

## **Table of Contents**

Cover image  
Title page  
Table of Contents  
Copyright  
Video table of contents  
Contributors  
Video contributors  
Dedication  
Preface  
List of Tables  
List of Illustrations

## **VOLUME 1**

### **Part 1. Retinal Imaging and Diagnostics**

#### **1. Fluorescein angiography: Basic principles and interpretation**

Introduction  
Basic principles  
Equipment  
Technique  
Interpretation  
Normal fluorescein angiogram  
Abnormal fluorescein angiogram  
Acknowledgments  
References

#### **2. Clinical applications of diagnostic indocyanine green angiography**

Introduction  
History  
Chemical and pharmacokinetics  
Toxicity  
Instrument comparison  
Injection technique  
Indocyanine green angiography interpretation  
References

### 3. Optical coherence tomography

Physical principles of optical coherence tomography

Quantitative analysis of optical coherence tomography data sets

Optical coherence tomography angiography

Normal macular anatomy

Spectral domain-based optical coherence tomography in retinal disorders

Future directions

Disclosures

Acknowledgments

References

### 4. Optical coherence tomography angiography (OCTA)

Overview

Principles of octa

OCTA algorithms

Image visualization

Quantitative metrics

Artifacts

Commercially available devices

Advantages and limitations of OCTA

Normal retinal and choroidal vascular anatomy and circulation

Understanding and interpreting OCTA

Retinal vascular disease

Degeneration

Macular neovascularization secondary to other disorders

Inflammatory disease

References

### 5. Autofluorescence imaging

Basic principles

Techniques of fundus autofluorescence imaging

Interpretation of fundus autofluorescence images

Recent developments in fundus autofluorescence imaging

Spectrally resolved FAF

Fluorescence lifetime imaging ophthalmoscopy (FLIO)

Clinical applications

References

## 6. Widefield imaging

Introduction

Historical perspective and nomenclature

Historical widefield imaging systems

Modern widefield imaging systems

Overview of imaging capabilities and optical principles

Clinical utility of widefield imaging

Limitations

Future directions

Conclusions

References

## 7. Advanced imaging technologies

Introduction: Retinal imaging to date

Adaptive optics: Imaging of single cells in the retina

Measuring visual function with adaptive optics

Imaging retinal function (optophysiology)

Vascular imaging and retinal blood flow

Imaging retinal melanin

Conclusions and future directions

Disclosures

References

## 8. Artificial intelligence and advanced imaging analysis

History of AI

Machine learning

Computer vision and advanced image analysis

Recent advances in computer vision: Deep learning

Components of deep learning model architecture

Deep learning model architectures

Training deep learning models

Beyond traditional deep learning models

The evaluation of AI models

Deep learning using fundus photography

Deep learning using OCT imaging

Deep learning using other retinal imaging

Regulatory

Gaps in technology

Immediate challenges with deployment of AI systems into retina clinics

Ethical questions on the impact of AI

Conclusions

Acknowledgments

References

## 9. Clinical electrophysiology

Introduction

The techniques and principles of interpretation

Inherited photoreceptor diseases

Inherited inner retinal disorders

Acquired retinal diseases

Inflammatory and autoimmune disorders

The role of electrophysiology in an era of precision medicine

Summary

Acknowledgments

References

## 10. Diagnostic ophthalmic ultrasound

Introduction

History of pulse echo phenomenon

Ophthalmic ultrasound: Physics and basic engineering

Clinical examination: B-scan of the posterior segment

Cross section B-scans of ocular pathology: Posterior segment ultrasonography

Pattern recognition from the inside-out: Vitreous, ocular wall, optic nerve, and orbit

Cross section B-scans of ocular pathology: Anterior segment ultrasonography

Anterior UHF ultrasonography: Pattern recognition examples

Pre- and postoperative ophthalmic ultrasound

Current and future development

References

## 11. Color vision and night vision

Overview

Rod and cone functions

Visual pathways for rod and cone functions

Dark adaptation functions: Assessment of the shift from day vision to night vision

Color vision

Variations in human color vision

Clinical evaluation of color vision

New developments in color vision research

Adaptive optics (AO) retinal imaging system

References

## 12. Visual acuity and contrast sensitivity

Visual acuity tests

Contrast sensitivity tests

References

### 13. Visual fields in retinal disease

Introduction

Principles of perimetry

Methods of visual field testing

Perimetry in specific retinal diseases

Other modalities of perimetry in retinal disease

Conclusions

References

## **Part 2. Basic Science and Translation to Therapy**

### **Section 1. Anatomy and Physiology**

#### 14. The development of the retina

Embryology of the eye

Specifying the eye field

Patterning the retinal, RPE, and anterior domains of the optic cup

Histogenesis of the retinal cell types

Inner retinal development

Photoreceptor development

Ganglion cell death

Retinal maturation

Conclusions

References

#### 15. Function and anatomy of the mammalian retina

Visual illusions and multiple channels

Neuronal communication: Chemical and electrical

Gross retinal morphology

Classification of retinal cells

Gene therapy to cure color blindness

New tools to identify ganglion cell types

Clinical relevance of functional anatomy

Conclusions

Acknowledgments

References

#### 16. Structure and function of rod and cone photoreceptors

Introduction

Photoreceptor fundamentals

Photoreceptor outer-segment structure

Phototransduction

Inner segment and connecting cilia

Photoreceptor synaptic terminal

Establishing synapses between photoreceptors and bipolar cells

Photoreceptor dysfunction and disease  
Influences of photoreceptor degeneration on the retinal circuitry  
References

17. Cell biology of the retinal pigment epithelium  
Embryology  
Anatomy and histology  
The retinal pigment epithelium transcriptome and proteome  
Specialized functions of the retinal pigment epithelium  
References

