discontinuous.
- Is a single channel, with a mean diameter of about 370 μm, which is transversed by tubules.
- Its inner wall comprises giant vacuoles that have direct communication with the intertrabecular spaces.
- The outer wall contains a single layer of endothelial cells that do not have pores.

Collecting Channels and Aqueous Veins

- Approximately 30 collecting channels connect Schlemm's canal with the aqueous veins.

JAYPEE BROTHERS

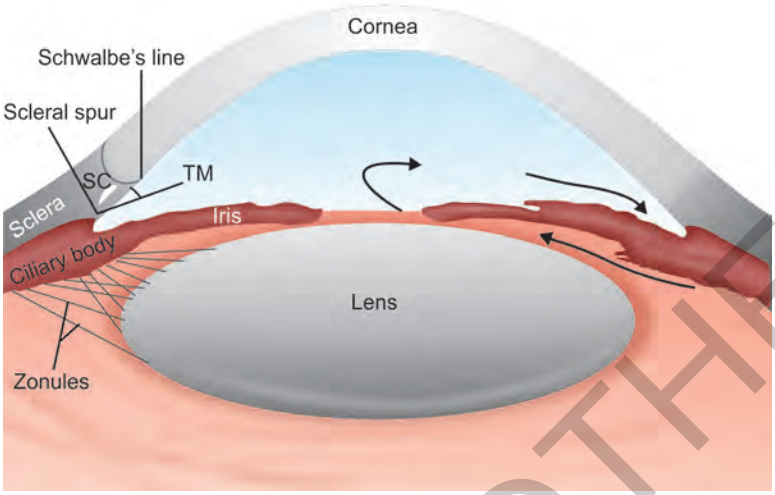


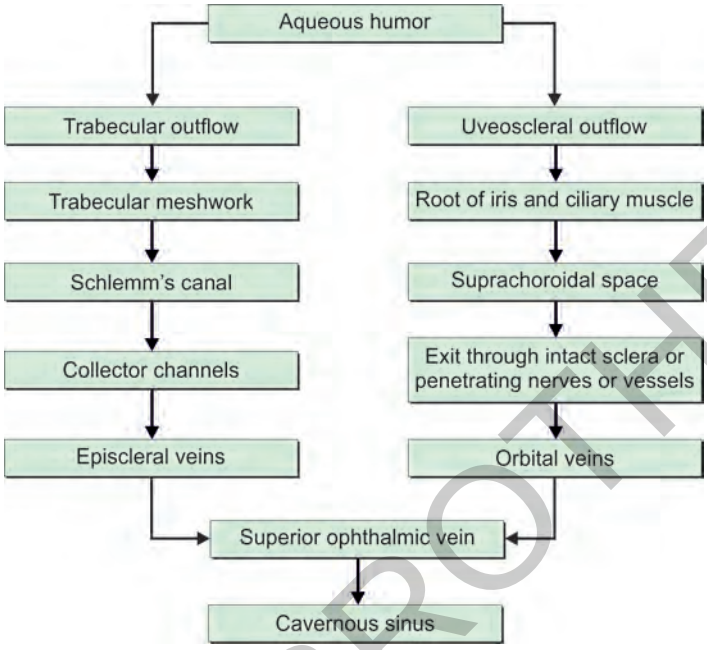
Fig. 3.2: The passage of aqueous humor. Arrows delineate the path of aqueous humor from the posterior chamber, through the pupil, into the anterior chamber angle. (TM: Trabecular meshwork; SC: Schlemm's canal).

Physiology

- Aqueous humor is secreted into the posterior chamber. It then passes around the lens through the pupil into the anterior chamber, where it leaves the chamber by flowing through the outflow pathway (Fig. 3.2).
- Aqueous humor has convection flow in the anterior chamber, where it flows downward near the cornea (cooler temperature) and flows upward near the lens (warmer temperature). Clinically, this movement may be visualized when we have particulate matter such as cells in the anterior chamber.
- Normal outflow facility varies widely (0.22–0.30 μL/min/mm Hg) and has an inverse relation with age. Outflow facility is measured by tonography method.
- Surgery, trauma, medications, and endocrine factors may affect outflow facility.
- The outflow is divided into two main mechanisms: trabecular and uveoscleral outflow (Flowchart 3.1).
  - Trabecular outflow (conventional)
    - A pressure-dependent outflow.
    - The TM is similar to a one-way valve that allows aqueous to leave the eye by bulk flow but resists flow in the other direction, independent of energy.
    - The major site of outflow resistance is believed to be the juxtacanalicular meshwork.

