
Contents

CHAPTER 1

Targets in Ocular Allergy

ALESSANDRA MICERA, SERGIO BONINI,
ALESSANDRO LAMBIASE, ROBERTO SGRULLETTA,
STEFANO BONINI

1.1	Introduction	1
1.2	Chronic Allergic Eye Diseases	2
1.3	Effector Cells and Cytokine Release	2
1.4	Chemokines and Adhesion Molecules	3
1.5	Neuropeptide and Growth Factor Involvement	4
1.6	Tissue Remodelling and the Contribution of Fibroblasts	5
1.7	Metabolism of Extracellular Matrix	6
1.8	Conclusions	7
	References	8

CHAPTER 2

Dry Eye: Inflammation of the Lacrimal Functional Unit

STEPHEN C. PFLUGFELDER, MICHAEL E. STERN

2.1	Introduction	11
2.1.1	Basics	11
2.1.2	Lacrimal Functional Unit	12
2.2	Specific Pathologies of the Lacrimal Functional Unit	14
2.2.1	Dysfunction of the Afferent System	14
2.2.2	Dysfunction of the Efferent System	15
2.2.3	Glandular Dysfunction	15
2.3	Lacrimal Keratoconjunctivitis Inflammation	16
2.3.1	Corneal Epithelial Disease	17
2.3.2	Conjunctival Epithelial Disease	17
2.3.3	Inflammation	18
2.4	Diagnosis	19
2.5	Therapies	21
	References	22

CHAPTER 3

Ocular Cicatricial Pemphigoid

MUNA AHMED, C. STEPHEN FOSTER

3.1	Introduction	25
3.2	Pathophysiology	26
3.3	Epidemiology	26
3.4	Clinical History	26
3.5	Clinical Signs	26
3.6	Staging	27
3.7	Diagnosis	28
3.7.1	Laboratory Tests	28
3.7.2	Conjunctival Biopsy	28
3.7.3	Histology	29
3.8	Treatment	29
3.8.1	Medical	29
3.8.2	Surgery	31
3.9	Collaborative Care	33
3.10	Prognosis	33
	References	34

CHAPTER 4

Immunomodulation for Corneal Transplantation

DOUGLAS J. COSTER, KERYN A. WILLIAMS

4.1	Introduction	35
4.2	Why Has Corneal Transplantation Fallen Behind Solid Organ Grafting?	36
4.3	Immunomodulation for Corneal Transplantation	36
4.4	Actuarial Survival Data on Corneal Transplantation	37
4.5	Options for Immunomodulation ...	38
4.6	Corneal Privilege	38
4.7	Mechanisms of Corneal Allograft Rejection	39

