

Cornea Subspecialty Day 2021

A Clear Vision for the New Decade

Program Directors

Sophie X Deng MD PhD, Vishal Jhanji MD, and Sonal S Tuli MD

In conjunction with the Cornea Society



Cornea Society
Advancing the treatment of corneal disease

Ernest N Morial Convention Center
New Orleans, Louisiana
Saturday, Nov. 13, 2021

Presented by:
The American Academy of Ophthalmology

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2021 Cornea Subspecialty Day Planning Group

On behalf of the American Academy of Ophthalmology and the Cornea Society, it is our pleasure to welcome you to New Orleans and Cornea Subspecialty Day 2021: A Clear Vision for the New Decade.



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Santen, Inc.: C
Stealth: S
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CME Credit

The Academy's CME Mission Statement

The purpose of the American Academy of Ophthalmology's Continuing Medical Education (CME) program is to present ophthalmologists with the highest quality lifelong learning opportunities that promote improvement and change in physician practices, performance, or competence, thus enabling such physicians to maintain or improve the competence and professional performance needed to provide the best possible eye care for their patients.

2021 Cornea Subspecialty Day Meeting Learning Objectives

Upon completion of this activity, participants should be able to:

- Use anterior segment imaging devices to assist with the diagnosis and management of corneal and ocular surface diseases
- Recognize ocular surface disorders that warrant surgical intervention and determine the ideal approach and timing of intervention
- Articulate and apply current best practices for the medical and surgical management of corneal infections and ocular surface inflammatory diseases
- Discuss the role and techniques of various keratoplasty and alternative treatments in the management of patients with corneal diseases
- Discuss the newest developments in pathogenesis and management of corneal diseases

2021 Cornea Subspecialty Day Meeting Target Audience

The intended target audience for this program is cornea surgeons, comprehensive ophthalmologists with an interest in anterior segment, and allied health personnel who are performing or assisting with cornea surgery.

Teaching at a Live Activity

Teaching instruction courses or delivering a scientific paper or poster is not an *AMA PRA Category 1 Credit™* activity and should not be included when calculating your total *AMA PRA Category 1 Credits™*. Presenters may claim *AMA PRA Category 1 Credits™* through the American Medical Association. To obtain an application form, please contact the AMA at www.ama-assn.org.

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The American Academy of Ophthalmology is committed to ensuring that all CME information is based on the application of research findings and the implementation of evidence-based medicine. The Academy seeks to promote balance, objectivity,

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2021 Cornea Subspecialty Day CME Credit

The American Academy of Ophthalmology is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

Friday Subspecialty Day Activity: Glaucoma, Neuro-Ophthalmology, Pediatric Ophthalmology, Refractive Surgery, and Retina (Day 1)

The American Academy of Ophthalmology designates this Other (blended live and enduring material) activity for a maximum of 12 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Saturday Subspecialty Day Activity: Cornea, Oculofacial Plastic Surgery, and Retina (Day 2)

The American Academy of Ophthalmology designates this Other (blended live and enduring material) activity for a maximum of 12 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Physicians registered as In Person and Virtual are eligible to claim the above CME credit.

How to Claim CME

Attendees can [claim credits online](#).

For AAO 2021, you can claim CME credit multiple times, up to the 50-credit maximum, through Aug. 1, 2022. You can claim some in 2021 and some in 2022, or all in the same year.

For 2021 Subspecialty Day, you can claim CME credit multiple times, up to the 12-credit maximum per day, through Aug. 1, 2022. You can claim some in 2021 and some in 2022, or all in the same year.

You do not need to track which sessions you attend, just the total number of hours you spend in sessions for each claim.

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The Academy provides nonmembers with verification of credits earned and reported for a single Academy-sponsored CME activity.

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You will be able to obtain a CME credit reporting/ proof-of-attendance letter for reimbursement or hospital privileges, or for nonmembers who need it to report CME credit:

Academy Members

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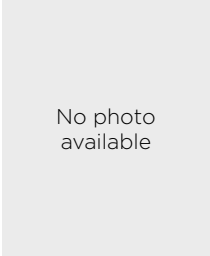
When you claim CME credits and complete the evaluation, a new browser window will open with a PDF of your certificate. Please disable your pop-up blocker. Your certificate will also be emailed to you.

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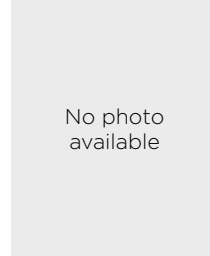
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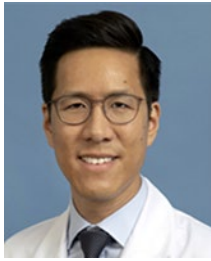
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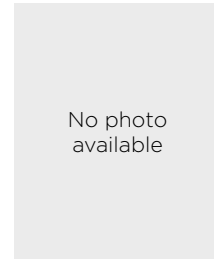
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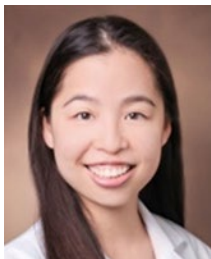
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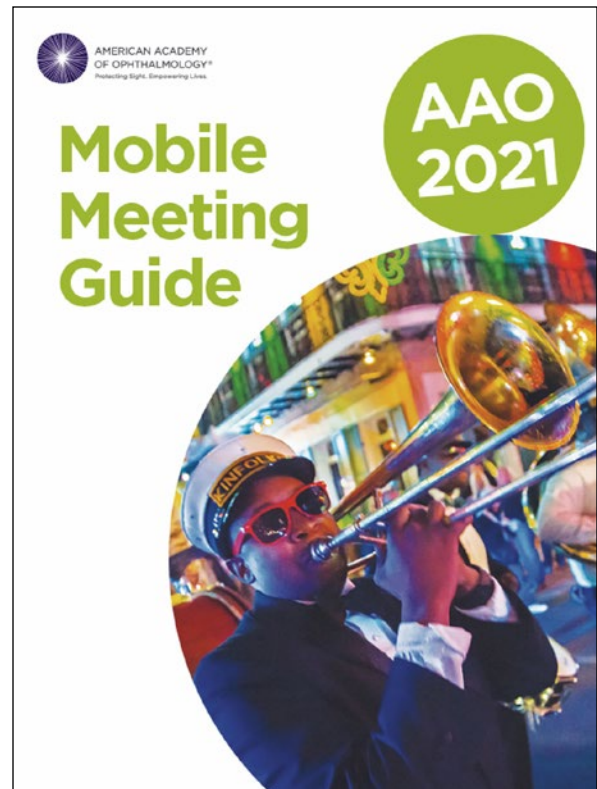


Sonal S Tuli MD
Gainesville, FL

Ask a Question Live During the Meeting Using the Mobile Meeting Guide

To ask the moderator a question during the meeting, follow the directions below.