18. Glial cells of the fovea  
Introduction  
Microglia  
Astroglia  
Müller glia  
Foveal glia  
Foveal development  
References

19. Retinal and choroidal vasculature: Retinal oxygenation  
Introduction  
History of retinal ischemia  
Normoxia  
Hyperoxia  
Hypoxia  
Adult retinal hypoxia and etiology  
Adult choroidal ischemia  
Conclusions  
References

20. Mechanisms of normal retinal adhesion  
Introduction  
Models for measuring retinal adhesion  
Adhesive force and environmental factors  
Mechanical forces inside the subretinal space  
Metabolic factors  
Subretinal fluid transport and subretinal protein  
Pharmacologic modification of adhesion  
Implications for vitreoretinal surgery  
Pathophysiology of serous detachment  
Conclusions and general implications  
References

## 21. Structure, function, and pathology of Bruch's membrane

Introduction, history, embryology

Structure of Bruch's membrane in young adults

Bruch's membrane in aging

Function of Bruch's membrane

Pathology of Bruch's membrane

Summary

References

## 22. Vitreous and vitreoretinal interface

Biochemistry

Anatomy and histology

Physiology

Pathology

Acknowledgments

References

## **Section 2. Basic Mechanisms of Injury in the Retina**

### 23. Mechanisms of oxidative stress in retinal injury

Introduction

Overview of oxidative stress in the retina

Retinal diseases related to oxidative stress

Oxidative injury to the retina

Retinal therapies targeting oxidative stress

Conclusions

References

### 24. Mechanisms of endoplasmic reticulum stress in retinal disease

Introduction

The endoplasmic reticulum

Endoplasmic reticulum stress and UPR signaling

Retinal diseases associated with ER stress

Summary

References

### 25. Cell death, apoptosis, and autophagy in retinal injury

Introduction

Modes of cell death

Autophagy and cell maintenance

Age-related retinal cell loss

Retinal damage: Death and repair

Therapeutic options

Conclusions

References

## 26. Inflammation and immune responses in retinal health and disease

Introduction

Innate defenses in the maintenance of retinal health

Autoinflammation and autoimmunity

Inflammation, vascular regulation, and pathologic angiogenesis (neovascularization)

Inflammation and age-related macular degeneration

Targeting inflammation through molecular stratification: Genetics and beyond

Conclusions

Acknowledgments

References

## 27. Basic mechanisms of pathologic retinal and choroidal angiogenesis

Introduction

Mechanisms of choroidal angiogenesis

Angiogenic and antiangiogenic factors in neovascularization

Conclusions

References

## 28. Blood–retinal barrier, immune privilege, and autoimmunity

Introduction

Blood–ocular barriers

Ocular autoimmunity and uveitis

Autoimmunity in human uveitis

Role of infection in autoimmunity

Conclusions

Acknowledgments

References

## 29. Mechanisms of diabetic macular edema and therapeutic approaches

Introduction: The global impact of diabetes and diabetic retinopathy

Overview of diabetic retinopathy, the blood retinal barrier, and edema

Characterization of diabetic macular edema and diagnostic imaging technologies

Histopathology of diabetic macular edema

Molecular and cellular mechanisms underpinning diabetic macular edema

Current treatments for diabetic macular edema

Summary

References



### 30. Cellular effects of detachment and reattachment on the neural retina and the retinal pigment epithelium

Introduction

Use and limitations of animal models in the study of retinal detachment

Cellular changes in response to retinal detachment

Chronic retinal detachment and proliferative vitreoretinopathy

Retinal reattachment

References

### 31. Retinal manifestations of neurodegeneration: A focus on Alzheimer disease

Introduction

Clinical and histopathologic evidence of optic nerve involvement in alzheimer disease

In vivo diagnostic imaging studies corroborate optic nerve atrophy

Histopathologic hallmarks of neurodegeneration in the retina

Histopathologic hallmarks of  $a\beta$  and tau pathology in the retina

Retinal amyloid and hyperspectral imaging of the retina

The melanopsin retinal ganglion cells in alzheimer disease and circadian rhythms

Pupillary function in alzheimer disease

Retinal vascular involvement in alzheimer disease

The retinal choroid

Future directions: Can novel ocular biomarkers be used to monitor or manage alzheimer disease?

Acknowledgments

References

## **Section 3. Genetics**

### 32. Genetic mechanisms of retinal disease

Introduction

Basic concepts in human genetics

The human genome

Genetic testing for inherited retinal diseases

Genetic testing methods

Conclusions

Acknowledgments

References

### 33. Mitochondrial genetics of retinal disease

Mitochondrial origins

Mitochondrial structure

Mitochondrial DNA

Mitochondrial function

Electron leakage and reactive oxygen species formation

Localization of mitochondria within the retina and optic nerve

Influences of mtDNA on cell function

References

#### 34. Epigenetic mechanisms of retinal disease

Introduction

Major factors of epigenetic regulation

Interplay between genetic and epigenetic factors

Epigenetic mechanisms in retinal development

Epigenetic mechanisms in retinal diseases

Perspectives and challenges of epigenetics

References

#### 35. Microbiome and retinal disease

Introduction

Dietary patterns are related to the risk for and progression of age-related macular degeneration

Summary

References

### **Section 4. Translational Basic Science**

#### 36. Gene therapy for retinal disease

Background: Preclinical gene therapy studies

History of retinal gene therapy

Current status of retinal gene therapy trials: Retinal diseases evaluated in human clinical trials

