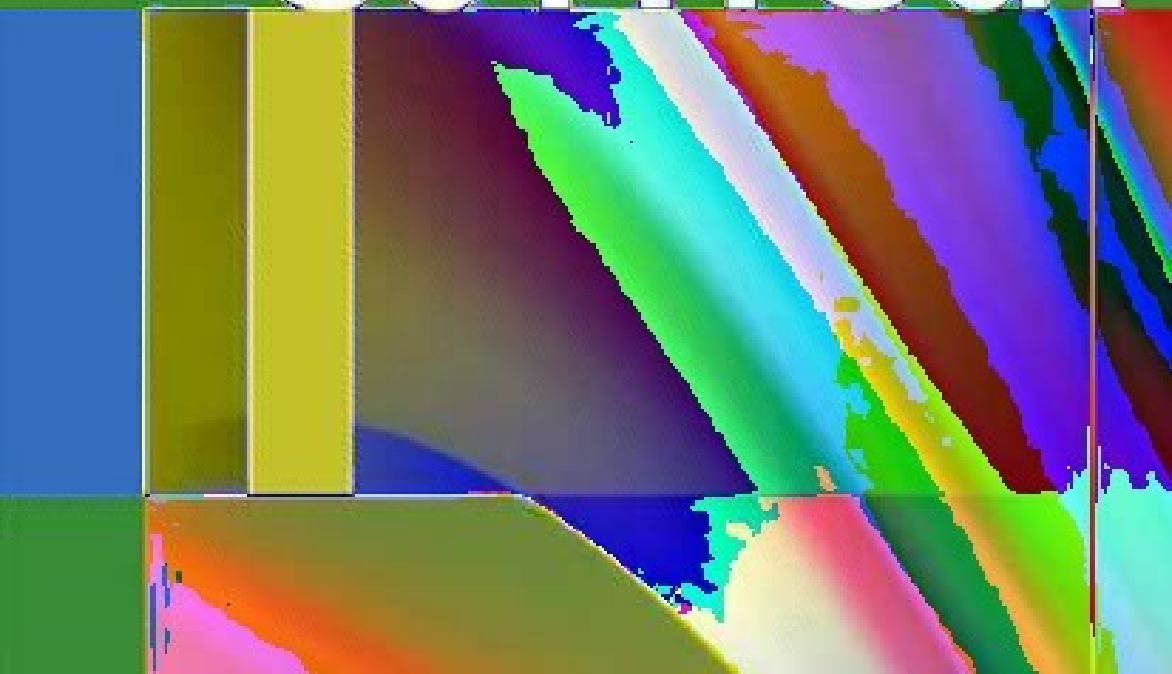


The
Fr
Ed

Corneal



Corneal Disease

Thomas Reinhard • Frank Larkin
Editors

Corneal Disease

Recent Developments in Diagnosis
and Therapy

 Springer

Editors

Prof. Dr. med. Thomas Reinhard
University Eye Hospital
Freiburg
Germany

Dr. Frank Larkin
Moorfields Eye Hospital
London
UK

ISBN 978-3-642-28746-6 ISBN 978-3-642-28747-3 (eBook)
DOI 10.1007/978-3-642-28747-3
Springer Heidelberg New York Dordrecht London

Library of Congress Control Number: 2012943838

© Springer-Verlag Berlin Heidelberg 2013

This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed. Exempted from this legal reservation are brief excerpts in connection with reviews or scholarly analysis or material supplied specifically for the purpose of being entered and executed on a computer system, for exclusive use by the purchaser of the work. Duplication of this publication or parts thereof is permitted only under the provisions of the Copyright Law of the Publisher's location, in its current version, and permission for use must always be obtained from Springer. Permissions for use may be obtained through RightsLink at the Copyright Clearance Center. Violations are liable to prosecution under the respective Copyright Law.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

While the advice and information in this book are believed to be true and accurate at the date of publication, neither the authors nor the editors nor the publisher can accept any legal responsibility for any errors or omissions that may be made. The publisher makes no warranty, express or implied, with respect to the material contained herein.

Printed on acid-free paper

Springer is part of Springer Science+Business Media (www.springer.com)

Preface

In this edition we have gathered a number of chapters on diagnosis and management of corneal disorders.