- Access at www.aao.org/mobile
- Select “Program,” “Handouts & Evals”
- Filter by Meeting: Cornea Meeting
- Select “Current Session”
- Select “Interact with this session (live)” to open a new window
- Choose “Ask a Question”



Cornea Subspecialty Day 2021: A Clear Vision for the New Decade

In conjunction with the Cornea Society

DATE: SATURDAY, NOV. 13, 2021

7:00 AM CONTINENTAL BREAKFAST

8:00 AM Welcome and Introductions
Sophie X Deng MD PhD*
Vishal Jhanji MD FRCOphth
Sonal S Tuli MD

Section I: Battles Against the Bugs

Moderator: Sophie X Deng MD PhD*

8:02 AM	Introduction	Sophie X Deng MD PhD*	
8:04 AM	COVID-19: The Elephant in the Room	James Chodosh MD MPH*	1
8:12 AM	Transmission of Coronavirus via Ocular Surface: Myth or Fact?	Shahzad I Mian MD*	2
8:20 AM	Impact of COVID-19 on Eyebanking and Keratoplasty	Jennifer Y Li MD	3
8:28 AM	Discussion		
8:33 AM	Neglected Pandemic of Contact Lens–Related Keratitis	Irene C Kuo MD	6
8:41 AM	Resistance in Microbial Keratitis (SCD)	Darlene Miller DHSc MPH CIC	8
8:49 AM	Herpes Zoster: Presentation and Management	Elisabeth J Cohen MD	11
8:57 AM	Case Presentation: Not Your Typical Infectious Keratitis	Zeba A Syed MD*	12
9:03 AM	Discussion		

Section II: Keratoplasty—Layer by Layer

Moderator: Vishal Jhanji MD FRCOphth

9:08 AM	Introduction	Vishal Jhanji MD FRCOphth	
9:10 AM	Tricks and Tips for a Successful Anterior Keratoplasty	Dalia Said MD	13
9:18 AM	DSAEK for Complex Eyes	Divya Srikumaran MD*	14
9:24 AM	DMEK for Complex Eyes	Nir Sorkin MD	15
9:30 AM	New DMEK Techniques	Isabel Dapena MD PhD*	17
9:38 AM	Corneal Xenotransplantation: Where Do We Stand?	Zuguo Liu MD*	19
9:46 AM	Case Presentation: Custom Keratoplasty	Audrey R Talley Rostov MD*	20
9:52 AM	Discussion		
10:02 AM	In These Unprecedented Times . . .	Darby D Miller MD	21
10:07 AM	REFRESHMENT BREAK and AAO 2021 EXHIBITS		

* Indicates that the presenter has financial interest. No asterisk indicates that the presenter has no financial interest.

Section III: Surgeries of the Anterior Segment

Moderator: Sonal S Tuli MD

10:37 AM	Introduction	Sonal S Tuli MD	
10:39 AM	No Zonules, No Problem!	Joanne F Shen MD	23
10:47 AM	The Cornea and Glaucoma Angle	Richard K Lee MD	26
10:55 AM	Iris Reconstruction and Replacement	Michael E Snyder MD*	27
11:03 AM	Discussion		
11:08 AM	Cataract Surgery in the Setting of Endothelial Dysfunction	Francis W Price Jr MD*	28
11:16 AM	Is FLACS a Preferred Choice in the Setting of Fuchs Endothelia Dystrophy?	Nicole R Fram MD*	29
11:24 AM	Cataract Surgery Considerations in Abnormal Corneas	Kristin M Hammersmith MD	30
11:32 AM	Do's and Don'ts of Corneal Crosslinking for Keratoconus	Preeya K Gupta MD*	32
11:40 AM	Case Presentation: What Is That Conjunctival Bump?	Carol L Karp MD	33
11:46 AM	Discussion		
11:51 AM	LUNCH and AAO 2021 EXHIBITS		

Section IV: Reconstruction of the Ocular Surface

Moderator: Vishal Jhanji MD FRCOphth

Virtual Moderator: Olivia L Lee MD*

1:11 PM	Introduction	Vishal Jhanji MD FRCOphth	
1:13 PM	Global Consensus on Limbal Stem Cell Deficiency	Friedrich E Kruse MD*	34
1:21 PM	Pterygium Surgery Complications and Management	Allan R Slomovic MD FRCSC MSc*	38
1:29 PM	Management of Autoimmune-Mediated Keratolysis	Kimberly C Sippel MD	40
1:37 PM	Discussion		
1:42 PM	Ocular Surface Squamous Neoplasia: Medical or Surgical Treatment	Darren G Gregory MD	44
1:50 PM	Forniceal and Conjunctival Reconstruction	Clara C Chan MD*	45
1:58 PM	Corneal Manifestations of New Systemic Medications	Winston D Chamberlain MD PhD*	46
2:06 PM	Case Presentation: Difficult Ocular Surface Construction	Swapna S Shanbhag MBBS	47
2:12 PM	Discussion		

Section V: Management of Ocular Surface Diseases

Moderator: Sonal S Tuli MD

Virtual Moderator: Olivia L Lee MD*

2:17 PM	Introduction	Sonal S Tuli MD	
2:19 PM	Therapeutic Scleral Contact Lenses	Alejandro Navas MD	48
2:27 PM	Smite the Mite! Novel Blepharitis Treatments	Christine Shieh MD*	50
2:35 PM	Fight the Blight With Light: Lasers for Blepharitis	Vatinee Y Bunya MD*	52
2:43 PM	Discussion		
2:48 PM	New Diagnostics for the Ocular Surface	Cynthia Matossian MD FACS*	54

* Indicates that the presenter has financial interest. No asterisk indicates that the presenter has no financial interest.

2:56 PM	Emerging Treatments for Dry Eye Disease	Amy Lin MD*	55
3:04 PM	Ocular Neuropathic Pain	Shruti Aggarwal MBBS	56
3:12 PM	Case Presentation: Not Your Typical Dry Eye	Stephen C Pflugfelder MD*	57
3:18 PM	Discussion		
3:23 PM	REFRESHMENT BREAK and AAO 2021 EXHIBITS		

Section VI: Therapies on the Horizon

Moderator: Sophie X Deng MD PhD*

Virtual Moderator: Olivia L Lee MD*

3:53 PM	Introduction	Sophie X Deng MD PhD*	
3:55 PM	Medical Treatment of Fuchs Endothelial Corneal Dystrophy	Kathryn A Colby MD PhD*	58
4:03 PM	Are We Ready for Cell Therapy for Corneal Endothelial Failure?	Shigeru Kinoshita MD*	60
4:11 PM	Stem Cell Therapy for Corneal Scars	Sayan Basu MBBS MS	61
4:19 PM	Induced Pluripotent Stem Cell-Derived Limbal Stem Cells	Kohji Nishida MD*	62
4:27 PM	New Treatments for Neurotropic Keratitis	Simon Fung MD MA FRCOphth*	63
4:35 PM	Emerging Artificial Corneas	Marjan Farid MD*	64
4:43 PM	Case Presentation: Think Out of the Box!	Jodhbir S Mehta MBBS PhD	65
4:49 PM	Discussion		
4:59 PM	Closing Remarks	Sophie X Deng MD PhD* Vishal Jhanji MD FRCOphth Sonal S Tuli MD	

* Indicates that the presenter has financial interest. No asterisk indicates that the presenter has no financial interest.

COVID-19: The Elephant in the Room

James Chodosh MD MPH

This presentation on ophthalmology during the COVID-19 pandemic will include a brief overview of the virology, epidemiology, means of transmission, prevention, and reported presentations of COVID-19 associated eye disease, as well as continued safety concerns for ophthalmologists and their patients.