4.8 The Afferent Limb:
Sensitization to Corneal Alloantigens 39

4.9 The Efferent Limb:
Histological Correlates 40

4.10 Current Approaches
to Immunomodulation
for Corneal Transplantation 41

4.10.1 Anti-inflammatory Measures 41

4.10.2 Atraumatic Microsurgical Technique 41

4.10.3 Topical Corticosteroids 41

4.10.4 HLA Matching for Class I
and Class II Antigens 41

4.10.5 Systemic Immunosuppression 42

4.10.6 Systemic Corticosteroids 42

4.10.7 Antiproliferative Agents 43

4.10.8 Calcineurin Blockers 43

4.10.9 Combination Therapy 44

4.10.10 Side Effects of Systemic
Immunosuppression 44

4.11 Novel Approaches
to Immunomodulation 45

4.11.1 Monoclonal Antibody Fragments .. 45

4.11.2 Gene Therapy 45

4.12 Conclusion 46

References 46

CHAPTER 5

Scleritis

ALISA KIM, SEAN DUMARS, SAMIR SHAH,
BARTLY MONDINO

5.1 Introduction 52

5.1.1 Classification 52

5.1.2 Anatomy 55

5.1.3 Pathogenesis 55

5.1.4 Histopathology 56

5.2 Clinical Presentation 57

5.2.1 History: Ocular Symptoms 57

5.2.2 Physical Examination:
Ocular Signs 58

5.2.3 Associated Ocular Manifestations .. 60

5.2.4 Systemic Diseases:
Clinical Evaluation 61

5.3 Diagnostic Tools 62

5.4 Medical Management 63

5.5 Surgical Management 64

References 65

CHAPTER 6

Clinical Aspects of MALT

ERICH KNOP, NADJA KNOP, UWE PLEYER

6.1 Introduction 67

6.2 Structure and Function of MALT ... 68

6.2.1 Structure of MALT 68

6.2.2 Eye-Associated Lymphoid Tissue
(EALT) 71

6.2.3 Basic Functions of MALT 74

6.3 Dry Eye Disease 76

6.3.1 Introduction 75

6.3.2 Epidemiology, Definition
and Characteristics of Dry Eye 76

6.3.3 Novel Therapeutic Approaches
to Dry Eye Disease 80

6.4 Ocular Allergy 81

6.4.1 Introduction 81

6.4.2 Epidemiology, Definition
and Characteristics
of Allergic Eye Disease 81

6.4.3 Course and Therapy Options
in Allergic Ocular Disease 84

6.5 Keratoplasty 84

6.5.1 Introduction 84

6.5.2 Immunological Characteristics
of Keratoplasty 85

References 87

CHAPTER 7

Immunogenetics

of Ocular Inflammatory Disease

RALPH D. LEVINSON

7.1 Introduction 91

7.2 Human Leukocyte Antigens 93

7.2.1 HLA Nomenclature 94

7.2.2 Class I HLA 94

7.2.3 Class II HLA 95

7.2.4 HLA Haplotypes
and Linkage Disequilibrium 95

7.2.5 HLA and Disease Pathogenesis 95

7.3 HLA Associations
with Ocular Inflammatory Disease . 96

7.3.1 Class I HLA Associations
with Ocular Inflammatory Disease . 96

7.3.2 Class II HLA Associations
with Ocular Inflammatory Disease . 98

7.3.3	HLA Associations with Ocular Infections	100
7.3.4	HLA Associations with External Ocular Inflammation.	100
7.3.5	HLA Associations with Extraocular Disease	100
7.4	Non-HLA Genes Associated with Ocular Inflammatory Disease	101
7.5	Other Ocular Diseases	102
7.6	Conclusion	102
	References	102

CHAPTER 8

Immune Mechanisms in Uveitis

LING CHEN, LYNN K. GORDON

8.1	Introduction	109
8.2	Animal Uveitis Models	110
8.2.1	Experimental Autoimmune Uveitis (EAU).	110
8.2.2	Endotoxin-Induced Uveitis (EIU)	116
8.2.3	Experimental Melanin-Protein- Induced Uveitis (EMIU)	116
8.2.4	Experimental Autoimmune Pigment Epithelial Membrane Protein- Induced Uveitis (EAPU).	117
8.3	Immune Mechanisms in Human Uveitis	117
8.3.1	HLA-Associated Human Uveitis	117
8.3.2	Behçet's Disease	119
8.3.3	Vogt-Koyanagi-Harada Syndrome	120
	References	121

CHAPTER 9

The Tip of the Iceberg: Current Knowledge of Uveitis in Juvenile Arthritis

UWE PLEYER, CLAUDIA SENGLER,
NATASA ORLIC, ROLF KEITZER

9.1	Introduction	125
9.2	Classification of Arthritis	126
9.3	Epidemiology	126
9.4	Pathogenesis	127
9.5	Risk Factors for the Development of Uveitis in JRA	128
9.6	Clinical Features of Uveitis in JCA	128
9.7	Complications of Uveitis in JCA	129
9.7.1	Macula Edema	130
9.8	Differential Diagnosis	130

9.9	Prognostic Factors for Uveitis.	131
9.9.1	Gender	132
9.9.2	Type of Arthritis	132
9.9.3	Onset of Arthritis	132
9.9.4	Severity of Uveitis at Onset	132
9.10	Correlation of Uveitis and Arthritis Activity	133
9.11	Treatment of Uveitis in JCA.	133
9.11.1	Topical Steroid Treatment	133
9.11.2	Nonsteroidal Anti-inflammatory Drugs (NSAID)	134
9.11.3	Systemic Immunomodulatory Agents	134
9.12	Recommendations for Ocular Screening in JCA	136
	References	136