Promises and challenges of bringing retinal gene transfer from bench to bedside

Conclusions

References

#### 37. Stem cells and cellular therapy for retinal degenerative diseases

Stem cells as therapeutics to treat retinal degenerative diseases

Definitions

Müller glial cells

Stem cell-derived photoreceptors

Stem cell-derived RPE cells

Human clinical trials using stem cells for the treatment of retinal diseases

Discerning the legitimacy of a human stem cell treatment

Concluding remarks

Acknowledgments

References

#### 38. Nanomedicine in ophthalmology

Introduction

General principles of nanotechnology and nanomedicine

Applications to ophthalmology

Obstacles to incorporation of nanotechnology into ophthalmology

Conclusions

References

## 39. Neuroprotection

History and definitions

Neuroprotection through the serotonin pathway

Neurotrophic factors for retinitis pigmentosa

CNTF protein and historical selection

CNTF phase I trial for human photoreceptor degeneration

New technology for endpoints for photoreceptor degenerations

Delivery of neurotrophins

Antioxidants

Neuroprotection with small molecules

Modulation of retinal milieu and neurotrophic factors through environmental components

References

## 40. Drug delivery

Introduction

A brief history of the field of drug delivery

Drug delivery

Gene delivery

Cellular delivery for sustained drug delivery

Routes of delivery to the retina

Pharmacokinetics in the eye

References

## 41. Retinal laser therapy: Biophysical basis and applications

Introduction

Basics of lasers

Interactions of light with tissue

Monitoring the retinal temperature

References

## **VOLUME 2**

### **Medical Retina**

#### **Section 1. Retinal Degenerations and Dystrophies**

## 42. Macular dystrophies

Introduction

The initial approach to a patient with macular dystrophy

Best macular dystrophy

Stargardt disease

Stargardt-like dominant macular dystrophy (SLDMD)

PROM1-associated macular dystrophy

Pattern dystrophy

Sorsby fundus dystrophy

Occult macular dystrophy  
Autosomal dominant radial drusen (doyne honeycomb retinal dystrophy, malattia leventinese)  
North carolina macular dystrophy  
Spotted cystic dystrophy  
Dominant cystoid macular dystrophy  
Fenestrated sheen macular dystrophy (FSMD)  
Drusen in immune complex–mediated and complement-mediated membranoproliferative glomerulonephritis  
Maternally inherited diabetes and deafness  
Acknowledgments  
References

#### 43. Retinitis pigmentosa and allied disorders

Early history  
Typical retinitis pigmentosa  
Syndromic retinitis pigmentosa  
Differential diagnosis-phenocopies of retinitis pigmentosa  
Differential diagnosis: Pseudoretinitis pigmentosa  
Basic science  
Genetic consultation  
Treatment  
Purported “cures” for RP  
Future management  
Acknowledgments  
References

#### 44. Abnormalities of rod and cone function

Introduction  
Stationary diseases associated with night blindness  
Stationary diseases of the cone system  
Progressive cone dystrophies  
Retinal dystrophies with pathognomonic ERG phenotypes  
Genetics of cone–rod dystrophies  
Conclusions  
References

#### 45. Hereditary vitreoretinal degenerations

Introduction  
Snowflake vitreoretinal degeneration  
VCAN-related vitreoretinopathies  
Autosomal dominant vitreoretinopathies  
Autosomal recessive vitreoretinopathies  
Chondrodysplasias associated with vitreoretinal degeneration  
X-linked retinoschisis  
Retinal nuclear receptor (NR2E3)-related diseases

Other vitreoretinal degenerations and vitreoretinopathies

References

46. Hereditary choroidal dystrophies

Introduction

Choroidal atrophy phenotypes

Gyrate atrophy of the choroid and retina

Choroideremia

Clinical phenotypes resembling hereditary choroidal dystrophies

Conclusions

References

## **Section 2. Retinal Vascular Disease**

47. Diabetic retinopathy: Etiologic mechanisms and genetics

Introduction

Anatomic lesions

Biochemical mechanisms in the pathogenesis of diabetic retinopathy

Genetic factors in the pathogenesis of diabetic retinopathy

Other ocular factors

Retinopathy in different forms of diabetes

Animal models in the study of diabetic retinopathy

Cell culture studies

Conclusions

References

48. Diabetes mellitus

Introduction

Prevalence of retinopathy

Glycemic control and retinopathy

Goals of treatment

Glycemic control: Pharmacologic treatment

Initiation and titration of therapy

References

49. Nonproliferative diabetic retinopathy and diabetic macular edema

Natural course of nonproliferative diabetic retinopathy

Clinical evaluation of nonproliferative diabetic retinopathy

Clinical evaluation of diabetic macular edema

Management of nonproliferative diabetic retinopathy and diabetic macular edema

Conclusions

References

## 50. Proliferative diabetic retinopathy

Pathogenesis of proliferative diabetic retinopathy

Natural course of proliferative diabetic retinopathy

Imaging of proliferative diabetic retinopathy

Origin and early recognition of preretinal new vessels

Relationship of proliferative diabetic retinopathy to type and duration of diabetes

Absence of proliferative diabetic retinopathy in individuals with diabetes of extreme duration

Proliferative diabetic retinopathy and blood glucose control

Early worsening of retinopathy with improved glycemic control

Systemic medications and proliferative diabetic retinopathy

Other risk factors for proliferative diabetic retinopathy

Management of proliferative diabetic retinopathy

Current techniques of panretinal photocoagulation

Regression of new vessels after initial photocoagulation and indications for retreatment