Impact of COVID-19 on Eyebanking and Keratoplasty

Jennifer Y Li MD

Since the start of the COVID-19 pandemic, the Eye Bank Association of America (EBAA) Medical Advisory Board (MAB) has been closely monitoring the ever-changing situation and the potential impact on donor corneal tissue. The Policy and Position Review Subcommittee (PPRS) of the MAB was tasked early on with developing guidelines for eye banks to help in determining donor eligibility criteria around COVID-19. The first guidelines were issued on February 3, 2020. There have been multiple updates since that time as the pandemic spread across the globe and as we have learned more about SAR-CoV-2. The guidelines were intended to help maintain the safety of the cornea donor pool while still meeting the needs of surgeons and recipients. The most recent update was released on June 4, 2021. The guidelines are included here for your information.¹

EBAA Updated Guidance and COVID-19 Screening Recommendations, June 4, 2021

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The impact of the COVID-19 shutdown from approximately March 2020 to May 2020 was profound on surgeons and eye banks alike. With almost all elective surgery on hold, eye banks were operating at less than 20% of the normal capacity and international placement of donor corneal tissue came to a virtual halt.² Fortunately, the recovery for domestic (US) eye banks has been relatively rapid since elective surgeries resumed in May 2020 in the United States. During the latter part of 2020, eye banks were able to recover back to about 80-85% of the normal volume.² Overall, in 2020 compared to 2019, total corneas donated were down 20% and the total grafts performed was down 23%.² While this has certainly impacted US domestic surgeries and patients, the more profound impact may ultimately be seen internationally where there is often insufficient corneal tissue to meet the needs of the population and a reliance on exported donor corneal tissue from countries like the United States.³

DONOR ELIGIBILITY

PCR Test Status*	COVID-19 Signs†	COVID-19 Symptoms‡	Plausible Alternative Etiology (Signs / Symptoms)	Close Contact§	Donor Fully Vaccinated¶	Eligibility	
Positive within the last 28 days	Yes or No	Yes or No	Yes or No	Yes or No	Yes or No	Not Eligible	
Negative (post-mortem or recent pre-mortem test)	Yes	Yes or No	Yes	Yes	Yes or No	Medical Director Review	
				No	Yes or No	Eligible	
			No	Yes	Yes	Yes or No	Medical Director Review
	No	Yes or No			Not Eligible		
	No	No	N/A	Yes	Yes	Eligible	
				No	No	Medical Director Review	
				No	Yes or No	Eligible	
		Yes	Yes or No	Yes	Yes	Yes	Medical Director Review
					No	No	Not Eligible
	Not done	Yes	Yes or No	Yes	Yes	Yes	Medical Director Review
No					Yes or No	Medical Director Review	
No				Yes or No	Yes or No	Not Eligible	
No		Yes	Yes	Yes	Yes	Medical Director Review	
				No	Yes or No	Medical Director Review	
		No	No	N/A	Yes	Yes	Medical Director Review
No	Yes or No				Eligible		

*PCR Test Status	
RT-PCR SARS-CoV-2 test performed 28 days prior to or less than 24 hours after death. If performed, but result is indeterminate or inconclusive, then donor should be deferred.	
†COVID-19 Signs	
Development of one of the following signs consistent with possible COVID-19 infection within the 28 days prior to death:	
<ul style="list-style-type: none"> • ARDS • Pneumonia • Pulmonary computed tomography (CT) showing “ground glass opacities” 	
‡COVID-19 Symptoms	
Development of acute symptoms consistent with COVID-19 infection within the 28 days prior to death	
One of the following: <ul style="list-style-type: none"> • Fever or chills • Cough • Shortness of breath or difficulty breathing • New loss of taste or smell 	OR two of the following: <ul style="list-style-type: none"> • Fatigue • Muscle or body aches • Headache • Sore throat • Congestion or runny nose • Nausea or vomiting • Diarrhea
§Close Contact	
Close contact is defined by the CDC as: <i>(If such contact occurs while not wearing recommended personal protective equipment)</i>	
a) being within approximately 6 feet (2 meters) of a COVID-19 case for a prolonged period of time; close contact can occur while caring for, living with, visiting, or sharing a health care waiting area or room with a COVID-19 case	OR b) having direct contact with infectious secretions of a COVID-19 case (e.g., being coughed on).
¶Vaccination	
Donor would be considered fully vaccinated, as defined by the CDC, at the time of death if he/she were:	
<ul style="list-style-type: none"> • 2 weeks after their second dose in a 2-dose series, such as the Pfizer or Moderna vaccines, or • 2 weeks after a single-dose vaccine, such as Johnson & Johnson’s Janssen vaccine 	

Figure 1

References

1. Eye Bank Association of America. "Regulatory Update." Covid-19 Updates. EBAA, 03 June 2021. <https://restoresight.org/covid-19-updates>.
2. Eye Bank Association of America. *2020 Eye Banking Statistical Report*. EBAA, 2021. https://restoresight.org/wp-content/uploads/2021/03/2020_Statistical_Report-Final.pdf.
3. AlMutlak M, Li JY, Bin Helayel H, Fairaq R. The future of corneal donation and transplantation; insights from Covid-19 pandemic [published online ahead of print, 2020 Aug 19]. *Cornea*. 2021 Mar 1;40(3):274-276.

The Neglected Pandemic of Contact Lens–Related Keratitis

Irene C Kuo MD

I. Numbers and Context

- A. 140,000 million contact lens (CL) wearers worldwide
- B. Annualized incidence 2-20 per 10,000 wearers with CL-related microbial keratitis (MK); about 30-300,000 with CL-related MK per year
- C. Context of overall microbial keratitis
 1. 1.5 million persons blind from MK worldwide each year
 2. World Health Organization Bulletin proposal that infectious corneal ulcer receive “neglected tropical disease” status¹
 3. Difference in etiologies between low to middle income countries and developed countries

II. Etiology of CL-Related Keratitis

- A. Problem with in vivo/ex vivo vs. in vitro studies; cell culture is not ideal.
- B. Host factors (“normal” cornea vs. cornea of a CL-wearer): how does CL wear render a cornea susceptible to infection?
 1. Epithelial barrier; impact of superficial injury
 2. Basal lamina
 3. Ocular surface microbiome—does the cornea have one?
 4. Biofilm
 5. Tear fluid and blinking and how they affect microbes
 6. Closed eye (overnight wear including orthokeratology and extended wear)
- C. Bacterial factors (focus on *Pseudomonas aeruginosa*, main etiology)
 1. Surface-expressed bacterial components: lipopolysaccharides, pili, flagellin
 2. Phagocytosis/lysosomal destruction vs. internalization and becoming *intracellular*
 3. Filamentation
- D. *Acanthamoeba*
 1. Trophozoite vs. cyst form
 2. Acanthaporin, protease MIP-133, phospholipases
 3. Polymicrobial infections (with bacteria)
 4. Increasing resistance?

