

Contents

Part I Optic Nerve

Chapter 1

Optic Neuritis and Multiple Sclerosis

Edward J. Atkins, Valérie Biousse,
Nancy J. Newman

1.1	Idiopathic Optic Neuritis	4
1.1.1	Clinically Isolated Syndrome	4
1.1.2	Clinical Features of Acute Idiopathic Optic Neuritis	4
1.1.3	Examination Findings in Acute Idiopathic Optic Neuritis	4
1.2	Natural History of Acute Idiopathic Optic Neuritis	4
1.2.1	Important Studies	4
1.2.2	Visual Prognosis	5
1.2.3	Risk of Recurrence of Optic Neuritis	5
1.2.4	Risk of Developing Multiple Sclerosis	5
1.2.5	Severity of Multiple Sclerosis in Patients Presenting with Optic Neuritis	10
1.3	Management of Acute Idiopathic Optic Neuritis	10
1.3.1	Diagnosis	11
1.3.2	Acute Therapeutic Options	12
1.3.3	Chronic Therapeutic Options	13
1.4	Pediatric Optic Neuritis	14

Chapter 2

Ischemic Optic Neuropathies

Anthony C. Arnold

2.1	Introduction	19
2.2	Anterior Ischemic Optic Neuropathy	20
2.2.1	Arteritic Anterior Ischemic Optic Neuropathy	20

2.2.1.1	Clinical Presentation	20
2.2.1.2	Pathophysiology	22
2.2.1.3	Differential Diagnosis	23
2.2.1.4	Clinical Course	23
2.2.1.5	Diagnostic Confirmation	23
2.2.1.6	Therapy	24
2.2.2	Nonarteritic Anterior Ischemic Optic Neuropathy (NAION)	25
2.2.2.1	Clinical Presentation	25
2.2.2.2	Pathophysiology	26
2.2.2.3	Risk Factors	27
2.2.2.4	Medications	29
2.2.2.5	Clinical Course	30
2.2.2.6	Differential Diagnosis	30
2.2.2.7	Therapy	31
2.2.2.8	Prevention	31
2.3	Posterior Ischemic Optic Neuropathy	32

Chapter 3

Optic Disc Drusen

François-Xavier Borruat

3.1	Introduction	37
3.2	Epidemiology	37
3.3	Pathology	38
3.4	Optic Canal Size	39
3.5	Associations	40
3.5.1	Inherited Retinal Degenerations	40
3.5.2	Angioid Streaks and Pseudoxanthoma Elasticum	40
3.5.3	Miscellaneous	40
3.6	Paraclinical Investigations	41
3.6.1	B-Scan Ultrasound	41
3.6.2	Scanning Laser Ophthalmoscope	41
3.6.3	Optical Coherence Tomography	43
3.6.4	Scanning Laser Polarimetry	44
3.6.5	Electrophysiology	44

3.6.6	Retinal Angiography	44
3.7	Complications	44
3.7.1	Visual Field Defects	44
3.7.2	Retinal Vascular Complications	46
3.7.3	Peripapillary Choroidal Neovascularization	46
3.7.4	Anterior Ischemic Optic Neuropathy	46
3.8	Therapy	46

Chapter 4

Inherited Optic Neuropathies

Marcela Votruba

4.1	Introduction	51
4.2	Primary Inherited Optic Neuropathies with Ocular Manifestations	52
4.2.1	Autosomal-Dominant Optic Atrophy	52
4.2.1.1	Clinical Features	52
4.2.1.2	Electrophysiology	55
4.2.1.3	Histopathology	55
4.2.1.4	Molecular Genetics and the Genetic Heterogeneity of ADOA	55
4.2.1.5	OPA4 Locus	58
4.2.1.6	OPA3 Locus: Autosomal-Dominant Optic Atrophy and Cataract (ADOAC)	58
4.2.2	Recessive Optic Atrophy	58
4.2.2.1	Clinical Features	58
4.2.2.2	OPA5 Locus	59
4.2.3	X-Linked Optic Atrophy	59
4.2.3.1	Clinical Features	59
4.2.3.2	OPA2 Locus	59
4.2.4	Mitochondrial Disease: Leber's Hereditary Optic Neuropathy	59
4.2.4.1	Clinical Features	59
4.2.4.2	Findings in Unaffected Relatives	60
4.2.4.3	Systemic Manifestations	60
4.2.4.4	Molecular Genetics	61
4.2.4.5	LHON-Associated Mitochondrial Mutations	62
4.2.4.6	Genotype-Phenotype Correlation	62
4.2.4.7	Evidence for an X-Linked Susceptibility Factor	63