Complications of PRP

Antiangiogenic therapies for proliferative diabetic retinopathy

Indications for vitrectomy

Conclusions

References

## 51. Telescreening for diabetic retinopathy

Introduction

Guidelines for telescreening program

Steps of telescreening

Technical considerations

Operational considerations

Quality assurance

Evaluating telescreening programs

Advances in telescreening

Conclusions

References

## 52. Hypertension

Introduction

Hypertensive retinopathy

Hypertensive choroidopathy

Hypertensive optic neuropathy

Emerging imaging technology to evaluate hypertensive retinopathy

Future directions

Conclusions

References

### 53. Retinal artery and capillary occlusions

Central retinal artery occlusion

Branch retinal artery occlusion

Cilioretinal artery occlusion

Combined retinal artery and vein occlusion

Cotton-wool spots

Paracentral acute middle maculopathy

References

### 54. Acquired retinal macroaneurysms

Clinical description

Diagnosis of retinal macroaneurysm

Natural course and treatment of retinal arterial macroaneurysms

References

### 55. Branch retinal vein occlusion

Introduction

Risk factors

Pathogenesis

Clinical features

Natural history

Clinical evaluation

Treatment options

Follow-up

Conclusions

References

### 56. Central retinal vein occlusion

Clinical features

Perfusion status

Pathogenesis

Risk factors and associations

Clinical evaluation

Follow-up

Conclusions

References

### 57. Macular telangiectasia type 2

Introduction

Classification of macular telangiectasia

Epidemiology

Clinical presentation

Retinal imaging

Staging and prognostic factors

Genetics

- Serine/glycine metabolism
- Association of systemic diseases
- Differential diagnosis
- Clinicopathologic correlation
- Therapeutic options
- Summary and future research directions
- References

## 58. Coats disease

- Introduction
- History
- Histopathology, etiology, and pathogenesis
- Clinical presentation
- Diagnostic testing
- Differential diagnosis
- Treatment
- Outcomes
- References

## 59. Hemoglobinopathies

- Prevalence
- Genetic modifiers
- Pathophysiology
- Systemic manifestations
- Ophthalmic clinical features
- Nonproliferative sickle retinopathy
- Proliferative sickle retinopathy
- Ophthalmic treatments
- Imaging
- Health maintenance and retinopathy screening
- Potential therapeutic options for the future
- References

## 60. Radiation retinopathy

- Introduction
- Etiology, pathogenesis, and histopathology
- Natural history and clinical features
- Classification
- Risk factors
- Incidence and dosimetry
- Differential diagnosis and diagnostic evaluation
- Prevention and treatment
- Prognosis
- Conclusions
- References



### 61. Ocular ischemic syndrome

Demographics and incidence

Etiology

Symptoms

Ancillary studies

Systemic associations

Differential diagnosis

Treatment

References

### 62. Systemic coagulopathy syndromes

Introduction

General considerations

Ophthalmic involvement

Differential diagnosis of choroidal ischemia

Conclusions

References

### 63. Pediatric retinal vascular diseases

Retinopathy of prematurity

International classification

Current concepts in management of retinopathy of prematurity

Other pediatric retinal vascular diseases

References

## **Section 3. Choroidal Vascular/Bruch's Membrane Disease**

### 64. Epidemiology and risk factors for age-related macular degeneration

Introduction

Classification

Prevalence and incidence

Quality of life

Sociodemographic factors

Ocular risk factors

Behavioral and lifestyle factors

Cardiovascular-related factors

Hormonal and reproductive factors

Inflammatory factors

Genetic factors

Summary and conclusions

References

## 65. Pathogenesis of age-related macular degeneration

Introduction: Age-related macular degeneration, a vascular-initiated, deposit-driven disease

Age-related macular degeneration by the layers

Classification of advanced age-related macular degeneration organized by extracellular deposits

Topography of photoreceptors, retinal pigment epithelium, and deposits

The drusen lifecycle: Clinical and lifespan aspects

Vision implicates soft drusen; choriocapillaris exonerates lipofuscin

Learning about subretinal drusenoid deposit using drusen as a model

Cell and molecular mechanisms of deposit formation; role of high-density lipoprotein genes

Role of the complement gene pathway

Conclusions

References

## 66. Age-related macular degeneration: Non-neovascular early AMD, intermediate AMD, and geographic atrophy

Introduction

Normal aging of the macula

Pathology of non-neovascular AMD

Prognosis and management of non-neovascular AMD

References

## 67. Neovascular age-related macular degeneration

Introduction

Histopathology

Etiology and classification

Diagnosis and characterization of macular neovascularization

Complications

Prevention and risk factors for development of neovascular exudative age-related macular degeneration