III. CL Types and Wear

- A. Extended wear vs. daily wear
- B. “New” material like silicone hydrogel with increased oxygen transmissibility
- C. OrthoK

IV. Patient Behaviors

- A. How to mold behavior
 1. Discrepancy between perception of one’s behavior and actual behavior
 2. Education may not be enough; awareness of correct behavior but choosing otherwise
- B. Age of wearer⁵
 1. Adolescents vs. young adults vs. other
 2. Sleeping in contact lenses, “topping off” the solution in the case, not changing the case, not seeing doctor annually, not replacing contact lenses at regular intervals, swimming in contact lenses, storing or rinsing in tap water

V. Strategies

- A. Treatments
 1. Multidrug-resistant *Pseudomonas aeruginosa* in United States, China, Europe (perhaps because of heavy fluoroquinolone use in animal husbandry) vs. restricted use in Australia
 2. *Acanthamoeba*
- B. Ophthalmic Advisory Committee of the Food and Drug Administration, American Academy of Ophthalmology, American Academy of Optometry, American Optometric Association, Contact Lens Association of Ophthalmologists: FDA-cosponsored workshop to revamp microbiological test methods for contact lenses, products, and accessories⁸
 1. Addition of 2 strains of *Pseudomonas* (invasive and cytotoxic) to American Type Culture Collection
 2. Realization of emerging pathogens
 3. Inclusion of real-world test parameters
 4. Role of soil in disinfection efficacy testing of CL care products
- C. Better education/training of CL wearers

- D. Targeted health communication strategies (“appeals to vanity” and “social norms marketing,” like antismoking efforts), prevention messages “shaped around lifestyle changes known to occur in young adults”
- E. Monitoring CL-related complications
 1. For U.S. practitioners: voluntary reporting to Food and Drug Administration (<https://www.accessdata.fda.gov/scripts/medwatch/index.cfm>)
 2. Possible need for help from agencies to focus on dispensing and education/training (or lack thereof)

References and Selected Readings

1. Ung L, Acharya NR, Agarwal T, et al. Infectious corneal ulceration: a proposal for neglected tropical disease status. *Bull World Health Organ.* 2019; 97(12):854-856.
2. Fleiszig SMJ, Kroken AR, Nieto V, et al. Contact lens-related corneal infection: intrinsic resistance and its compromise. *Prog Retin Eye Res.* 2020; 76:100804.
3. Niederkorn JY. The biology of *Acanthamoeba keratitis*. *Exp Eye Res.* 2021; 202:108365.
4. Bui TH, Cavanagh HD, Robertson DM. Patient compliance during contact lens wear: perceptions, awareness, and behavior. *Eye Contact Lens.* 2010; 36(6):334-339.
5. Cope JR, Collier SA, Nethercut H, Jones JM, Yates K, Yoder JS. Risk behaviors for contact lens-related eye infections among adults and adolescents—United States, 2016. *MMWR Morb Mortal Wkly Rep.* 2017; 66(32):841-845.
6. Badenoch PR. A turning point for contact lens-associated microbial keratitis? *Clin Exp Ophthalmol.* 2019; 47(6):701-703.
7. Thulasi P, Saeed HN, Rapuano CJ, et al. Oral miltefosine as salvage therapy for refractory *Acanthamoeba keratitis*. *Am J Ophthalmol.* 2021;223:75-82.
8. Hampton D, Tarver ME, Jacobs DS, et al. Special commentary: Food and Drug Administration, American Academy of Ophthalmology, American Academy of Optometry, American Optometric Association, and the Contact Lens Association of Ophthalmologists Cosponsored Workshop: Revamping microbiological test methods for contact lenses, products, and accessories to protect health and ensure safety. *Eye Contact Lens.* 2015; 41(6):329-333. <https://www.accessdata.fda.gov/scripts/medwatch/index.cfm>.

Resistance in Microbial Keratitis

Time for “That (Antibiotic Stewardship) Talk?”

Darlene Miller DHSc MPH CIC

Introduction

Antimicrobial resistance in microbial keratitis is a current and expanding public health concern. Cumulative and increasing reports of clinical failures and poor patient outcomes following fluoroquinolone monotherapy is a call to arms to re-exam and modify our current recommendations and approach. Emerging resistance among nonbacterial pathogens (herpes simplex virus, *Fusarium*, and *Acanthamoeba*) is also quite alarming (see Table 1). Employing the principles and protocols of an effective antimicrobial stewardship program could be a key weapon in reducing the incidence and emergence of antimicrobial resistance in microbial keratitis.

Table 1. Antimicrobial Resistance Among Microbial Keratitis Pathogens

Current Practice and Recommendations for Antimicrobial Management of Microbial Keratitis, USA ^a		% Susceptible, In Vitro Coverage-BPEI Isolates, N = 833, 2016-2020	Comment (s)
Bacterial: no smear, no culture (community)	Fluoroquinolone (moxifloxacin)	Less activity against <i>Pseudomonas aeruginosa</i> and <i>Serratia marcescens</i> . Emerging fluoroquinolone resistance is a combination and interaction of subinhibitory concentrations, increased mutations, and multiple efflux pumps. In vitro efficacy for the <i>Staphylococci</i> is less than 80%, while <i>S. pneumoniae</i> and the <i>S. viridans</i> group in vitro susceptibility profiles both remain above 90%.	
No smear, no culture (small abrasions, peripheral infiltrates)	Treatment/prophylaxis with a fluoroquinolone	As above	
No organisms	Fortified (tobramycin/vancomycin)	94.8%	Sensitivity profiles vary by location and patient population.
	Fluoroquinolone (levofloxacin)	85.3%	
Gram-positive cocci	Cefazolin	25%	
	Vancomycin	100%	
	Fluoroquinolone (moxifloxacin)	61%	
Gram-negative rods	Tobramycin	95.5%	
	Gentamicin	96.1%	
	Ceftazidime	94.7%	
	Fluoroquinolone (ciprofloxacin)	97%	
<i>Mycobacteria</i> species	Amikacin	78%	Profile for most common isolate—the <i>Mycobacteria abscessus</i> complex
	Clarithromycin	84%	
	Fluoroquinolone	<20%	
<i>Nocardia</i> species	Trimethoprim sulfamethoxazole	100%	
	Amikacin	Increased amikacin resistance (20%-40%) among new emerging species	

(table continues on next page)

Fungal Keratitis	Antifungal Therapy	
Positive confocal or smear	Antifungal	
Yeast	5% natamycin Amphotericin B (0.15%-0.5%) Voriconazole	Polyenes have good activity against <i>Candida</i> species. Good activity against <i>Candida</i> species
Filamentous fungi	5% natamycin Voriconazole 1%	Poor penetration may lead to subinhibitory concentrations Broad spectrum-some activity against <i>Aspergillus</i> , <i>Curvularia</i> , and <i>Paecilomyces</i>
AK	Antiamoebic Therapy	
Negative smear, “ring infiltrate,” clinical signs consistent with AK	(Biguanide monotherapy) PHMB (0.02-0.06%-polyhexamethylene biguanide)	Currently more than 26 species and 20 <i>Acanthamoeba</i> genotypes. Genotype T4 is the most common recovered from AK patients. Genotypes respond differently to amoebic therapy. NonT4 <i>Acanthamoeba</i> genotypes (ie, T5-A lenticulata) may be less responsive and have poorer outcomes, including the need for cornea transplant. Exposure to subinhibitory PHMB concentrations in contact lens solutions may select for tolerant and or resistant isolates among all genotypes.
Positive smear or confocal	Combination therapy with a diamidine (propamidine isethionate 0.1% Brolene) and PHMB Miltefosine oral (orphan drug in USA) Antifungals (voriconazole, posaconazole, itraconazole)	Recently approved for treatment of <i>Acanthamoeba</i> . Mixed results. Fulminant inflammatory response with prolonged use observed in some patients. Have mixed results. High in vitro resistance.
Viral Keratitis	Antiviral Therapy	
HSV epithelial keratitis	Topical: trifluridine, ganciclovir Systemic: acyclovir, famciclovir, valacyclovir	Long-term prophylaxis with acyclovir can lead to resistance as high as 6%. Cross resistance to the analogs valacyclovir, ganciclovir, and famciclovir also occurs (all dependent on thymidine kinase). More common in patients with recurrent disease. Alternative for acyclovir-resistant strains include foscarnet, cidofovir, and trifluridine.
HSV stromal keratitis	Oral antiviral for 10 weeks. Topical corticosteroids	
HSV endothelial keratitis	Topical steroid and oral antiviral	

^a United States of AmericaAbbreviations: AK, *Acanthamoeba* keratitis; HSV, herpes simplex virus.