Miller, Girgis, Karp and Alfonso discuss mycobacterial keratitis, uncommon but increasingly encountered following ocular surgery or trauma. Diagnosis and medical therapy remain challenging for this infection.

Sueke, Horsburgh, Gilbert, Shankar, Neal and Kaye present a pragmatic approach to antibacterial chemotherapy in keratitis. Corneal specialists working in referral clinics will be particularly interested in their forward look to new antibacterial agents.

While familial keratoconus is very uncommon in Europe and North America, there is an increasing interest in information we can discover on keratoconus pathogenesis from apparently unaffected relatives with subclinical ectasia signs. Willoughby and Lechner review their own work and the recent published literature.

Imaging techniques have become a valuable component in diagnosis of corneal diseases, ranging from infections to corneal dystrophies. Labbé, Denoyer and Baudouin further show that confocal microscopy and ocular coherence tomography may facilitate clinical follow-up after corneal surgery.

Cursiefen and Bock discriminate between haem- and lymph-angiogenesis. They demonstrate that novel anti-angiogenic agents directed at blood or lymph vessels can significantly improve allograft survival by regression of corneal vessels pre- as well as post- transplantation.

For keratoplasty it is vital that corneal surgeons have access to cornea banks with robust and effective quality and risk management systems. Pels and Pollock illustrate that this is especially true in respect to the increasing practice of eye bank preparation of donor posterior lamellar cornea for endothelial keratoplasty procedures.

Few corneal surgeons undertake corneal transplantation in infants with any regularity. Surgical technical and post-operative management challenges in this transplant recipient group are very different to older patients, as Kim and Rootman describe. We expect that David Rootman's comparatively huge experience in infant keratoplasty will be a useful reference to those readers faced with occasional infant candidates for surgery.

We hope you enjoy reading this book.

Thomas Reinhard

Frank Larkin

Contents

1	New Aspects in the Diagnosis and Therapy of Mycobacterial Keratitis	1
	Darlene Miller, Dalia Girgis, Carol Karp, and Eduardo C. Alfonso	
2	New Developments in Antibacterial Chemotherapy for Bacterial Keratitis	19
	H. Sueke, J. Shankar, T.J. Neal, M. Horsburgh, R. Gilbert, and Stephen B. Kaye	
3	Heredity of Keratoconus	37
	Colin E. Willoughby and Judith Lechner	
4	Advance in Corneal Imaging	53
	Antoine Labbé, Alexandre Denoyer, and Christophe Baudouin	
5	Antiangiogenic Treatment Options in the Cornea	71
	Claus Cursiefen and Felix Bock	
6	Storage of Donor Cornea for Penetrating and Lamellar Transplantation	91
	Elisabeth Pels and Graeme Pollock	
7	Infant Keratoplasty	107
	Peter Kim and David S. Rootman	
	Index	123

Contributors

Eduardo C. Alfonso, M.D. Department of Ophthalmology,
University of Miami Miller School of Medicine, Miami, USA

Christophe Baudouin, M.D., Ph.D. Department of Ophthalmology III,
Quinze-Vingts National Ophthalmology Hospital, Paris, France

Felix Bock Department of Ophthalmology, University of Cologne,
Köln, Germany

Claus Cursiefen, M.D., FEBO Department of Ophthalmology,
University of Cologne, Köln, Germany

Alexandre Denoyer, M.D. Department of Ophthalmology III,
Quinze-Vingts National Ophthalmology Hospital, Paris, France

R. Gilbert St. Paul's Eye Unit, Royal Liverpool University Hospital, 8Z Link,
Liverpool, UK

Dalia Girgis, M.D. Department of Ophthalmology, University of Miami
Miller School of Medicine, Miami, USA

M. Horsburgh Institute of Integrative Biology, University of Liverpool,
Liverpool, UK

Carol Karp, M.D. Department of Ophthalmology, University of Miami
Miller School of Medicine, Miami, USA

Stephen B. Kaye St. Paul's Eye Unit, Royal Liverpool University Hospital,
8Z Link, Liverpool, UK

Peter Kim, MBBS (Hons), FRANZCO Department of Ophthalmology,
Toronto Western Hospital, University of Toronto, Toronto, ON, Canada

Antoine Labbé, M.D., Ph.D. Department of Ophthalmology III,
Quinze-Vingts National Ophthalmology Hospital, Paris, France