4.2.4.8	The Pathophysiology of LHON	63
4.3	Primary Inherited Optic Neuropathies with Significant Systemic Features	64
4.3.1	Autosomal-Dominant Optic Atrophy and Neurological Defects	64
4.3.2	Autosomal-Recessive Optic Atrophy "Plus"	64
4.3.3	Costeff's Syndrome	64
4.3.4	Behr's Syndrome	64
4.3.5	Wolfram Syndrome, DIDMOAD	64
4.4	Conclusions	65

Chapter 5

Optic Nerve Tumours

Tim D. Matthews

5.1	Introduction	69
5.1.1	Gliomas	69
5.1.1.1	NF1	71
5.1.2	Meningiomas	71
5.1.2.1	Retino-Choroidal Collaterals	72
5.2	Imaging	74
5.2.1	Gliomas	74
5.2.1.1	Typical	74
5.2.1.2	Masquerade	74
5.2.2	Meningiomas	75
5.2.2.1	Typical	75
5.2.2.2	Masquerade	76
5.3	Management	76
5.3.1	Gliomas	76
5.3.1.1	Paediatric	77
5.3.1.2	Adult	78
5.3.2	Meningiomas	79
5.4	Conclusions	80

Chapter 6

Traumatic Optic Neuropathy: Recommendations and Neuroprotection

Solon Thanos, Stephan Grewe, Tobias Stupp

6.1	Introduction	83
6.1.1	Optic Nerve Anatomy	83
6.1.2	Traumatic Optic Neuropathy	84

6.2	Review of Previous Studies on TONs	84	7.3.1	Scanning Laser Ophthalmoscopy and Tomography	103
6.3	Histopathology of TON	87	7.3.1.1	The Rodenstock System	105
6.4	Mechanisms of TON-Induced Ganglion Cell Death	89	7.3.1.2	The Heidelberg Laser Tomographic Scanner	105
6.5	Diagnosis of TON	89	7.3.1.3	The Zeiss Confocal Scanning Laser Ophthalmoscope and TopSS™ Topographic Scanning System	106
6.6	Therapeutic Concepts of TON	91	7.3.2	The Heidelberg Retinal Tomograph II	106
6.6.1	Steroids	91	7.3.3	Scanning Laser Polarimetry ("GDx")	107
6.6.2	Neuroprotection	91	7.3.4	Optical Coherence Tomography	109
6.6.3	Surgical Decompression	91	7.3.4.1	Using OCT for Glaucoma Evaluation	111
6.6.4	The Role of Ophthalmologists	91	7.3.4.2	Other Uses of OCT	111
6.7	Outlook on Regeneration of the Optic Nerve	92	7.3.4.3	Ultrahigh-Resolution OCT (UHR-OCT)	112
6.8	Current Clinical Practice and Recommendations	93	7.4	Imaging of the Optic Nerve and Alzheimer Disease	113

Part II Investigations

Chapter 7

Imaging the Nerve Fiber Layer and Optic Disc

Marc Dinkin, Michelle Banks,
Joseph F. Rizzo III

7.1	Introduction	100
7.2	Overview of Early Imaging Techniques	100
7.2.1	Optic Nerve Head Drawings	100
7.2.2	Direct Ophthalmoscopy of the Nerve Fiber Layer	100
7.2.3	Retinal Nerve Fiber Layer Photography	100
7.2.4	Stereoscopic Optic Nerve Head Photography	101
7.2.5	Optic Nerve Head Analyzers	102
7.2.5.1	The Topcon IMAGENet	102
7.2.5.2	The Humphrey Retinal Analyzer	102
7.2.5.3	The Rodenstock Optic Nerve Head Analyzer	102
7.2.5.4	The Glaucoma-Scope	103
7.3	Modern Techniques for Optic Nerve and Retinal Nerve Fiber Layer Imaging	103