Antimicrobial Stewardship: What Is It? How Does It Work?

Antimicrobial stewardship is a coordinated program to promote the appropriate use of antimicrobials, improve patients' outcomes, and reduce microbial resistance. Activity includes educating, measuring, and monitoring how antimicrobials are prescribed by physicians and used by patients.

Top 5 Reasons It Might Be Time for the "Antibiotic Stewardship" Talk and Microbial Keratitis

1. Despite the widespread prescribing and use of empirical, broad-spectrum antimicrobials, microbial keratitis remains a leading cause of visual impairment and blindness worldwide.
2. Current and emerging multidrug resistance is evident among the most common corneal pathogens (herpes simplex virus, *Staphylococci*, *Pseudomonas* species), as well as the less common pathogen species (*Fusarium*, *Mycobacteria*, *Nocardia*), and nonpseudomonal gram-negative rods (*Klebsiella*, *Proteus*, *Stenotrophomonas*, and *Achromobacter* and *Acinetobacter*).
3. Treating with the inappropriate antimicrobial and or exposure to subinhibitory antimicrobial concentrations can lead to increased adverse effects, including poorer patient outcomes, increased cost, compromised ocular surface, and unbalanced microbiome.
4. Prescribing and use of broad-spectrum antimicrobials for non-sight threatening abrasions, infiltrates, and "just in case" prophylaxis may lead to the selection of antimicrobial tolerant and or resistant microbial strains in individual patients.

5. Knowledge gap: Resistance in microbial keratitis is a dynamic interplay between infecting micro-organism, corneal health, and the selected antimicrobial. Key players:
 - a. The organism: Who is there? What are they doing? How are they doing? What can you do about it? What should you do about it?
 - b. Cornea health: Patient-specific data-identified risk factors (contact lens wear, trauma, surgery, systemic disease, prior antibiotic exposure, and immune status)
 - c. The drug: Which one? How much? (dose), how often? (dosing frequency), which route? (topical, oral, intrastromal), and for how long? (10 days? 1 month?)
 - d. YOU/healthcare provider: practice, education, interest, prescription profile

Selected Readings

1. Austin A, Lietman T, Rose-Nussbaumer J. Update on the management of infectious keratitis. *Ophthalmology* 2017; 124(11):1678-1689.
2. Miller D. Update on the epidemiology and antibiotic resistance of ocular infections. *Middle East Afr J Ophthalmol.* 2017; 24(1):30-42.
3. Sanchez GV, Fleming-Dutra KE, Roberts RM, Hicks LA. Core elements of outpatient antibiotic stewardship. *MMWR Recomm Rep.* 2016; 65(no. RR-6):1-12.

Case Presentation: Not Your Typical Infectious Keratitis

Zeba A Syed MD

I. Case Presentation

- A. 56-year-old male with a history of recurrent herpes simplex virus (HSV) epithelial and stromal keratitis presents with worsening vision and pain in the right eye.
- B. The patient had an extensive 10+ year history of HSV epithelial and stromal flare-ups that had not been successfully controlled with prophylactic regimens of acyclovir 400 mg PO b.i.d. or valacyclovir 500 mg PO q.d.; his presenting prophylactic regimen was valacyclovir 1 g b.i.d., and he has had 1 prior flare-up on this regimen.
- C. Examination demonstrated a corneal epithelial defect with ~75% stromal thinning along with an associated hypopyon and fibrinous stands in the anterior chamber.
- D. Valacyclovir was increased to 1 g t.i.d.; however, the patient clinically deteriorated, increasing suspicion for an alternate etiology for his findings.
- E. Corneal cultures were performed, which returned positive for *Mycobacterium* and *Pseudomonas* despite the absence of a frank corneal infiltrate.
- F. Upon initiation of appropriate antibiotics, the anterior chamber reaction improved; amniotic membrane was used to facilitate epithelialization.
- G. Given concern for reactivation of HSV epithelial keratitis as the underlying predisposing risk factor for bacterial infection, the patient was transitioned to famciclovir 500 mg PO b.i.d.
- H. The patient has been flare-free on this prophylactic regimen for over 3 years.

II. Teaching Points

- A. Prophylactic medication, dose, and frequency for HSV keratitis varies across individuals, and a “one size fits all” approach should not be adopted in its management.
- B. Clinicians should maintain a high index of suspicion for bacterial superinfection of HSV keratitis flare-ups that display atypical features or do not respond to escalated antiviral therapy.
- C. Often, a multipronged approach is needed for healing in HSV keratitis, involving amniotic membrane or tarsorrhaphy to facilitate epithelialization.

Selected Readings

1. Boisjoly HM, Pavan-Langston D, Kenyon KR, Baker AS. Superinfections in herpes simplex keratitis. *Am J Ophthalmol.* 1983; 96(3):354-361.
2. Burrell S, Boutolleau D, Azar G, et al. Phenotypic and genotypic characterization of acyclovir-resistant corneal HSV-1 isolates from immunocompetent patients with recurrent herpetic keratitis. *J Clin Virol.* 2013; 58(1):321-324.
3. Choong K, Walker NJ, Apel AJ, Whitby M. Aciclovir-resistant herpes keratitis. *Clin Exp Ophthalmol.* 2010; 38(3):309-313.
4. Loutsch JM, Sainz B Jr, Marquart ME, et al. Effect of famciclovir on herpes simplex virus type 1 corneal disease and establishment of latency in rabbits. *Antimicrob Agents Chemother.* 2001; 45(7):2044-2053.

Tricks and Tips for a Successful Anterior Lamellar Keratoplasty

Dalia G Said MD and Harminder S Dua CBE

Outline

Deep anterior lamellar keratoplasty (DALK) is the gold standard technique for replacing corneas in which the disease process involves the stroma and spares the endothelium. It has the advantage of eliminating endothelial graft rejection and hence improves graft survival and provides a stronger graft–host junction. Additionally, the technique allows early removal of sutures and eliminates the need for long-term steroid use with the consequent complications of cataract and glaucoma. However, visual compromise related to astigmatism issues with sutures remains a challenge.

The discovery of the pre-Descemet layer (PDL, Dua layer, Dua-Fine layer)¹ has improved our understanding of this challenging procedure, notably that it is impervious to air and offers a highly elastic, robust plane of cleavage between it and the posterior corneal stroma. This has led to an in-depth understanding of the behavior of air and viscoelastic² in separating corneal lamellae and has enlightened surgeons to introduce modifications and improvements in the surgical techniques to achieve a successful DALK.