Treatment

Patient education and rehabilitation

References

## 68. Pharmacotherapy of age-related macular degeneration

Introduction

Neovascular age-related macular degeneration

Non-neovascular AMD

Summary

References

## 69. Pathologic myopia

Epidemiology

Pathogenesis

Histopathology

Animal models

Optical coherence tomography-based classification of myopic maculopathy

Conclusions

References

## 70. Angioid streaks

Introduction

Histopathology

Systemic associations

Ocular manifestations and clinical course

Ocular imaging and diagnosis

Optical coherence tomography angiography

Therapy

Conclusions

References

## 71. Ocular histoplasmosis

Historical perspective

Clinical features of ocular histoplasmosis

Relationship of ocular disease to systemic infection

Epidemiology of ocular histoplasmosis

Pathogenesis

Natural history of ocular histoplasmosis and public health implications

Treatment

References

## 72. Pachychoroid disease and its association with polypoidal choroidal vasculopathy

Introduction and definition

Evolving concept of pachychoroid as a potential pathogenic mechanism

Pachychoroid disease spectrum

Pachychoroid pigment epitheliopathy

Pachychoroid neovasculopathy

Polypoidal choroidal vasculopathy/aneurysmal pachychoroid neovasculopathy

Peripapillary pachychoroid syndrome

Management considerations

Pachychoroid phenotypes and age-related macular degeneration

Future research and conclusions

Financial disclosures

References

### 73. Central serous chorioretinopathy

Introduction

Definition, pathogenesis, risk factors, epidemiology, and demographics

Clinical features

Differential diagnosis

Multimodal imaging

Natural history

Treatment

Conclusions

References

### 74. Uveal effusion syndrome and hypotony maculopathy

Uveal effusion syndrome

Hypotony maculopathy

References

## **Section 4. Inflammatory Disease/Uveitis Inflammation**

### 75. Sympathetic ophthalmia

Introduction

Epidemiology

Pathogenesis

Immunopathology

Clinical findings

Diagnosis

Differential diagnosis

Course and complications

Therapy

Prevention

Prognosis

References

### 76. Vogt–Koyanagi–Harada disease

Introduction and historical aspects

Epidemiology

Clinical description

Pathology and pathogenesis

Investigations

Differential diagnosis

Treatment

Complications and management

Prognosis

Conclusions

References

## 77. White spot syndromes and related diseases

Introduction

Birdshot chorioretinopathy

Placoid diseases

Multifocal choroiditis/punctate inner choroidopathy

Multiple evanescent white dot syndrome

Acute zonal occult outer retinopathy

Acute macular neuroretinopathy

Acknowledgments

References

## 78. Autoimmune retinopathies

Introduction

Clinical features and investigations

Phenotypes potentially related to autoimmune retinopathy

Treatment and prognosis

Conclusions

References

## 79. Sarcoidosis

General considerations

Course and prognosis

Ocular manifestations

Posterior segment disease

Diagnosis

Fundus imaging

Course and prognosis

Therapy

Conclusions

References

## 80. Intermediate uveitis

Introduction

Epidemiology and demographics

Presentation and clinical findings

Imaging

Differential diagnosis and workup

Histopathology and pathophysiology

Treatment

Clinical course and complications

References

## 81. Rheumatic disease

Introduction

Disease-specific section

Ocular complications of rheumatologic therapies

References

Infections

## 82. HIV-associated infections

Introduction

Epidemiology of HIV infection and AIDS

Occupational exposure to HIV

HIV virology and pathogenesis

Therapy of HIV infections

Clinical spectrum of HIV

Infection control related to HIV

Ocular findings in AIDS: An overview

Noninfectious retinopathy

Infectious retinopathy

Fungal diseases

Bacterial retinitis

Invasive diagnostic techniques for retinal disease

Antiretroviral therapy

References

## 83. Mycobacterial infections

Introduction

Pulmonary and extrapulmonary tuberculosis

Ocular tuberculosis

Adnexal tuberculosis

Laboratory evaluation

Treatment

References

## 84. Eales disease

Introduction

Clinical features and natural history

Pathology and pathogenesis

Differential diagnosis

Diagnostic workup for eales disease

Epidemiologic spectrum of retinal vasculitis

Management

Summary

References

## 85. Spirochetal infections

Introduction

Syphilitic uveitis

Uveitis associated with lyme disease

Ocular leptospirosis

References

## 86. Ocular toxoplasmosis

Introduction

Pathogenesis

Ocular disease

Laboratory

Outcomes and complications

Treatment and prevention

References

## 87. Helminthic disease

Introduction

Ocular toxocariasis

Diffuse unilateral subacute neuroretinitis

Onchocerciasis

Cysticercosis

References

## 88. Endogenous endophthalmitis: Bacterial and fungal

Epidemiology and risk factors

Clinical assessment of the patient

Medical evaluation of the patient

Endogenous bacterial endophthalmitis

Endogenous fungal endophthalmitis

Treatment strategies

Suggested management

References

## 89. Acute retinal necrosis syndrome

Introduction

Symptoms and clinical course

Patient population

Etiology

Pathologic features

Differential diagnosis

Treatment and prognosis

References

## 90. Drug toxicity of the posterior segment

Disruption of the retina and retinal pigment epithelium

Vascular damage and/or occlusion

Cystoid macular edema

Retinal folds

Crystalline retinopathy

Uveitis

Miscellaneous

Summary

Acknowledgments

References

## 91. Photic retinal injuries: Mechanisms, hazards, and prevention

Introduction

Photomechanical retinal interactions

Photothermal retinal interactions

Laser accidents

Photochemical retinal interactions

Photic retinopathy accidents

Safety standards

Conclusions

References

## 92. Traumatic chorioretinopathies

Introduction

Direct ocular injury

Indirect ocular injury

Conclusions

References

## 93. Retinal and choroidal disorders in pregnancy (pregnancy-related diseases)

Retinal and choroidal disorders in pregnancy

Preexisting conditions

Diagnostic testing and therapy

Conclusions

References



## 94. Optic disc anomalies, drusen, pits, hypoplasia, and associated retinal pathology

Optic disc anomalies

Anatomy

Optic disc drusen

Optic disc pits

Congenital optic nerve hypoplasia

References

## 95. Retina-related clinical trials: A resource bibliography

Introduction

Diabetic retinopathy and diabetic macular edema

Vascular occlusions

Age-related macular degeneration and other conditions associated with choroidal neovascularization