CHAPTER 10

Herpes Viruses in Ocular Inflammation

BAHRAM BODAGHI, PHUC LEHOANG

10.1	Introduction	141
10.2	Fundamental Virology	143
10.3	Epidemiology	143
10.4	Pathophysiology	144
10.4.1	Experimental Viral Uveitis	144
10.4.2	Experimental Models to Study Viral Retinitis	145
10.5	Clinical Features	145
10.5.1	Anterior Uveitis	145
10.5.2	Viral Retinopathies	147
10.5.3	Differential Diagnosis	149
10.5.4	Putative Viral-Associated Uveitis	150
10.6	Diagnosis	150
10.6.1	Obtention of Ocular Fluids	151
10.6.2	Herpes Viruses	151
10.6.3	Search for Antiviral Antibodies	152
10.7	Treatment	153
10.7.1	Anterior Uveitis	153
10.7.2	Viral Retinopathies	154
	References	157

CHAPTER 11

Cytomegalovirus and the Eye

MARC D. DE SMET

11.1	Introduction	161
11.2	Populations at Risk	161

11.2.1	HIV Associated Immunosuppression	161
11.2.2	Immunosuppression in Non-HIV Settings.....	162
11.3	Appearance and Course.....	163
11.3.1	Manifestation Prior to Initial Treatment	163
11.3.2	Manifestations Under Therapy.....	164
11.3.3	Differential Diagnosis	165
11.3.4	Investigations	166
11.4	Therapeutic Agents	166
11.4.1	Ganciclovir.....	166
11.4.2	Valganciclovir	167
11.4.3	Foscarnet	167
11.4.4	Other Agents	167
11.5	Screening and Treatment Algorithms	167
11.5.1	CMV in HIV Infected Patients	168
11.5.2	CMV in Other Immunosuppressive States	168
11.6	Management of Complications.....	168
11.6.1	Immune Recovery	168
11.6.2	Retinal Detachment	168
	References	169

CHAPTER 12

Behçet's Disease

MANFRED ZIERHUT, NICOLE STÜBIGER,
CHRISTOPH DEUTER, INA KÖTTER

12.1	Introduction	173
12.2	Definition and Epidemiology of BD	174
12.2.1	Definition.....	174
12.2.2	History	174
12.2.3	Epidemiology	174
12.3	Genetics of BD	178
12.4	Immunology	182
12.4.1	T Cells	182
12.4.2	NK Cells	183
12.4.3	Neutrophils	183
12.4.4	Endothelial Dysfunction	183
12.4.5	Coagulation and Fibrinolytic Pathway Abnormalities	184
12.5	General (Extraocular) Manifestations of BD	184
12.5.1	Oral Aphthous Ulcerations	184
12.5.2	Genital Ulcerations.....	185
12.5.3	Skin Lesions.....	185
12.5.4	Pathergy Phenomenon	185

12.5.5	Skeletal System	185
12.5.6	Gastrointestinal Manifestations	186
12.5.7	Neurological Manifestations	186
12.5.8	Vascular Manifestations.....	186
12.5.9	Rare Manifestations	187
12.5.10	Life Expectancy	187
12.6	Ocular Involvement	187
12.6.1	Anterior Segment Changes	188
12.6.2	Posterior Segment Changes	188
12.6.3	Complications	189
12.6.4	Diagnosis	190
12.7	Therapy	190
12.7.1	Local Treatment	191
12.7.2	Systemic Treatment.....	191
12.7.3	Surgical Treatment	194
12.7.4	Practical Treatment Recommendations	194
	References	195

CHAPTER 13

Choroiditis:**General Considerations and Classification**

CARL P. HERBORT

13.1	Introduction	202
13.2	Indocyanine Green Angiography (ICGA)	202
13.2.1	Physicochemical Properties of Indocyanine Green (ICG)	202
13.2.2	Standard ICG Angiographic Protocol for Inflammatory Diseases	204
13.2.3	Principles for the Interpretation of ICGA [9, 10].....	204
13.2.4	Differences Between Fluorescein and Indocyanine Green Angiography	205
13.2.5	Clinico-pathologic-angiographic Correlations	205
13.2.6	Relevance of ICGA in Ocular Inflammatory Diseases	205
13.3	The Concepts of Inflammatory Choriocapillaropathy and Stromal Choroiditis [12].....	206
13.3.1	Primary Inflammatory Choriocapillaropathy (PICCP)	206
13.3.2	Stromal Choroiditis	207
13.3.3	Secondary Inflammatory Choriocapillaropathy	207
	References	207