Judith Lechner School of Medicine, Dentistry and Biomedical Sciences,
Centre for Vision and Vascular Science, Queen's University Belfast,
Royal Victoria Hospital, Belfast, UK

Darlene Miller, DHSc. Department of Ophthalmology,
University of Miami Miller School of Medicine, Miami, USA

T.J. Neal Department of Microbiology, Royal Liverpool University Hospital,
Liverpool, UK

Elisabeth Pels, Ph.D. Cornea Bank Amsterdam, Euro Tissue Bank, Beverwijk,
The Netherlands

Graeme Pollock, Ph.D. Lions Eye Donation Service Melbourne,
Royal Victorian Eye and Ear Hospital, Melbourne, VIC, Australia

David S. Rootman, M.D., FRCSC Department of Ophthalmology and Visual
Sciences, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada

J. Shankar St. Paul's Eye Unit, Royal Liverpool University Hospital, 8Z Link,
Liverpool, UK

H. Sueke St. Paul's Eye Unit, Royal Liverpool University Hospital, 8Z Link,
Liverpool, UK

Colin E. Willoughby School of Medicine, Dentistry and Biomedical Sciences,
Centre for Vision and Vascular Science, Queen's University Belfast,
Royal Victoria Hospital, Belfast, UK

New Aspects in the Diagnosis and Therapy of Mycobacterial Keratitis

1

Darlene Miller, Dalia Girgis, Carol Karp,
and Eduardo C. Alfonso

Core Messages

- Mycobacterial keratitis is a rare but sight-threatening infection caused by both slow growing (Runyoun Groups I-III) and rapid growing (Runyoun Group IV) members of the genus *Mycobacterium* following trauma or ocular surgery.
- Mycobacteria are aerobic, nonmotile, nonspore-forming bacilli, ubiquitous in nature and difficult to eradicate with common disinfectants and topical antimicrobials due to the high lipid content of their cell walls.
- Delay in clinical and laboratory diagnosis and confirmation contributes to the protracted clinical course associated with the disease.
- Medical therapy and management remain a challenge.
- Surgical intervention is often required to cure and control the disease.

Mycobacterial keratitis is a rare event [1]. In general, infection rates constitute less than 2% of reported infectious microbial keratitis cases [2, 3]. Rates may vary by geographical locations and have been as high as 8% in some reported series from Asia (Reddy, Lalthia, Huang). Trends in recovery of mycobacteria from keratitis increased in number and diversity in the last decade (Fig. 1.1 and Table 1.1). Disease recognition, confirmation and management, however, remain challenging. Clinical diagnosis is problematic due to delay in presentation, low index of suspicion, mimicry of fungal or viral keratitis, and prior antibiotic and/or corticosteroid therapy. Traditional risk factors have included trauma with metal objects, soil and/or

D. Miller, DHSc. • D. Girgis, M.D. (✉) • C. Karp, M.D. • E.C. Alfonso, M.D.
Department of Ophthalmology, University of Miami Miller
School of Medicine, 900 N.W., 17th Street, Miami 33136, USA
e-mail: dmiller@med.miami.edu; dgirgis@uwhealth.org;
ckarp@med.miami.edu; ealfonso@med.miami.edu

vegetable matter or following surgical interventions such as radial keratotomy, photorefractive keratectomy, cataract surgery, or contact lens wear (Fig. 1.2). Current and emerging risk factors are mainly health care related and include surgical procedures (LASIK, LASEK, DSEK), smart plugs, and other biomaterials (Fig. 1.3). In several patients, no identifiable risk factor has been documented [4–7].