1. The big bubble technique (BB) involves separation of the stroma from the PDL (type 1 BB). This is the most popular technique, as it leaves behind the patient's PDL, Descemet membrane (DM), and the endothelium, with no residual diseased stroma. With this technique perforations and consequent double chamber are unlikely to occur by virtue of the strength and elasticity of the PDL.³ The type 1 BB is achieved in 80% of cases. Various techniques, including using femtolasers or intraoperative OCT, have been suggested to increase the chance of a BB formation.⁴
2. In around 20% of cases, a type 2 (and mixed) BB is achieved, in which only the patient's DM and endothelium are left behind. This is a thin-walled bubble; thus the risks of perforation, rupture of the bubble, and the need to convert to a penetrating graft (PKP) increase significantly. In cases with a mixed BB, similar disadvantages and precautions pertain as with type 2 BB.
3. If the attempts to achieve BB have failed, lamellar dissection layer by layer or stromal air injection to whiten the cornea followed by stromal hydration is our recommended technique. Visual results with this technique have been shown to be comparable to those of the BB technique in some studies, but the variability in the depth of stromal dissection between different surgeons can influence the results.³
4. The use of viscoelastic to achieve a BB is another technique, aiming to inject a small volume of viscoelastic in the deep stroma to cleave the PDL.⁵ However, an intrastromal visco-bubble can form without reaching the PDL. This mimics a type 1 BB, and DALK can be associated with a variable amount of stroma.⁵

This presentation will demonstrate the different steps to achieve a successful DALK, including the different techniques (BB and stromal hydration) as well as tips to increase the chance of type 1 BB formation and tricks to differentiate between the different types of bubbles and what to do when you have an incomplete bubble. Complications and their management, such as micro- or macroporations and premature or inadequate opening of the bubble, will be illustrated. Precautions during suturing, management of double chamber, and postoperative management after DALK will also be discussed.

References

1. Dua HS, Faraj LA, Said DG, Gray T, Lowe J. Human corneal anatomy redefined: a novel pre-Descemet's layer (Dua's layer). *Ophthalmology* 2013; 120:1778-1785.
2. Ross AR, Said DG, El-Amin A, et al. Deep anterior lamellar keratoplasty: dissection plane with viscoelastic and air can be different. *Br J Ophthalmol*. 2018; 102:1646-1652.
3. Dua HS, Said DG. Deep anterior lamellar keratoplasty (DALK): science and surgery. In: D.M. Albert, et al., eds. *Albert and Jakobiec's Principles and Practice of Ophthalmology*. Switzerland: Springer Nature; 2021.
4. Au J, Goshe J, Dupps WJ Jr, Srivastava SK, Ehlers JP. Intraoperative optical coherence tomography for enhanced depth visualization in deep anterior lamellar keratoplasty from the PIONEER study. *Cornea* 2015; 34:1039-1043.
5. Güell JL, Aristizábal-Montes D. Visco-bubble technique for deep anterior lamellar keratoplasty. *J Emmetropia*. 2014; 5:65-68.

DSAEK for Complex Eyes

Divya Srikumaran MD

Introduction

Selective endothelial keratoplasty, including Descemet-stripping automated endothelial keratoplasty (DSAEK) and Descemet membrane endothelial keratoplasty (DMEK), is the most commonly performed keratoplasty procedure in the United States. It has become the preferred procedure over penetrating keratoplasty for the treatment of endothelial dysfunction due to its faster visual recovery and improved safety profile. Modern-day endothelial keratoplasty techniques, pioneered by Dr. Gerrit Melles, have evolved over the past 2 decades from deep lamellar endothelial keratoplasty (DLEK) to DSAEK, including variations in graft thickness such as ultrathin (less than 100-micron graft) or nanothin (less than 50-micron graft), to, most recently, DMEK.

DMEK vs. DSAEK

The advantages of DMEK over DSAEK include more rapid and improved visual acuity outcomes as well as decreased risk of rejection. While early rates of endothelial cell loss and rebubbling rates may be higher with DMEK compared to DSAEK during the surgeon learning curve, evidence suggests the rates are similar with increased experience.¹⁻³ Two randomized trials comparing DMEK and ultrathin DSAEK were published recently, one from the United States and one from the Netherlands.^{4,5} Both trials demonstrated improved visual acuity outcomes, with a higher proportion of eyes achieving 20/25 or better vision for DMEK over DSAEK, with comparable complications and endothelial cell loss.^{4,5} A subsequent nonrandomized case series suggested that nanothin DSAEK may also provide visual acuity outcomes comparable to those of DMEK.⁶ Though the numbers of DMEK procedures performed annually continue to increase, DSAEK is still more commonly performed, likely to due the technical difficulty of DMEK.⁷

Complex Cases

While data regarding the superiority of DMEK over DSAEK for uncomplicated cases performed by experienced surgeons is growing, less is known about comparative outcomes in complex cases. DSAEK may be preferred over DMEK for eyes with complex anterior chamber anatomy, including anterior chamber IOLs, sutured IOLs, aphakia, tube shunt devices, trabeculectomy, large iris defects, hypotony, and eyes with very deep anterior chambers (such as in high myopia or with prior vitrectomy). In such cases, DMEK can be more challenging since the air/SF₆ gas bubble might be difficult to maintain in the anterior chamber, and thus the DMEK graft may be more prone to detachment (whereas the stromal-to-stromal interface of DSAEK can facilitate graft attachment). In such eyes, the DMEK graft can also be very difficult to unfold and/or position, and/or the graft could migrate posteriorly. Similarly in patients with significant medical comorbidities and social situations that might prevent adequate postoperative positioning, DSAEK may be the preferred procedure. In eyes with prior or concurrent vitrectomy,

reports have demonstrated comparable postoperative visual acuity outcomes but higher rates of complications in DMEK cases with prior vitrectomy compared to DSAEK, and as specifically shown in another study, patients over the age of 90 had higher rates of rebubbling.^{8,9} However, a different study comparing DMEK and DSAEK in patients with prior glaucoma surgery demonstrated comparable complications rates and better visual acuity in the DMEK group.¹⁰ Additional studies are needed to optimize case selection for DSAEK vs. DMEK in complex eyes.

References

- Deng SX, Lee WB, Hammersmith KM, et al. Descemet membrane endothelial keratoplasty: safety and outcomes: a report by the American Academy of Ophthalmology. *Ophthalmology* 2018; 125(2):295-310.
- Marques RE, Guerra PS, Sousa DC, Gonçalves AI, Quintas AM, Rodrigues W. DMEK versus DSAEK for Fuchs' endothelial dystrophy: a meta-analysis. *Eur J Ophthalmol.* 2019; 29(1):15-22.
- Schrittenlocher S, Schaub F, Hos D, Siebelmann S, Cursiefen C, Bachmann B. Evolution of consecutive Descemet membrane endothelial keratoplasty outcomes throughout a 5-year period performed by two experienced surgeons. *Am J Ophthalmol.* 2018; 190:171-178.
- Chamberlain W, Lin CC, Austin A, et al. Descemet endothelial thickness comparison trial: a randomized trial comparing ultrathin Descemet stripping automated endothelial keratoplasty with Descemet membrane endothelial keratoplasty. *Ophthalmology* 2019; 126(1):19-26.
- Dunker SL, Dickman MM, Wisse RPL, et al. Descemet membrane endothelial keratoplasty versus ultrathin Descemet stripping automated endothelial keratoplasty: a multicenter randomized controlled clinical trial. *Ophthalmology* 2020; 127(9):1152-1159.
- Kurji KH, Cheung AY, Eslani M, et al. Comparison of visual acuity outcomes between nanothin Descemet stripping automated endothelial keratoplasty and Descemet membrane endothelial keratoplasty. *Cornea* 2018; 37(10):1226-1231.
- Eye Bank Association of America. Eye Banking Statistical Report. EBAA website. Available from: <https://restoresight.org/what-we-do/publications/statistical-report/>.
- Mimouni M, Sorkin N, Slomovic J, et al. Descemet membrane endothelial keratoplasty versus Descemet stripping automated endothelial keratoplasty in complicated vitrectomized eyes. *Curr Eye Res.* Epub ahead of print 2021 Mar 4; 1-8. doi: 10.1080/02713683.2021.1892150.
- Parker JS, Ham L, Parker CP, Parker JS, Dockery PW, Melles GRJ. DMEK in super-seniors: clinical outcomes of Descemet membrane endothelial keratoplasty performed in patients ≥ 90 years old. *Curr Eye Res.* 2020; 45(9):1031-1035.
- Lin SR, Prapaipanich P, Yu F, et al. Comparison of endothelial keratoplasty techniques in patients with prior glaucoma surgery: a case-matched study. *Am J Ophthalmol.* 2019; 206:94-101.