JAYPEE BROTHERS

Flowchart 3.1: Aqueous humor outflow pathways.



- Aqueous flows both across and between the endothelial cells lining the inner wall of Schlemm's canal.
- After Schlemm's canal, the aqueous flows into a plexus of collector channels and subsequently drains into the venous system (aqueous veins, episcleral veins, the anterior ciliary and superior ophthalmic veins, and finally drains into the cavernous sinus).

▪ Uveoscleral outflow (posterior or unconventional)
- A pressure-independent outflow.
- Any nontrabecular outflow is termed uveoscleral outflow.
- Accounts for approximately 35–55% of total aqueous outflow in younger humans.
- Seems to be influenced by age; it is significantly reduced in older people compared with younger individuals.
- *The proposed passage of aqueous*: from the anterior chamber through the root of the iris, uveal meshwork, and the anterior face of the ciliary muscle into the supraciliary and suprachoroidal spaces. Ultimately, the fluid exits the eye through either the intact sclera or along the penetrating nerves or vessels.
- Despite the existence of ion fluxes, there is no significant net fluid passage through vitreoretinal interface, iris vasculature, or cornea.

JAYPEE BROTHERS

- Pumping model in aqueous humor dynamics
  - Is an alternative to the bulk flow model
  - Depends on tissue compliance rather than static resistance
  - Receives power from transient increase in IOP such as
    - Systole of the cardiac cycle.
    - Blinking.
    - Eye movement.
  - The model is supported by the clinical evidence of pulsatile flow into Schlemm's canal

WHAT IS THE RELATION BETWEEN AQUEOUS HUMOR AND INTRAOCULAR PRESSURE?

- The relation of aqueous humor formation and outflow to IOP in a normal eye is summarized by the Goldmann equation:
  - $P_0 = (F/C) + P_V$
  - P_0: IOP (mm Hg); F: rate of aqueous formation (µL/min); C: facility of outflow (µL/min/mm Hg); P_V: episcleral venous pressure (mm Hg).
- In modified Goldmann equation:
  - $P_0 = [(F\text{-USO})/\text{CTM}] + P_V$
  - USO: uveoscleral outflow; CTM: facility of outflow via the TM.

Aqueous Humor Composition

- Table 3.1 summarizes important constituents of the aqueous humor.
- The most remarkable differences between aqueous and plasma constituents are the low protein (200 times less) and high ascorbate (20 times greater) concentrations in the aqueous relative to plasma.
- The high ascorbate concentration, as an antioxidant, may help protect anterior chamber structures (such as trabecular cells) from ultraviolet phototoxicity.
- The excess lactate of the aqueous results from glycolytic activity of the lens, cornea, and other ocular structures.
- The aqueous humor composition dynamically changes as it flows from the posterior chamber, through the pupil, and into the anterior chamber. Dilutional exchanges and active processes across the anterior hyaloid face of the vitreous, the surface of the lens, the blood vessels of the iris, and the corneal endothelium are contributed to this change.

WHAT CHANGES IN GLAUCOMA?

Altered Aqueous Humor Dynamics in Glaucoma

- Glaucoma is inherently linked to the aqueous humor dynamics.
- Disturbance of outflow facility is the major cause of glaucoma.

JAYPEE BROTHERS

Table 3.1: Ingredients of the aqueous humor.