Retinopathy of prematurity

Posterior uveitis

Other retinal and retina-related conditions

Vitreo-retinal surgery

## **VOLUME 3**

### **Part 1. Surgical Retina**

#### **Section 1. The Pathophysiology of Retinal Detachment and Associated Problems**

## 96. Pathogenetic mechanisms of retinal detachment

Introduction

Pathophysiology of retinal detachment

Rhegmatogenous retinal detachment

Tractional retinal detachment

Combined tractional and rhegmatogenous retinal detachment

Exudative and hemorrhagic retinal detachment

Conclusions

References

## 97. Nonrhegmatogenous retinal detachment

Introduction

Idiopathic

Vascular

Inflammatory and infectious

Degenerative

Tumor and malignancy

Disc anomalies

Other conditions

Conclusions

References

## 98. Degenerative retinoschisis

Definitions and pathology

Retinoschisis

Retinoschisis with retinal breaks

Schisis detachment

Progressive rhegmatogenous retinal detachment associated with retinoschisis

Conclusions

Acknowledgments

References

## 99. Pathogenesis of proliferative vitreoretinopathy

Introduction

Pathogenesis of PVR

The pharmacologic management of PVR

Biomarkers and genetic profiling

Conclusions

References

## 100. Pathophysiology of ocular trauma

Introduction

Anatomic change

Histopathologic findings

Experimental models

Wound healing and traumatic proliferative vitreoretinopathy

Special conditions

Therapeutic aspects

Conclusions

References

## **Section 2. Retinal Reattachment: General Surgical Principles and Techniques**

### 101. The biomechanics of scleral buckles in the treatment of retinal detachment

Introduction

Effects of scleral buckles on the geometry of the eye

Effects of scleral buckles on retinal pigment epithelium and the retina

Conclusions

References

### 102. Techniques of scleral buckling

Introduction

Preparation for surgery

Surgical steps

Final examination of the retina

Closure

Documentation  
Outcomes  
Postoperative complications  
References

### 103. Principles and techniques of vitreoretinal surgery

Introduction  
Vitreoretinal surgical anatomy  
Mechanics of vitreoretinal surgery  
Infusion system management  
Vitreous cutter considerations  
Fluidics  
Control systems  
Microscope requirements  
Tool ergonomics  
Surgical steps  
Lens management  
Epiretinal membrane management  
Management of subretinal proliferation  
Extrusion techniques  
Interfacial surface tension management  
Retinectomy  
Hemostasis  
Retinopexy  
Panretinal photocoagulation  
Subconjunctival pharmacotherapeutics  
Surgical algorithms  
Conclusions  
References

### 104. Intraoperative OCT imaging

Background and historical prospective  
OCT in the operating room: Integrative advances  
Surgeon feedback platform enhancements  
Surgical findings with intraoperative OCT in vitreoretinal conditions  
Conclusions  
References

### 105. Primary vitrectomy in rhegmatogenous retinal detachment

Introduction  
Pathogenesis of rhegmatogenous retinal detachment  
Categories of rhegmatogenous retinal detachment  
Patient selection for primary vitrectomy  
Principles of vitrectomy  
Surgical techniques

- Surgical outcomes
- Prognostic factors
- Complications
- Perspectives
- References

#### 106. Pneumatic retinopexy

- Introduction
- History
- Basic principles
- Surgical technique
- Special procedures
- Summary of procedure
- Postoperative management
- Results
- Complications
- Utilization of pneumatic retinopexy
- Conclusions
- References

#### 107. Special adjuncts to treatment

- Intraocular gas
- Perfluorocarbon liquid in vitreoretinal surgery
- Silicone oil in vitreoretinal surgery
- Heavy tamponade
- Chromovitrectomy
- References

#### 108. Optimal procedures for retinal detachment repair

- Introduction
- Round hole retinal detachment
- Detachment because of retinal dialyses
- Retinal detachment secondary to "U" (horseshoe) tears
- Conclusions
- References

#### 109. Prevention of retinal detachment

- Introduction
- Risk factors for retinal detachment
- Symptomatic eyes
- Asymptomatic eyes without high-risk factors
- Asymptomatic nonfellow eyes with high-risk factors
- Asymptomatic patients with retinal detachment in the fellow eye
- Prophylactic therapy in eyes undergoing vitreoretinal surgery
- Treatment methods

Results and complications of prophylactic therapy  
Conclusions  
References

### **Section 3. Complicated Forms of Retinal Detachment**

#### 110. Proliferative vitreoretinopathy

Introduction  
Pathophysiology  
Risk factors for the development of PVR  
Clinical signs and diagnosis of PVR  
Classification of PVR  
Prevention of PVR  
Surgery for PVR  
Postoperative management  
Complications after PVR surgery  
Results of surgery for PVR  
When is surgery for PVR not justified?  
References

#### 111. Retinotomies and retinectomies

Introduction  
Drainage retinotomy  
Retinotomy to gain access to the subretinal space  
Relaxing retinectomy  
References

#### 112. Giant retinal tear

Introduction  
Etiology  
Pathogenesis  
Historical aspects of management of giant retinal tears  
Preoperative evaluation  
Role of nonsurgical treatment  
Role of simple scleral buckling  
Vitreous surgery  
Results  
Management of the fellow eye  
References

#### 113. Surgery for ocular trauma: Principles and techniques of treatment

Extent of ocular injuries  
Ocular trauma classification  
Closed-globe injuries  
Open-globe injuries