DMEK in Complex Eyes

Nir Sorkin MD

I. Introduction

Descemet membrane endothelial keratoplasty (DMEK) has been established as a safe and effective technique in the management of endothelial failure, showing superiority over other keratoplasty techniques. However, it may be more technically challenging to perform as manifested by its relatively steep learning curve. While the majority of eyes undergoing DMEK have no specific characteristics that could complicate the procedure, some eyes may present circumstances that make them more complex for DMEK.

II. The Complexity of Defining “Complex”

There is no universal definition for a complex DMEK eye. Complexity varies between eyes, depending on the specific characteristics that make an eye complex. Also, complexity is dependent upon surgeon experience. Many times, a complex eye can have more than one complex characteristic. Complex characteristics are not limited to intraoperative considerations, as some eyes can present postoperative DMEK management challenges as well. Lastly, since these cases are less common, there is less published data on DMEK performed in these scenarios.

III. Which Characteristics Make a Complex DMEK Eye?

Some examples include anterior synechiae or shallow anterior chambers (ACs), previous vitrectomy or high myopia with deep (non-shallowing) ACs, presence of a glaucoma filter or a glaucoma-drainage-device (GDD), presence of a penetrating keratoplasty (PK) or Descemet stripping automated endothelial keratoplasty (DSAEK) graft, and altered lens-iris diaphragm such as in aphakia, aniridia, or an IOL that is either dislocated, fixated, or present in the AC.

IV. What Have We Learned Recently About DMEK in Some of Those Scenarios?

A. Vitrectomized eyes

1. Challenge: AC does not shallow.
2. What we have learned:
 - a. Use of pars plana infusion to control AC depth
 - i. Good early outcomes
 - ii. High rate of retinal complications and adverse events
 - b. Double-bubble technique (one small bubble above and one large bubble beneath the graft) for the purpose of fixating and unfolding the graft
 - i. Good early outcomes

ii. Prolonged unfolding time

iii. Further research required to establish safety and efficacy

c. Temporary diaphragm (temporary hydrophilic methacrylate sheet) in the AC to flatten the AC and facilitate graft unfolding

i. High detachment rate

ii. Further research required to establish safety and efficacy

d. Better outcomes shown with DSAEK – DSAEK may be preferred in this scenario.

B. Aphakia and/or aniridia

1. Challenges

a. Insufficient lens-iris diaphragm to allow DMEK unfolding and positioning

b. High risk of graft dislocating into the vitreous cavity

2. What we have learned:

a. Endothelium-in pull-through

i. Very high graft failure rates

ii. DSAEK showed better outcomes.

b. Staged procedure: ant. segment reconstruction first (IOL fixation ± iris reconstruction or artificial iris implantation) followed by DMEK

i. Promising early outcomes

ii. Further research required

c. Until further data is available – DSAEK may be preferred in this scenario.

C. Presence of a trabeculectomy or a GDD

1. Intraoperative challenges

a. GDD gets in the way.

b. Hard to achieve tamponade; potentially more detachments

2. Postoperative challenge: High rates of rejection and secondary failure

3. What we have learned:

a. DMEK detachment rates are probably not higher in this scenario compared to Fuchs.

b. To reduce rejection/failure:

i. Should we be more aggressive with steroids?

- ii. Should we use steroid-sparing rejection prophylaxis?
 - iii. Should we use posterior GDD tubes?
 - c. Rejection and secondary failure rates similar in DSAEK and DMEK
 - d. Better visual outcome with DMEK
- D. Presence of a failed PK
1. Intraoperative challenges: Different corneal curvatures, graft-host interface (irregular and weak)
 2. Postoperative challenge: high detachment rates
 3. What we have learned:
 - a. Avoid the graft-host junction; graft size affects detachment rate.
 - b. Use air bubble to unscroll the graft.
 - c. Femtosecond-assisted descemetorhexis—reduced detachment rates

Selected Readings

1. Sorkin N, Einan-Lifshitz A, Ashkenazy Z, et al. Enhancing Descemet membrane endothelial keratoplasty in postvitrectomy eyes with the use of pars plana infusion. *Cornea* 2017; 36(3):280-283.
2. Hayashi T, Kobayashi A. Double-bubble technique in Descemet membrane endothelial keratoplasty for vitrectomized eyes: a case series. *Cornea* 2018; 37(9):1185-1188.
3. Yoeruek E, Bartz-Schmidt KU. Novel technique for improving graft unfolding in vitrectomized eyes using a temporary diaphragm in Descemet membrane endothelial keratoplasty. *Cornea* 2018; 37(10):1334-1336.
4. Mimouni M, Sorkin N, Slomovic J, et al. Descemet membrane endothelial keratoplasty versus Descemet stripping automated endothelial keratoplasty in complicated vitrectomized eyes. *Curr Eye Res*. Epub ahead of print 2021 Mar 4:1-8. doi: 10.1080/02713683.2021.1892150.
5. Santaella G, Sorkin N, Mimouni M, et al. Outcomes of Descemet membrane endothelial keratoplasty in aphakic and aniridic patients. *Cornea* 2020; 39(11):1389-1393.
6. Ang M, Tan D. Anterior segment reconstruction with artificial iris and Descemet membrane endothelial keratoplasty: a staged surgical approach. *Br J Ophthalmol*. Epub ahead of print 2021 Feb 26. doi: 10.1136/bjophthalmol-2020-317906.
7. Bonnet C, Ghaffari R, Alkadi T, et al. Long-term outcomes of Descemet membrane endothelial keratoplasty in eyes with prior glaucoma surgery. *Am J Ophthalmol*. 2020; 218:288-295.
8. Sorkin N, Mimouni M, Kisilevsky E, et al. Four-year survival of Descemet membrane endothelial keratoplasty in patients with previous glaucoma surgery. *Am J Ophthalmol*. 2020; 218:7-16.
9. Lin SR, Prapaipanich P, Yu F, et al. Comparison of endothelial keratoplasty techniques in patients with prior glaucoma surgery: a case-matched study. *Am J Ophthalmol*. 2019; 206:94-101.
10. Alshaker S, Mimouni M, Batawi H, et al. Four-year survival comparison of endothelial keratoplasty techniques in patients with previous glaucoma surgery. *Cornea*. Epub ahead of print 2020 Dec 16. doi: 10.1097/ICO.0000000000002585.
11. Pasari A, Price MO, Feng MT, Price FW Jr. Descemet membrane endothelial keratoplasty for failed penetrating keratoplasty: visual outcomes and graft survival. *Cornea* 2019; 38(2):151-156.
12. Sorkin N, Mimouni M, Santaella G, et al. Comparison of manual and femtosecond laser-assisted Descemet membrane endothelial keratoplasty for failed penetrating keratoplasty. *Am J Ophthalmol*. 2020; 214:1-8.