Chapter 8

Functional Neuroanatomy of the Human Visual System: A Review of Functional MRI Studies

Mark W. Greenlee, Peter U. Tse

8.1	Introduction	119
8.2	Imaging the Lateral Geniculate Nucleus	121
8.3	Functional Maps of the Visual Field	121
8.4	Striate and Extrastriate Visual Areas in Human Visual Cortex (V1, V2, V3)	121
8.5	Receptive Field Size as a Function of Retinal Eccentricity	122
8.6	Alternative Methods of Retinotopic Mapping	124
8.7	Columnar Structures within Human V1	125
8.8	Orientation Specificity of BOLD Responses in Visual Cortex	125

8.9 Visual Maps of Higher Visual Function: V4 126

8.10 Visual Maps of Higher Visual Function: V3A, V3B and KO 126

8.11 Segmenting Extrastriate Areas and MT+ into Functional Subregions 127

8.12 Responses to Optic Flow ... 128

8.13 Disparity and Motion-in-Depth Stimulation 129

8.14 Interface Between Visual and Oculomotor Systems 129

8.15 Parietal Lobe Maps of Visuotopic Space 130

8.16 Working Memory for Visual Stimuli 130

8.17 Role of V1 in Visual Consciousness 132

8.18 Summary 132

Chapter 9
Investigating Visual Function with Multifocal Visual Evoked Potentials

Michael B. Hoffmann

9.1 Introduction 139

9.2 Multifocal Principle and Characteristics of Multifocal VEPs 140

9.2.1 Basics – Multifocal Stimulation, First- and Second-Order Kernels 140

9.2.2 Stimulus Display for mfVEP Recordings 143

9.2.3 Recording mfVEPs and Practical Considerations 143

9.2.4 Dependence of mfVEPs on Visual Cortex Morphology 146

9.3 Assessment of mfVEPs 148

9.3.1 Response Magnitude 148

9.3.2 Response Latency 149

9.4 mfVEP Investigations of Diseases 151

9.4.1 mfVEP in Glaucoma 152

9.4.2 mfVEP in Optic Neuritis 153

9.4.3 mfVEP in Albinism 154

9.5 Conclusion 157

Part III Retinal Disorders

Chapter 10
Autoimmune Retinopathies

Jennifer K. Hall, Nicholas J. Volpe

10.1 Autoimmune Disease Overview 163

10.2 Autoimmune Retinopathy Overview 164

10.3 Paraneoplastic Retinopathies 164

10.3.1 Cancer-Associated Retinopathy 164

10.3.1.1 Clinical Presentation 166

10.3.1.2 Diagnostic Studies 166

10.3.1.3 Pathophysiology 166

10.3.1.4 Treatment 168

10.3.2 Melanoma-Associated Retinopathy 168

10.3.2.1 Clinical Presentation 168

10.3.2.2 Diagnostic Studies 168

10.3.2.3 Pathophysiology 169

10.3.2.4 Treatment 169

10.3.3 Bilateral Diffuse Uveal Melanocytic Proliferation .. 169

10.3.3.1 Clinical Presentation 170

10.3.3.2 Diagnostic Studies 170

10.3.3.3 Pathophysiology 170

10.3.3.4 Treatment 171

10.4 Autoimmune-Related Retinopathy and Optic Neuropathy 171

10.5 Acute Outer Retinopathies with Blind Spot Enlargement 172

10.5.1 Acute Idiopathic Blind Spot Enlargement ... 173

10.5.1.1 Clinical Presentation 173

10.5.1.2 Diagnostic Studies 173