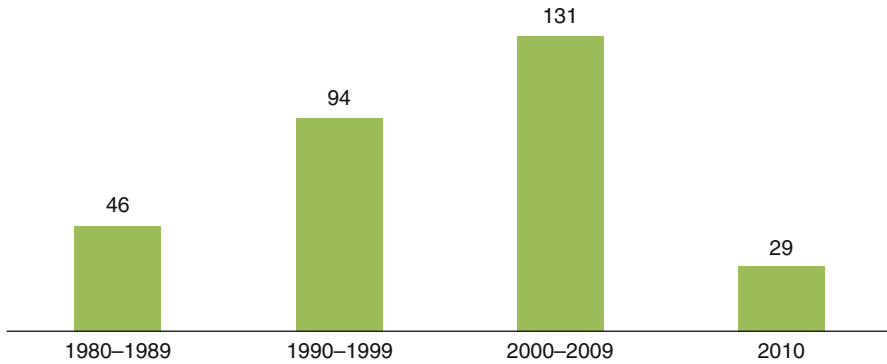


Fig. 1.1 Trends in mycobacterial keratitis cases (literature)

Table 1.1 Frequency and diversity of mycobacterial species recovered from keratitis (published reports 1980–2010), $N=300$

Mycobacteria classification	Sample source		Isolates	
	LASIK flap, cornea bed	Non-LASIK scrapings, biopsy	# of isolates	% of isolates
Runyon group				
Group I – Photochromogens (Slow growing >7 days for colonies to appear on solid media after subculture; pigment upon light exposure)				
<i>M. asiaticum</i>		1	1	0.33
<i>M. marinum</i>		1	1	0.33
Total	0	2	2	0.66
Group II – Scotochromogens (Slow growing-pigment in dark or light)				
<i>M. flavescens</i>		1	1	0.33
<i>M. gordonae</i>	2	3	5	1.67
<i>M. szulgai</i>	7	1	8	2.67
Total	9	5	14	4.67
Group III – Nonchromogens (Slow growing; nonpigmented)				
<i>M. avium</i> complex	0	2	2	0.67
<i>M. nonchromogenicum</i>	0	1	1	0.33
<i>M. terrae</i>	1		1	0.33
<i>M. triviale</i>	0	1	1	0.33
Total	1	4	5	1.67

Table 1.1 (continued)

Mycobacteria classification	Sample source		Isolates	
	LASIK flap, cornea bed	Non-LASIK scrapings, biopsy	# of isolates	% of isolates
Runyon group				
Group IV – Rapid Growers (<7 days for colonies to appear on solid media after subculture)				
<i>M. abscessus</i>	7	15	22	7.33
<i>M. chelonae</i>	37	123	130	53.33
<i>M. fortuitum</i>	4	38	42	14.00
<i>M. immunogenum</i>	5	0	5	1.67
<i>M. immnogenum</i>	2	0	2	0.67
<i>M. smegmatis</i>	0	1	1	0.33
Total	55	177	232	77.33
<i>Nontuberculosis Mycobacteria, not otherwise speciated (NTM, NOS)</i>	5	42	47	15.67
Total isolates	70	230	300	
% of isolates	23.33	76.67		

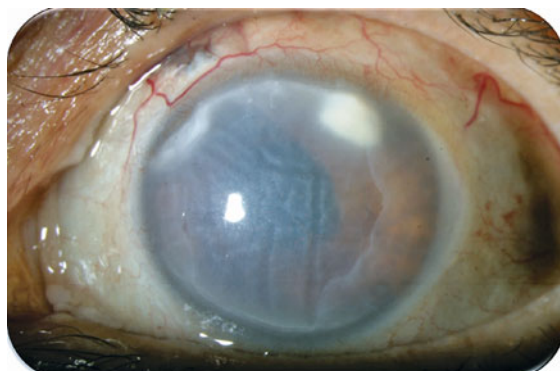


Fig. 1.2 *M. chelonae* mycobacteria following CE/IOL/trabectomy

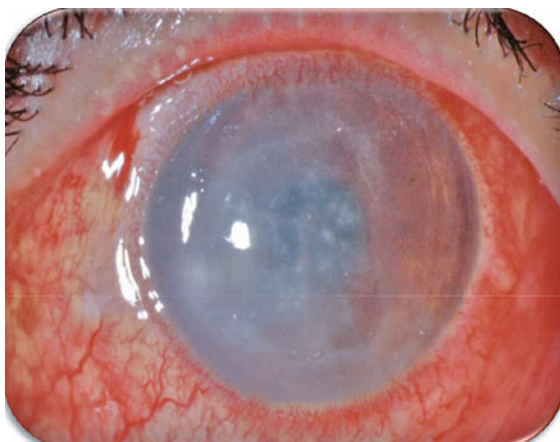


Fig. 1.3 Post LASIK *Mycobacteria abscessus* keratitis