Components	*Aqueous concentration (plasma concentration)/ explanation*
Inorganic ions	
Sodium (mmol/kg H_2O)	• 163 (146)
Chloride (mmol/kg H_2O)	• 134 (109)
Potassium	• Similar to plasma
Magnesium	• Similar to plasma
Iron, copper, zinc	• Approximately: 1 mg/mL; similar to plasma
Calcium	• ½ plasma
Phosphate	• ≤ ½ of plasma
Bicarbonate (mmol/kg H_2O)	• 20 (28)
Organic anions	
Lactate	• Always > plasma; the most abundant organic anions in the aqueous
Ascorbate (mmol/kg H_2O)	• 1.06 (0.04); is actively transported by a Na^+-dependent L-ascorbic acid transporter
Carbohydrates	
Glucose	• About 70% of plasma; facilitated diffusion
Inositol	• 10× of plasma
Glutathione and urea	
Glutathione (μm/L)	• 1–10 (<5); diffusion or active transport
Urea	• 80–90% of plasma; passive diffusion
Proteins	
Proteins	• 0.02 g/100 mL; 1/200–1/500 of plasma protein (7 g/100 mL); albumin and transferrin constitute about 50% of all protein content
Proteinases and inhibitors	
Proteinases	• For example, cathepsin D (degradation of neuropeptides and peptide hormones); cathepsin O (normal cellular protein degradation and turnover)
Proteinase inhibitors	• For example, α_2-macroglobulin; α_1-antitrypsin
Enzymes	
Hyaluronidase	• May be important in the normal regulation of the outflow resistance through the trabecular meshwork
Carbonic anhydrase	• Is present in trace amounts; may be important in the catalysis of the equilibrium between bicarbonate and $CO_2 + H_2O$
Lysozyme	• Antibacterial role, level may raise tenfold or more in ocular inflammation

Contd...

JAYPEE BROTHERS

Contd...

Components	*Aqueous concentration (plasma concentration)/ explanation*
Neurotrophic and neuroendocrine proteins	
Bioactive neuroendocrine markers	• For example, neurotensin, angiotensin, endothelins, and natriuretic peptides; may contribute to IOP regulation or aqueous secretion
Neuropeptide-processing enzymes	• For example, prohormone convertases, carboxypeptidase E, and peptidylglycine α-amidating monooxygenase
Neuropeptides and peptide hormones	• For example, secretogranin II, galanin, neurotensin, and natriuretic peptides
Growth-modulatory factors	
Growth-modulatory factors	• For example, TGFβ-1 and 2, aFGF and bFGF, IGF-I, IGFBPs, VEGF, and transferrin; play an important role in modulating the proliferation, differentiation, and wound healing of ocular tissues.
Oxygen and carbon dioxide	
Oxygen	• Partial pressure of about 55 mm Hg (roughly one third of its concentration in the atmosphere); derived from the blood supply to the ciliary body and iris. Source of oxygen for corneal endothelium, lens, and the endothelial lining of the trabecular meshwork
Carbon dioxide	• 40–60 mm Hg; contributes approximately 3% of the total bicarbonate; the relative proportions of CO_2 and HCO_3^- determine the pH of the aqueous (7.5–7.6). CO_2 is constantly lost from the aqueous humor by diffusion through the cornea into the atmosphere

(aFGF: Acidic fibroblast growth factor; bFGF: Basic fibroblast growth factor; IGF-I: Insulin-like growth factor I; IGFBPs: Insulin-like growth factor binding proteins; IOP: Intraocular pressure; TGF: Transforming growth factor; VEGF: Vascular endothelial growth factor).

- In open-angle glaucoma, the pathology seems to be an increase in the resistance to aqueous humor flow in TM.
- In closed-angle glaucoma, the TM is blocked by the peripheral iris (peripheral anterior synechia, PAS), and therefore, the aqueous cannot reach the TM.
- The degree of angle closure directly corresponds to the outflow facility. For example, outflow facility diminishes to half, if ½ of the angle is closed.

JAYPEE BROTHERS

IMPORTANT STUFF FOR CLINICAL PRACTICE: APPLIED ANATOMY AND PHYSIOLOGY

- Examination of outflow facility
  - Due to total internal reflection, the TM can not be visualized by unaided slit-lamp examination; a goniolens should be placed over the cornea to be able to evaluate the outflow pathway.
  - In open-angle glaucoma, the TM is visible in gonioscopy.
  - In closed-angle glaucoma, iris apposition to TM or PAS is seen. To differentiate iris apposition from PAS, indentation gonioscopy should be employed.
  - Visible blood in Schlemm's canal may be due to hypotony, increased episcleral venous pressure, Sturge–Weber syndrome, carotid-cavernous fistula, superior vena cava syndrome, sickle cell disease, or orbital varices.
- Glaucoma medications
  - Aqueous humor dynamic is the major target for most of the glaucoma medications. Table 3.2 summarizes the effect of these medications on different steps of aqueous humor production and outflow.

Table 3.2: Effect of different classes of glaucoma medications on the aqueous humor dynamics.