10.5.1.3 Pathophysiology 173

10.5.1.4 Treatment 176

10.5.2 Multiple Evanescent White Dot Syndrome 176

10.5.2.1 Clinical Presentation 176

10.5.2.2 Diagnostic Studies 176

10.5.2.3 Pathophysiology 177

10.5.2.4 Treatment 178

10.5.3 Acute Zonal Occult Outer Retinopathy 178

10.5.3.1 Clinical Presentation 178
 10.5.3.2 Diagnostic Studies 178
 10.5.3.3 Pathophysiology 179
 10.5.3.4 Treatment 179
 10.5.3.5 AZOOR Complex of Disease 179
 10.6 Summary 180

Chapter 11

Retinal Research: Application to Clinical Practice

Ludwig Aigner, Claudia Karl

11.1 Introduction 185
 11.1.1 Retinitis Pigmentosa 185
 11.1.2 Age-Related Macular Degeneration 186
 11.1.3 Glaucoma 186
 11.2 Cell Death in the Retina 186
 11.2.1 Major Characteristics and Pathways of Apoptosis 187
 11.2.1.1 Caspase-Dependent Apoptosis 187
 11.2.1.2 Caspase-Independent Apoptosis 188
 11.3 Therapeutic Strategies in Degenerative Retinal Diseases 189
 11.3.1 Strategies for Neuroprotection 189
 11.3.1.1 Animal Models in Retinal Degeneration Research 189
 11.3.1.2 Strategies for Neuroprotection Interfering with the Induction Phase of Apoptosis 190
 11.3.1.3 Strategies for Neuroprotection Interfering with the Early Phase of Apoptosis 191
 11.3.1.4 Strategies Using Neuroprotective Cytokines that Showed Effects in Other Tissues 191
 11.3.2 Cell Therapy for the Diseased Retina 192
 11.3.2.1 Cell Transplantation in the Retina 193
 11.3.2.2 Application of Transgenes or Genetically Engineered Stem and Progenitor Cells 198

11.3.2.3 Endogenous Cell Replacement in the Retina 199

Part IV Systemic disease

Chapter 12

Chorioretinal Lesions in Infectious Diseases of Neuroophthalmic Interest

Yan Guex-Crosier

12.1 Introduction 206
 12.2 Ocular Zoonosis 206
 12.2.1 Ocular Toxoplasmosis 206
 12.2.1.1 Congenital Toxoplasmosis .. 206
 12.2.1.2 Reactivation of Toxoplasmosis in Immunocompetent Patients 207
 12.2.1.3 Ophthalmic Toxoplasmosis in AIDS Patients 209
 12.2.1.4 Neurologic Manifestation of Toxoplasmosis in AIDS Patients 209
 12.2.1.5 Radiologic Manifestation of Toxoplasmosis in AIDS ... 209
 12.2.2 Toxocariasis 210
 12.2.2.1 Introduction 210
 12.2.2.2 Ocular Manifestations 210
 12.2.2.3 Neurologic Manifestations 210
 12.2.3 Diseases Transmitted by Ticks 210
 12.2.3.1 Introduction 210
 12.2.3.2 Tick-Borne Encephalitis 210
 12.2.3.3 Lyme Disease 211
 12.2.4 Cat Scratch Disease 214
 12.2.4.1 Introduction 214
 12.2.4.2 Ocular and Neuroophthalmologic Manifestations 214
 12.2.4.3 Neurologic Manifestations 215
 12.2.4.4 Therapy 215
 12.3 Sexually Transmitted Diseases 215
 12.3.1 Syphilis 215
 12.3.1.1 Introduction 215
 12.3.1.2 Ocular and Neuroophthalmologic Manifestations 215
 12.3.1.3 Diagnostic Tests 216