CHAPTER 14

Primary Inflammatory Choriocapillaropathies

LUCA CIMINO, ALESSANDRO MANTOVANI,
CARL. P. HERBORT

14.1	Introduction	210
14.2	Angiographic Signs in Inflammatory Choriocapillaropathies	211
14.2.1	Angiographic Signs in Inflammatory Choriocapillaropathies	213
14.3	Patient History, Systemic and Ocular Symptoms and Signs in Primary Inflammatory Choriocapillaropathies	213
14.4	Practical Attitude in Primary Inflammatory Choriocapillaropathies (PICCP)	214
14.5	Specific Entities	215
14.5.1	Multiple Evanescent White Dot Syndrome (MEWDS)	215
14.5.2	Acute Idiopathic Blind Spot Enlargement (AIBSE)	216
14.5.3	Acute Posterior Multifocal Placoid Pigment Epitheliopathy (APMPPE) or Acute Multifocal Ischaemic Choriocapillaropathy (AMIC)	217
14.5.4	Multifocal Choroiditis (MFC), Including Punctate Inner Choroiditis (PIC), Diffuse Subretinal Fibrosis and Presumed Ocular Histoplasmosis Syndrome (POHS)	219
14.5.5	Serpiginous Choroiditis	222
14.6	Rare Entities	224
14.6.1	Acute Zonal Occult Outer Retinopathy (AZOOR) and Acute Annular Outer Retinopathy (AAOR)	224
14.6.2	Acute Macular Neuroretinopathy (AMN)	225
14.7	Overlapping Clinical Pictures in PICCPs: The Choriocapillaris as the Common Denominator of PICCPs	226
14.7.1	Association of Different PICCPs in the Same Patient	226
14.7.2	Intermediary Forms of PICCP	226
14.7.3	Unclassifiable Primary Inflammatory Choriocapillaropathies	227
14.8	Conclusion	228
	References	228

CHAPTER 15

Stromal Choroiditis

NADIA BOUCHENAKI, CARL O. HERBORT

15.1	Introduction	233
15.2	Specific Entities	234
15.2.1	Primary Stromal Choroiditis	234
15.2.2	Stromal Choroiditis as a Random Involvement of a Systemic Disease ..	243
15.2.3	Other Infectious Choroiditides	249
	References	251

CHAPTER 16

Immunomodulatory Therapy in Uveitis

STEPHAN R. THURAU, GERHILD WILDNER

16.1	Introduction	255
16.2	Cytotoxic Drugs	257
16.2.1	Azathioprine	258
16.2.2	Methotrexate	258
16.2.3	Mycophenolate Mofetil	259
16.2.4	Leflunomide	259
16.2.5	Cyclophosphamide	259
16.2.6	Chlorambucil	260
16.3	Antibiotics	261
16.3.1	Sulphasalazine	261
16.4	Calcineurin Inhibitors	261
16.4.1	Cyclosporine A (CsA)	261
16.4.2	Tacrolimus (FK506)	262
16.4.3	Sirolimus (Rapamycin)	262
16.5	Immunomodulatory Substances ...	262
16.5.1	Thalidomide	262
16.5.2	Anti-TNF- α Treatment	263
16.5.3	Interferon- α	265
16.5.4	Daclizumab	266
16.6	Oral Tolerance Induction	266
16.6.1	Retinal Autoantigens as Tolerogens ..	266
16.6.2	HLA-peptide B27PD as Oral Tolerogen	267
	References	268