Stage	*Medications*	*Effect*
• Aqueous production	• Carbonic anhydrase inhibitors*	Decrease
	• β-adrenergic antagonists (beta-blockers)†	
	• α2-adrenergic agonists	
• Trabecular outflow	• Prostaglandin analogs (bimatoprost, unoprostone isopropyl)	Increase
	• Miotics‡	
	• Adrenergic agonists	
• Uveoscleral outflow	• Cycloplegics	Increase
	• Brimonidine	
	• Prostaglandin analogs (latanoprost, travoprost, bimatoprost)	
• Episcleral venous pressure	• Apraclonidine HCL	Decrease

*The enzyme carbonic anhydrase provides the bicarbonate ion for active secretion into the eye.

†The most prevalent adrenergic receptors in the ciliary epithelium is β2-receptors. β-adrenergic antagonists may affect active transport through alterations in the efficiency or the number of Na+/K+ pump.

‡Miotics decrease the uveoscleral outflow.

JAYPEE BROTHERS

  - Nocturnal elevation of IOP in glaucoma may not be effectively controlled with adrenergic-based glaucoma therapies.
  - Long-term suppression of aqueous production and redirection of outflow from trabecular to the uveoscleral pathway may lead to underperfusion of TM with subsequent detrimental morphologic and functional effects.
- Breakdown of blood–aqueous barrier
  - Etiology
    - Traumatic
      - *Mechanical*: Paracentesis; corneal abrasion; blunt trauma; intraocular surgery; stroking of the iris
      - *Physical*: Radiotherapy; nuclear radiation
      - *Chemical*: Alkali; irritants (e.g. nitrogen mustard)
    - Pathophysiologic
      - Vasodilation (histamine, sympathectomy); corneal and intraocular infections; intraocular inflammation; prostaglandins; anterior segment ischemia
    - Pharmacologic
      - Melanocyte-stimulating hormone; cholinergic drugs (especially cholinesterase inhibitors); plasma hyperosmolarity
  - Pathophysiology
    - The aqueous protein level may rise 10–100 times, particularly in the high-molecular-weight polypeptides.
    - The aqueous contents of inflammatory mediators, immunoglobulins, fibrin, and proteases increase, and the balance among the various growth factors is disrupted.
  - Sign
    - Because of high protein content of aqueous humor, the resultant light scattering (Tyndall effect) makes the slit beam visible as it passes across the anterior chamber. Clinically, this observation is known as flare.
  - Clinical sequelae
    - Fibrinous exudate and clot; cyclitic membranes; peripheral or posterior synechia; abnormal neovascular response (in turn can further exacerbate breakdown of the barrier); abnormal hyperplastic response of the lens epithelium, corneal endothelium, TM, and iris; formation of complicated cataracts
- Glaucoma surgeries
  - *Filtering surgeries*: creating a new outflow pathway to drain aqueous humor from anterior chamber to the subconjunctival and subtenon's space
    - *Trabeculectomy*: creating a window under a partial-thickness sclera flap

JAYPEE BROTHERS

  - *Shunt surgeries*: aqueous humor is drained from the anterior chamber through the tube of shunt to the plate of shunt fixed over the sclera
- Laser trabeculoplasty induces trabecular cell division and cause an alteration in the production of cytokines in the TM that finally improves TM outflow facility
- *Cyclodestructive procedures*: reduce aqueous production
  - *Cyclocryotherapy*: applying cryo probe on the sclera over the ciliary processes area.
  - *Transscleral cyclophotocoagulation*: the G-probe of a diode laser is placed on the sclera over the ciliary processes area.
  - *Endoscopic cyclophotocoagulation*: inserting an endoscope containing a diode laser probe and an illumination to apply laser to the ciliary processes.
- Cyclodialysis decreases the IOP by substantial increase in uveoscleral outflow.