12.3.1.4 Therapy 216

12.3.2 Human Immunodeficiency Virus (HIV) and Ocular Infection 216

12.3.2.1 Introduction 216

12.3.2.2 HIV Retinopathy 217

12.3.2.3 CMV Retinitis 218

12.4 Encephalopathies Due to Viral and Non-Conventional Agents 220

12.4.1 Lymphocytic Choriomeningitis Virus 220

12.4.2 Creutzfeldt–Jakob Disease 220

12.4.3 JC Virus and Progressive Multifocal Leukoencephalopathy 221

12.4.4 Herpetic Encephalopathy and Acute Retinal Necrosis Syndrome 222

12.5 Conclusion 222

Chapter 13
Giant Cell Arteritis

Aki Kawasaki

13.1 Pathophysiology of Giant Cell Arteritis 227

13.1.1 Epidemiology 227

13.1.2 Triggering Event 228

13.1.3 Tropism to Certain Vascular Beds 228

13.1.4 Macrophage Recruitment and Vascular Injury 229

13.1.5 Systemic Inflammation 230

13.2 Clinical (Non-Ophthalmic) Manifestations of GCA 231

13.2.1 Natural History 231

13.2.2 Systemic Signs and Symptoms 231

13.2.3 Headache and Craniofacial Pain 231

13.2.4 Auditory Manifestations ... 232

13.2.5 Neurologic Manifestations 232

13.2.6 Occult GCA 232

13.3 Visual Manifestations of GCA 233

13.3.1 Transient Visual Loss 233

13.3.2 Anterior Ischemic Optic Neuropathy 234

13.3.3 Other Types of Ischemic Visual Loss 235

13.3.4 Diplopia 235

13.3.5 Orbital Manifestations 236

13.4 Clinical Subtypes of GCA ... 236

13.4.1 Systemic Inflammatory Syndrome 236

13.4.2 Cranial Arteritis 236

13.4.3 Large-Vessel Vasculitis 237

13.5 Laboratory Investigations in GCA 238

13.5.1 Erythrocyte Sedimentation Rate 238

13.5.2 C-Reactive Protein 239

13.5.3 Thrombocytosis 239

13.5.4 Interleukin-6 and Other Cytokines 239

13.5.5 Anemia 240

13.5.6 Others 240

13.6 Diagnosis of GCA 240

13.6.1 Temporal Artery Biopsy 241

13.6.2 American College of Rheumatology Criteria .. 241

13.6.3 Role of Ultrasound 243

13.6.4 Other Non-Invasive Imaging of the Cranial Arteries 243

13.7 Treatment and Prognosis of GCA 244

13.7.1 Corticosteroids 244

13.7.1.1 Starting Dose 245

13.7.1.2 Maintenance Dose 245

13.7.1.3 Tapering Regimen 245

13.7.1.4 Duration of Treatment 245

13.7.2 Visual Outcome on Corticosteroids 245

13.7.3 Methotrexate 246

13.7.4 Other Adjuvant Therapies .. 246

13.7.5 Treatment of Large-Vessel Involvement 247

Part V Oculomotility

Chapter 14
Cerebral Control of Eye Movements

Charles Pierrot-Deseilligny

14.1 Introduction 254

14.2 Brainstem 255

14.2.1 Horizontal Eye Movements 255
 14.2.1.1 Final Common Pathway 255
 14.2.1.2 Premotor Structures and Afferent Pathways 257
 14.2.2 Vertical Eye Movements 259
 14.2.2.1 Final Common Pathway 259
 14.2.2.2 Premotor Structures and Brainstem Afferents ... 259
 14.3 Suprareticular Structures ... 261
 14.3.1 Cerebellum 261
 14.3.2 Cerebral Hemispheres 262
 14.4 Abnormal Eye Movements 263
 14.4.1 Nystagmus 263
 14.4.2 Non-Nystagmic Abnormal Eye Movements 264

Chapter 15
Chronic Progressive External Ophthalmoplegia – A Common Ocular Manifestation of Mitochondrial Disorders