CHAPTER 17

Vitrectomy in Uveitis

MATTHIAS D. BECKER, ARND HEILIGENHAUS,
MARC DE SMET, JANET DAVIS

17.1	Introduction	273
17.2	General Approach to PPV in Uveitis	273
17.2.1	Patient Selection	273
17.2.2	Timing of Surgery	273
17.2.3	Technical Considerations.....	274
17.2.4	Diagnostic Procedures	274
17.3	Perioperative Management	274
17.3.1	Assessment of Other Ocular Disease	274
17.3.2	Concomitant Medical Management .	275
17.4	Combined Surgery	277
17.4.1	Cataract Surgery	277
17.4.2	Membrane Peeling	278
17.4.3	Cryotherapy	278
17.4.4	Diagnostic PPV	278
17.5	Postoperative Complications	279
17.5.1	Hypotony	279
17.5.2	Retinal Detachment	279
17.5.3	Vitreous Haemorrhage	280
17.5.4	Uveitis Recurrence	280
17.6	PPV in Specific Diseases	280
17.6.1	Fuchs Uveitis Syndrome	280
17.6.2	Behçet's Disease	280
17.6.3	Intermediate Uveitis	280
17.6.4	Childhood Uveitis	281
17.6.5	Infectious Uveitis	281
	References	283
	 Subject Index	 285

Contributors

AHMED, MUNA, MD
Ocular Immunology and Uveitis Service,
Department of Ophthalmology,
Harvard Medical School,
243 Charles Street, Boston, MA 02114, USA

BECKER, MATTHIAS, Prof. Dr.
Interdisciplinary Uveitis Center,
Department of Ophthalmology,
University of Heidelberg,
Im Neuenheimer Feld 400,
69120 Heidelberg, Germany

BODAGHI, BAHRAM, MD, PhD
Professor of Ophthalmology
Department of Ophthalmology,
Pitié-Salpêtrière Hospital,
47 Bd. de l'Hôpital,
Paris 75013, France

BONINI, SERGIO, MD
Professor of Ophthalmology
University of Rome Tor Vergata,
Via Cassia Antica 35,
Rome 191, Italy

BONINI, STEFANO, MD
Professor of Ophthalmology
Interdisciplinary Centre
for Biomedical Research (CIR), Laboratory
of Ophthalmology, "Campus Bio-Medico",
University of Rome, Rome, Italy

BOUCHENAKI, NADIA, MD
Inflammatory Eye Diseases Unit,
Fondation A de Rothschild,
Clinique Générale Beaulieu,
Geneva, Switzerland

CHEN, LING, MD, MS
Jules Stein Eye Institute,
100 Stein Plaza,
Los Angeles, CA 90095, USA
CIMINO, LUCA, MD
Ocular Immunology Unit,
Division of Ophthalmology,
Arcispedale S. Maria Nuova,
Reggio Emilia, Italy

COSTER, DOUGLAS J., MD
Professor of Ophthalmology
Department of Ophthalmology,
Flinders University of South Australia,
Flinders Medical Centre,
Bedford Park, SA 5042, Australia

DAVIS, JANET, MD
University of Miami,
Bascom Palmer, 900 NW 17th Street,
Miami, FL 33136, USA

DE SMET, MARC, MD
Professor of Ophthalmology
Department of Ophthalmology,
Academic Medical Centre,
University of Amsterdam, Meibergdreef 9,
Amsterdam AZ 1105, The Netherlands

DEUTER, CHRISTOPH, Dr.
Universitäts-Augenklinik,
Schleichstraße 12,
72076 Tübingen, Germany

DUMARS, SEAN, MD
Jules Stein Eye Institute,
100 Stein Plaza, Los Angeles, CA 90095, USA

FOSTER, C. STEPHEN, MD
Professor of Ophthalmology
Massachusetts Eye & Ear Infirmary,
Harvard Medical School,
243 Charles Street,
Boston, MA 02114-3069, USA

GORDON, LYNN K., MD, PhD
Jules Stein Eye Institute,
100 Stein Plaza,
Los Angeles, CA 90095, USA

HEILIGENHAUS, ARND, Prof. Dr.
St. Franziskus Hospital,
Hohenzollernring 74,
48145 Münster, Germany

HERBORT, CARL P., MD, PD, MER
Professor of Ophthalmology
Department of Ophthalmology,
University of Lausanne,
La Source Eye Centre,
2 Ave. des bergières,
Lausanne 1004, Switzerland