SUGGESTED READING

1. Aqueous humor. In: Chalam KV, Ambati BK, Beaver HA, Grover S, Levine LM, Wells T, et al. (Eds). Fundamentals and Principles of Ophthalmology. San Francisco, CA: American Academy of Ophthalmology; 2011-2012. pp. 265-72.
2. Civan M. The Eye's Aqueous Humor, 2nd edition. Elsevier Inc.; 2008.
3. Coca-Prados M, Escribano J. New perspectives in aqueous humor secretion and in glaucoma: the ciliary body as a multifunctional neuroendocrine gland. Prog Retin Eye Res. 2007;26(3):239-62.
4. Gabelt BT, Kaufman PL. Changes in aqueous humor dynamics with age and glaucoma. Prog Retin Eye Res. 2005;24(5):612-37.
5. Intraocular pressure and aqueous humor dynamics. In: Glaucoma. San Francisco, CA: American Academy of Ophthalmology; 2011-2012. pp. 17-31.
6. Johnson M. 'What controls aqueous humour outflow resistance?'. Exp Eye Res. 2006;82(4):545-57.
7. Kiel JW, Hollingsworth M, Rao R, et al. Ciliary blood flow and aqueous humor production. Prog Retin Eye Res. 2011;30(1):1-17.
8. Malihi M, Sit AJ. Aqueous humor dynamics and implications for clinical practice. Int Ophthalmol Clin. 2011;51(3):119-39.
9. Production and flow of aqueous humor. In: Levin LA, Nilsson SFE, Ver Hoeve J, Wu SM (Eds). Adler's Physiology of the Eye, 11th edition. Elsevier Inc.; 2011. pp. 274-307.

JAYPEE BROTHERS

or detailed information on ophthalmology books, visit our website **www.jaypeebrothers.com,** for detailed information on ophth

Manual of GLAUCOMA

Manual of Glaucoma has been possible due to the contributions of many leading glaucoma experts from across the globe.

The book aims to be a ready reckoner for both, the glaucoma practitioner and the ophthalmologist in training. Fully illustrated in color, with both clinical photos and schematic drawings, the manual explains all the complex concepts and clinical situations in a lucid and easy manner. Comprehensive tables and flowcharts make the book easy to read. It is a handy guide during clinical practice as well as during exams.



Shibal Bhartiya MD is currently working as a senior consultant, glaucoma surgeon at Fortis Memorial Research Institute, Gurgaon, Haryana, India. She has a special interest in glaucoma diagnosis and management, and ocular surface diseases. She was a Senior Clinical Research Fellow in the Glaucoma services of the Department of Clinical Neurosciences, University of Geneva, Switzerland, and pursued her Doctorate en Medicine (currently enrolled) under Dr Tarek Shaarawy, at the University of Geneva and associated hospitals. Prior to that, she did her glaucoma training as Senior Research Associate in the Cornea and Glaucoma services at Dr RP Center for Ophthalmic Sciences, AIIMS, New Delhi, India.

She has published extensively in glaucoma, contributing several chapters to books and peer reviewed journals alike. She has co-edited the prestigious *ISGS Textbook of Glaucoma Surgery*, and is the managing editor of the *Video Atlas of Glaucoma Surgery*. An avid educator and researcher, she has been responsible for the design and execution of many clinical trials in both clinical and basic research.

Dr Bhartiya has lectured at, and chaired various sessions in regional, and international meetings. She serves as a reviewer for many ophthalmology journals, and is the Managing Editor of the *Journal of Current Glaucoma Practice*, the official journal of the International Society of Glaucoma Surgery.



Parul Ichhpujani MS is currently an Assistant Professor at the Department of Ophthalmology, Government Medical College and Hospital, Chandigarh, India. She takes care of the Glaucoma and Neuro-ophthalmology services at her Center. She has done her Glaucoma training from Advanced Eye Center, Postgraduate Institute of Medical Education and Research, Chandigarh, India and a subsequent Clinical Research fellowship, under Dr George L Spaeth, at Wills Eye Institute, Philadelphia, USA. She is an avid researcher and an academician having co-authored a book, *Pearls in Glaucoma Therapy*; edited two books, *Expert Techniques in Ophthalmology* and *Glaucoma: Basic and Clinical Perspectives* and contributed several research articles and book chapters in national as well as international books. Dr Ichhpujani has lectured at regional, national and international surgical meetings and serves as a reviewer for many ophthalmology journals.

Available at all medical bookstores or buy online at www.jaypeebrothers.com

JAYPEE BROTHERS
Medical Publishers (P) Ltd.
www.jaypeebrothers.com

Join us on facebook.com/JaypeeMedicalPublishers

Shelving Recommendation
OPHTHALMOLOGY

ISBN 978-93-5152-964-4