Marcus Deschauer, Stephan Zierz

15.1 Introduction 267
 15.2 Clinical Features 268
 15.2.1 Ophthalmoplegia and Ptosis 268
 15.2.2 CPEO Plus: Multisystemic Involvement 268
 15.2.2.1 Muscle Impairment 268
 15.2.2.2 Visual Impairment 268
 15.2.2.3 Specific CPEO Plus Syndromes 268
 15.3 Genetics 270
 15.3.1 General Mitochondrial Genetics 270
 15.3.2 Single Deletions of mtDNA 270
 15.3.3 Defects of Intergenomic Communication with Multiple Deletions of mtDNA 271
 15.3.4 Point Mutations of mtDNA 272
 15.3.5 Coenzyme Q Deficiency 273
 15.3.6 Genotype–Phenotype Correlation 273
 15.4 Diagnostics 274
 15.4.1 Myohistological Investigations 275
 15.4.2 Biochemical Investigations 275

15.4.3 Molecular Genetic Investigations 275
 15.5 Treatment 276
 15.5.1 Pharmacological Therapy .. 276
 15.5.2 Symptomatic Treatment ... 277
 15.5.3 Gene Therapy 277
 15.6 Differential Diagnosis 278
 15.6.1 Oculopharyngeal Muscular Dystrophy 278
 15.6.2 Myasthenic Syndromes 278
 15.6.3 Congenital Fibrosis of the Extraocular Muscles 279
 15.6.4 Ocular Myositis 279
 15.6.5 Endocrine Ophthalmopathy 279
 15.6.6 Myotonic Dystrophy 279
 15.6.7 Facioscapulohumeral Muscular Dystrophy 279
 15.6.8 Congenital Myopathies 279

Chapter 16
Treatment of Specific Types of Nystagmus

Marianne Dieterich

16.1 Introduction 284
 16.2 Peripheral Vestibular and Ocular Motor Disorders 284
 16.2.1 Acute Peripheral Vestibulopathy, Vestibular Neuritis 284
 16.2.1.1 Etiology 286
 16.2.1.2 Therapeutic Recommendations 287
 16.2.2 Superior Oblique Myokymia 288
 16.2.2.1 Etiology 288
 16.2.2.2 Therapeutic Recommendations 288
 16.3 Supranuclear Ocular Motor Disorders 289
 16.3.1 Central Vestibular Disorders 289
 16.3.1.1 Vestibular Syndromes in the Sagittal (Pitch) Plane 289
 16.3.2 Central Ocular Motor Disorders 294
 16.3.2.1 Acquired Pendular Nystagmus 294
 16.3.2.2 Opsoclonus and Ocular Flutter 296

Part VI Rehabilitation

Chapter 17

Rehabilitation in Neuroophthalmology

Susanne Trauzettel-Klosinski

17.1	Introduction	301
17.2	Psychophysics of Normal Reading	302
17.3	Diseases of the Visual Pathways and their Functional Deficits	303
17.3.1	Optic Neuropathies	303
17.3.1.1	Central Scotomas	303
17.3.1.2	Arcuate Scotomas: Nerve Fiber Bundle Defects	305
17.3.1.3	Ring Scotomas	305
17.3.1.4	Constricted Fields	305
17.3.1.5	The Impact of Visual Field Defects on Reading Performance	305
17.3.2	Optic Chiasmal Syndromes	307
17.3.3	Suprachiasmatic Lesions of the Visual Pathways	307
17.3.3.1	Hemianopic Reading Disorder	308
17.3.3.2	Hemianopic Orientation Disorder	310
17.3.4	Cortical Visual Impairment	311
17.4	Diagnostic Procedures to Examine Reading Ability	311
17.5	Rehabilitation Programs	312
17.5.1	Visual Aids in Reading Disorders	312
17.5.2	Visual and Other Aids in Spatial Orientation Problems	313
17.5.3	Training	314
17.5.3.1	Training for Patients with Circumscribed Scotomas in the Central Field	314
17.5.3.2	Training for Patients with Homonymous Field Defects	315
17.5.4	Counseling Regarding Public Support	316
17.6	Summary and Conclusions	316
	Subject Index	321