Sympathetic ophthalmia

Application of online resources and newer technology to ocular trauma

Prevention

References

114. Surgery for proliferative diabetic retinopathy

Introduction

Requirements for surgery in diabetic patients

Indications and timing of surgery

Surgical procedure in diabetic patients

Complications of surgery in diabetic patients

Postoperative care

Results of surgery as reported and indicated by medical surveys

Conclusions

References

115. Management of combined inflammatory and rhegmatogenous retinal detachment

Introduction

Epidemiology

Pathophysiology

Clinical examination and findings

Management

Prognosis

Conclusions

References

116. High myopia and the vitreoretinal complications

Introduction

Retinal detachment from peripheral breaks

Epidemiology of surgical macular complications

Etiology and pathophysiology

Clinical findings

Treatment of foveoschisis and macular holes with or without retinal detachment

Postoperative complications

Conclusions

References

117. Surgical management of retinopathy of prematurity

Introduction

Classification system

Histopathologic features, clinically relevant cell biology, and pathophysiology

Clinical considerations

Surgical therapy

References

## 118. Surgery for pediatric vitreoretinal disorders

General aspects

Surgical considerations and techniques

Injuries

Conclusions

References

### **Section 4. Vitreous Surgery for Macular Disorders**

## 119. Epiretinal membranes, vitreoretinal traction, cystoid macular edema, and submacular hemorrhage

Introduction

Epiretinal membranes

Vitreomacular traction and cystoid macular edema

Submacular hemorrhage

Conclusions

References

## 120. Macular hole

Introduction

History

Epidemiology and risk factors for primary full-thickness macular holes

Pathogenesis from posterior vitreous detachment to impending MH

Clinical and imaging features of full-thickness macular holes

Differential diagnosis

Secondary macular hole

Surgery for macular hole

Results of surgery

Complications of macular hole surgery

Vitreolysis as a nonsurgical treatment for macular hole

References

## 121. Retinal pigment epithelium and choroid translocation in patients with age-related macular degeneration

Epidemiology

Alternative treatments for AMD

Surgical treatment

Rationale for reconstitution of retinal pigment epithelium

Transplantation of a full-thickness patch from the midperiphery

Surgery

Finding a cleavage plane between sclera and choroid

Results in neovascular AMD

Retinal pigment epithelium transplantation in dry AMD

Surgical aspects in dry AMD

Conclusions for patient benefit in geographic atrophy

Retinal pigment epithelium–choroid translocation and future stem cell treatments for AMD

## References

### **Section 5. Vitreous Surgery: Additional Considerations**

#### 122. Infectious endophthalmitis

Introduction

Organisms that cause endophthalmitis

Experimental endophthalmitis

Clinical findings

Therapy

Future directions

Conclusions

References

#### 123. Diagnostic and therapeutic vitrectomy for uveitis

Introduction

Diagnostic vitrectomy

Therapeutic vitrectomy

Conclusions

References

#### 124. Vitreous, retinal, and choroidal biopsy

Introduction

Vitreous biopsy

Transvitreal retinal biopsy

Transvitreal and transscleral choroidal biopsy

Fine-needle biopsy

Complications of intraocular biopsy

Conclusions

References

#### 125. Transplantation frontiers

Introduction

History of ocular cell transplantation

Background and rationale for RPE transplantation in age-related macular degeneration

Cell selection for RPE transplantation

Cell delivery strategies

Iatrogenic retinal detachment

Results of RPE transplants in humans

Immune response to RPE transplants

RPE graft failure

RPE replacement: Future directions

Background and rationale for photoreceptor transplantation in retinal dystrophies

Results of photoreceptor transplants in experimental animals

Transplantation aimed at photoreceptor cell rescue



Transplantation aimed at photoreceptor cell replacement  
Stem cells in photoreceptor transplantation  
Results of photoreceptor transplants in humans  
Photoreceptor transplantation: Future directions  
Conclusions  
References

## 126. Artificial vision

Introduction  
Background and history of artificial vision  
Visual prostheses  
PRIMA  
STS  
BVT  
Electrotherapeutics  
Optogenetics  
Conclusions  
Disclosures  
References

## 127. Pharmacology during surgery

Introduction  
Pharmacologic vitreolysis  
Enzymatic vitreolysis: Microplasmin, plasmin, and others  
Antiproliferative agents in the management of proliferative vitreoretinopathy  
Tissue plasminogen activator in vitreoretinal surgery  
Visualization of the vitreoretinal interface  
VEGF inhibitors in vitreoretinal surgery  
Endophthalmitis  
Autologous blood and platelet concentrate  
Summary  
References

## 128. Complications and challenges in vitreoretinal surgery

Introduction  
Subluxated intraocular lens  
Trauma with contact lens  
Subfoveal perfluoro-n-octane heavy liquid  
Intraocular scissors  
Dexamethasone implant migration into the anterior chamber  
Dexamethasone implant induced retinal break  
Iatrogenic retinal break during silicone oil removal  
Iatrogenic breaks during proliferative vitreoretinopathy surgery  
Globe perforation during posterior sub-Tenon triamcinolone injection  
Scleral perforation during scleral buckling procedure

Macular fold  
Choroidal detachment as a complication of pars plana vitrectomy  
Challenging macular hole surgery  
Complications during chandelier light assisted scleral buckling surgery  
Scleral buckling surgery with slit-lamp microscope  
Autologous internal limiting membrane flap technique for optic nerve pit maculopathy  
Scleral inlay for recurrent optic nerve pit maculopathy

## **Part 2. Tumors of the Retina, Choroid, and Vitreous**

### **Section 1. Tumors of the Retina**

#### 129. Retinoblastoma

Introduction  
Genetics of retinoblastoma  
Retinoblastoma: The disease  
TNM classification system  
Diagnosis of retinoblastoma  
The approach to the child with cancer  
Treatment methods and techniques  
Conclusions  
References

#### 130. Cavernous hemangioma

Introduction  
Clinical findings  
Differential diagnosis  
Ancillary studies  
Natural history  
Treatment  
Pathology  
Systemic and familial involvement  
Genetics  
References

#### 131. Hemangioblastoma of the retina and von Hippel–Lindau disease

Introduction  
von Hippel–Lindau disease  
History  
The VHL gene and protein  
Clinical features of ocular von Hippel–Lindau disease  
Pathology of ocular lesions  
Diagnosis and surveillance of von Hippel–Lindau disease  
Treatment of ocular von Hippel–Lindau disease  
Conclusions

## References

### 132. Tuberous sclerosis and the eye

Introduction

Genetic diagnostic criteria

Systemic manifestations

Ocular manifestations

Genetics and pathophysiology

Organ-specific surveillance and treatment approaches

References

### 133. Phakomatoses

Introduction

Definition of hamartia, hamartoma, chorista, and choristoma

Neurofibromatosis

Encephalofacial hemangiomas (Sturge–Weber syndrome)

Racemose hemangiomas (Wyburn-Mason syndrome)

Retinal cavernous hemangiomas

Organoid nevus syndrome

Phacomatosis pigmentovascularis

Oculodermal melanocytosis

Other phakomatoses

Combined systemic hamartomas

Conclusions

References

### 134. Retinal metastases

Introduction

Checkpoint inhibition and tumor cell mutations

Review of case reports

Summary

References

### 135. Remote effects of cancer: Paraneoplastic autoimmune retinopathies

Introduction

Cancer-associated retinopathy (CAR)