KEITZER, ROLF, Dr.
Otto Heubner Center for Paediatric
and Adolescent Medicine,
Augustenburger Platz 1,
13353 Berlin, Germany

KIM, ALISA, MD
Jules Stein Eye Institute,
100 Stein Plaza,
Los Angeles, CA 90095, USA

KNOP, ERICH, Prof. Dr.
Augenklinik Charité,
Campus Virchow Klinikum,
Augustenburger Platz 1,
13353 Berlin, Germany

KNOP, NADJA, Dr.
Augenklinik Charité,
Campus Virchow Klinikum,
Augustenburger Platz 1,
13353 Berlin, Germany

KÖTTER, INA, Dr.
Universitäts-Augenklinik,
Schleichstraße 12,
72076 Tübingen, Germany

LAMBIASE, ALESSANDRO, MD
Laboratory of Ophthalmology,
Interdisciplinary Centre
for Biomedical Research (CIR),
“Campus Bio-Medico”, University of Rome,
Rome, Italy

LEHOANG, PHUC, MD, PhD
Professor of Ophthalmology
Department of Ophthalmology,
Pitié-Salpêtrière Hospital,
47 Bd. de l'Hôpital, Paris 75013, France

LEVINSON, RALPH D., MD
Assistant Professor of Ophthalmology
Jules Stein Eye Institute,
100 Stein Plaza, UCLA,
Los Angeles, CA 90095, USA

MANTOVANI, ALESSANDRO, MD
Division of Ophthalmology,
Ospedale Valduce, Como, Italy

MICERA, ALESSANDRA, MD
Interdisciplinary Centre
for Biomedical Research (CIR), Laboratory
of Ophthalmology, “Campus Bio-Medico”,
University of Rome, Rome, Italy

MONDINO, BARTLY, MD
Professor of Ophthalmology
Jules Stein Eye Institute,
100 Stein Plaza,
Los Angeles, CA 90095, USA

PFLUGFELDER, STEPHEN C., MD
Biological Sciences, Allergan Inc.,
2525 Dupont Drive, Irvine, CA 92612, USA

PLEYER, UWE, Prof. Dr.
Augenklinik Charité,
Campus Virchow Klinikum,
Augustenburger Platz 1,
13353 Berlin, Germany

ORLIC, NATASA, Dr.
Augenlinik Charité,
Campus Virchow Klinikum,
Augustenburger Platz 1,
13353 Berlin, Germany

SEGLER, CLAUDIA, Dr.
Otto Heubner Center for Paediatric
and Adolescent Medicine,
Augustenburger Platz 1,
13353 Berlin, Germany

SGRULLETTA, ROBERTO, MD
Laboratory of Ophthalmology,
Interdisciplinary Centre
for Biomedical Research (CIR),
“Campus Bio-Medico”,
University of Rome, Rome, Italy

SHAH, SAMIR, MD
Jules Stein Eye Institute,
100 Stein Plaza, Rm,
Los Angeles, CA 90095, USA

STERN, MICHAEL E., MD
Professor of Ophthalmology
Biological Sciences,
Allergan Inc., 2525 Dupont Drive,
Irvine, CA 92612, USA

STÜBINGER, NICOLE, Dr.
Universitäts-Augenklinik,
Schleichstraße 12,
72076 Tübingen, Germany

THURAU, STEPHAN R., Prof. Dr.
Section of Immunobiology,
Department of Ophthalmology,
Ludwig-Maximilians University,
Mathildenstraße 8,
80336 Munich, Germany

GERHILD, WILDNER, Dr.
Section of Immunobiology,
Department of Ophthalmology,
Ludwig-Maximilians University,
Mathildenstraße 8,
80336 Munich, Germany

WILLIAMS, KERYN A., MD
Department of Ophthalmology,
Flinders University of South Australia,
Flinders Medical Centre,
Bedford Park, SA 5042, Australia

ZIERHUT, MANFRED, Prof. Dr.
Universitäts-Augenklinik,
Schleichstraße 12,
72076 Tübingen, Germany



<http://www.springer.com/978-3-540-20045-1>

Uveitis and Immunological Disorders

Pleyer, U.; Mondino, B. (Eds.)

2005, XVII, 291 p., Hardcover

ISBN: 978-3-540-20045-1