Melanoma-associated retinopathy (MAR)

Paraneoplastic vitelliform maculopathy (PVM)

Paraneoplastic optic neuropathies (PON)

Bilateral diffuse uveal melanocytic proliferation (BDUMP)

Conclusions

References

### 136. Optic disc melanocytoma

Introduction

Clinical features

Differential diagnosis

Pathology and pathogenesis

Diagnostic approaches

Management

Conclusions

References

### 137. Congenital hypertrophy of the retinal pigment epithelium

Introduction

Epidemiology and demographics

Clinical findings and classification

Differential diagnosis

References

### 138. Combined hamartoma of the retinal pigment epithelium and retina

Historical review

Epidemiology

Clinical manifestations

Diagnostic evaluation

Differential diagnosis

Clinical course

Etiology and pathogenesis

Histopathology

Treatment

References

## **Section 2. Tumors of the Choroid**

### 139. Choroidal nevi

Introduction

Prevalence of choroidal nevus

Clinical presentation

Histopathology of choroidal nevus

Clinical differential diagnosis of choroidal nevus

Ancillary studies

Management of choroidal nevus

Secondary changes in the neighboring tissues

Choroidal nevi and systemic disease

Acknowledgments

References

#### 140. Epidemiology of posterior uveal melanoma

Introduction

Incidence

Host factors

Hormones and reproductive factors

Environmental factors

Conclusions

References

#### 141. Prognosis of posterior uveal melanoma

Globe-conserving therapies and prognosis

Clinical prognostic indicators for metastasis

Histopathologic prognostic indicators for metastasis

Molecular prognostic indicators for metastasis

Marker integration

Liquid biopsies

Psychological impact

Improving prognosis with early treatment of uveal melanoma

Conclusions

References

#### 142. Molecular genetics of choroidal melanoma

Introduction

Genomic landscape of uveal melanoma

Epidemiology and genetic predisposing conditions

Conclusions

Acknowledgments

References

#### 143. Pathology of choroidal melanoma

Introduction

Processing of specimens

Gross appearance of choroidal melanoma

Histopathologic features of tumor cells and their prognostic relevance

Other histopathologic characteristics and their prognostic relevance

Special types of uveal melanoma

Histologic changes after treatment

Acknowledgments

Appendix: Histologic differential diagnoses

References

#### 144. Overview of management of posterior uveal melanoma

Introduction

Conditions that predispose to uveal melanoma

Zimmerman hypothesis

Posterior uveal melanoma management

Radiotherapy

Laser photocoagulation

Transpupillary thermotherapy

Photodynamic therapy

Local resection

Enucleation

Orbital exenteration

Observation

AURA-011 (AU-011) nanoparticle therapy

Genetic testing

Management and prevention of systemic metastasis

Conclusions

References

#### 145. Enucleation for choroidal melanomas

Introduction

Purpose of enucleation

Enucleation technique

Conclusions

Acknowledgments

References

#### 146. Brachytherapy for choroidal melanoma

Introduction

Dosimetry

Isotope selection

Plaque design

Indications for treatment

Plaque placement technique

Local tumor response

Recurrences

Visual outcomes and radiation complications

Management of radiation-related complications

Adjuvant therapy

Conclusions

References

#### 147. Charged-particle irradiation of uveal melanoma

Introduction

Treatment

Results

Conclusions

References

#### 148. Surgical resection of choroidal melanoma

Introduction

Exoresection

Endoresection

Secondary local resection for toxic tumor after radiotherapy

Conclusions

Acknowledgments

References

#### 149. Laser treatment of choroidal melanoma

Introduction

Transpupillary thermotherapy

Photodynamic therapy

Photoactivated therapy

Experimental laser techniques

References

#### 150. Systemic evaluation and management of patients with metastatic uveal melanoma

Introduction

Physical examination

Pathology, genetics, and molecular biology

Ethical considerations of screening and biopsy

High-risk disease

Treatment of metastatic disease

References

#### 151. Collaborative ocular melanoma study

Introduction

Background

Design of the collaborative ocular melanoma study (COMS)

Methods

Chronology of the COMS

Findings from the COMS trial of I-125 brachytherapy for medium choroidal melanoma

Findings from the COMS trial of pre-enucleation radiation for large choroidal melanoma

Findings from the COMS nonrandomized prospective study of small choroidal melanoma

Histopathologic findings from enucleated eyes

Other published findings

Conclusions

## References

### 152. Choroidal metastases

Introduction

Symptoms and clinical findings

Diagnostic evaluation

Differential diagnosis

Systemic evaluation

Management

Prognosis

Conclusions

References

### 153. Choroidal osteoma

Introduction

Definition and incidence

Clinical features

Differential diagnosis

Pathology and pathogenesis

Familial choroidal osteoma

Systemic associations

Diagnostic approaches

Management

Prognosis

Conclusions

References

### 154. Circumscribed choroidal hemangioma

Introduction

Clinical features

Differential diagnosis

Ancillary studies

Pathology

Treatment

Conclusions

References

## **Section 3. Hematologic and Miscellaneous Tumors**

### 155. Miscellaneous uveal tumors

Introduction

Epithelial tumors of the ciliary body: Congenital

Epithelial tumors of the ciliary body: Acquired

Melanocytic tumors

Neurogenic tumors



Myogenic tumors

Miscellaneous

The role of diagnostic biopsy for uveal tumors

Conclusions

References

156. Leukemias and lymphomas

Introduction

Systemic classification of leukemia and lymphoma

Leukemia

Lymphomas

References

157. Primary vitreoretinal lymphoma

Introduction

Epidemiology

Etiology and pathogenesis

Clinical findings

Diagnosis

Differential diagnosis

Treatment

Prognosis

References

Index