New DMEK Techniques

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Introduction

Descemet membrane endothelial keratoplasty (DMEK) has shown outstanding clinical outcomes, becoming the procedure of choice for treating endothelial disease.¹⁻³ As a result, the number of endothelial keratoplasty treatments has increased significantly over recent years, resulting in a high demand for good quality endothelial grafts.⁴ However, as there is worldwide shortage of corneal tissue, there is an urgent need for new techniques that can allow for a more efficient use of donor corneal grafts, increasing the pool of patients that can be treated worldwide.⁵⁻⁸ Furthermore, in order to keep improving the results of the modern lamellar keratoplasty techniques, refinement into more minimally invasive surgery is needed. In this presentation, we would like to discuss the advantages and disadvantages of new DMEK techniques that have been developed to facilitate a more beneficial use of corneal tissue.

Background Observations

From DMEK in patients with Fuchs endothelial corneal dystrophy (FECD), we have learned that a cornea can still clear “spontaneously” in the presence of a detached or upside-down graft, given the potential of donor and/or recipient endothelial cells to migrate.^{9,10} This important finding initiated the concepts of Descemet membrane endothelial transfer (DMET) and Descemet stripping only (DSO).¹⁰⁻¹⁶ In both techniques, a descemetorrhexis is performed, stimulating the migration of the peripheral endothelial cells to cover the created “gap.”¹⁰⁻¹⁶ Unlike in DSO, in DMET a free-floating donor graft is transplanted which theoretically could further stimulate the clearance process. These procedures seem to achieve corneal clearance in some patients; however, the clearance time is relatively long and the patterns of clearance may differ significantly among patients,¹⁷ suggesting that the procedures may only be valid for some patients with certain type and/or severity of FECD, who perform better—being, in general, those with central FECD. Furthermore, the postoperative endothelial cell density seems to remain lower than in standard DMEK, making unpredictable the time that the cornea will remain clear after the procedure. Moreover, DMET has been shown to fail in providing satisfactory results in the long term.¹¹ In DSO, as the descemetorrhexis is much smaller (4-5 mm vs. ~9.0 mm in DMET), the results seem to be improved, especially when combined with the use of topical Rock-inhibitor eyedrops.¹²⁻¹⁶ Nevertheless, more studies in a larger group of patients and with a longer follow-up time are needed in order to better evaluate the results of this procedure.

Hemi- and quarter-DMEK are also new DMEK techniques developed in the past several years.⁶⁻⁸ In hemi-DMEK, a half-moon nontrephined DMEK graft is transplanted, while quarter-DMEK uses only one quarter, but with a smaller descemetorrhexis. In these procedures central corneal clearance is much faster compared with DSO, but the endothelial cell density still remains lower than in standard DMEK, probably due to the

migration of endothelial cells that still happens in order to cover the “bare” stromal gaps surrounding the graft.⁶⁻⁸ Furthermore, the quarter-/semi-lunar shaped grafts seem to present a higher tendency to detach than circular grafts.⁶⁻⁸ To circumvent these issues, the technique has been refined into what we have named “customized-DMEK.” This technique completely adapts the size of the descemetorrhexis and the diameter of the graft to the extent of the disease, generally meaning a smaller descemetorrhexis and (circular) graft covering the damaged area, leaving minimal bare areas to maintain the high endothelial cell density and with a circular shape to diminish the risk of graft detachment. By replacing only the affected part of the endothelium and implanting a smaller graft, positioned centrally, theoretically there is a better preservation of the peripheral host cells, a chance of visual restoration identical to standard DMEK and potentially a lower risk of allograft rejection.

Conclusion

In the past few decades, many developments have occurred in the treatment of endothelial disease. Not only have grafts steadily become thinner, smaller, and more specific, but the increasing knowledge about the behavior of the endothelium, both in health and disease, have prompted further developments in DMEK and in the treatment of FECD dystrophy.

References

1. Birbal RS, Baydoun L, Ham L, et al. Effect of surgical indication and preoperative lens status on Descemet membrane endothelial keratoplasty outcomes. *Am J Ophthalmol.* 2020; 212:79-87.
2. Birbal RS, Ni Dhubbghaill S, Bourgonje VJA, et al. Five-year graft survival and clinical outcomes of 500 consecutive cases after Descemet membrane endothelial keratoplasty. *Cornea* 2020; 39:290-297.
3. Vasiliauskaite I, Oellerich S, Ham L, et al. Descemet membrane endothelial keratoplasty: ten-year graft survival and clinical outcomes. *Am J Ophthalmol.* 2020; 217:114-120.
4. Eye Bank Association of America. Eye Banking statistical report 2019; 4.
5. Baydoun L, Zygoura V, Hsien S, et al. Clinical feasibility of using multiple grafts from a single donor for quarter-DMEK. *Acta Ophthalmol.* 2018; 96:e656-e658.
6. Birbal RS, Hsien S, Zygoura V, et al. Outcomes of hemi-Descemet membrane endothelial keratoplasty for Fuchs endothelial corneal dystrophy. *Cornea* 2018; 37:854-858.
7. Birbal RS, Ni Dhubbghaill S, Baydoun L, et al. Quarter-Descemet membrane endothelial keratoplasty: one- to two-year clinical outcomes. *Cornea* 2020; 39:277-282.
8. Zygoura V, Baydoun L, Ham L, et al. Quarter-Descemet membrane endothelial keratoplasty (quarter-DMEK) for Fuchs endothelial corneal dystrophy: 6 months clinical outcome. *Br J Ophthalmol.* 2018; 102:1425-1430.

9. Balachandran C, Ham L, Verschoor CA, Ong TS, van der Wees J, Melles GR. Spontaneous corneal clearance despite graft detachment in Descemet membrane endothelial keratoplasty. *Am J Ophthalmol.* 2009; 148:227-234.e1.
10. Bleyen I, Saelens IE, van Dooren BT, van Rij G. Spontaneous corneal clearing after Descemet's stripping. *Ophthalmology* 2013; 120:215.
11. Birbal RS, Parker J, Dirisamer M, et al. Descemet membrane endothelial transfer: ultimate outcome. *Cornea* 2018; 37:141-144.
12. Arbelaez JG, Price MO, Price FW Jr. Long-term follow-up and complications of stripping Descemet membrane without placement of graft in eyes with Fuchs endothelial dystrophy. *Cornea* 2014; 33:1295-1299.
13. Koenig SB. Planned Descemetorhexis without endothelial keratoplasty in eyes with Fuchs corneal endothelial dystrophy. *Cornea* 2015; 34:1149-51.
14. Moloney G, Petsoglou C, Ball M, et al. Descemetorhexis without grafting for Fuchs endothelial dystrophy-supplementation with topical ripasudil. *Cornea* 2017; 36:642-648.
15. Davies E, Jurkunas U, Pineda R 2nd. Predictive factors for corneal clearance after Descemetorhexis without endothelial keratoplasty. *Cornea* 2018; 37:137-140.
16. Garcerant D, Hirschall N, Toalster N, Zhu M, Wen L, Moloney G. Descemet's stripping without endothelial keratoplasty. *Curr Opin Ophthalmol.* 2019; 30:275-285.
17. Dirisamer M, Dapena I, Ham L, et al. Patterns of corneal endothelialization and corneal clearance after Descemet membrane endothelial keratoplasty for Fuchs endothelial dystrophy. *Am J Ophthalmol.* 2011; 152:543-555.e1.

Corneal Transplantation: Where Do We Stand?

Zuguo Liu MD

Corneal disease is the leading cause of blindness around the world. Corneal transplantation is the most important method of treating the diseases and recovering the vision. However, the shortage of cornea donors is a major barrier to cornea transplant operations. Animal corneas have been investigated as a possible replacement for human corneal grafts for a long time. Recently, progress has been made in utilizing genetically engineered (GE) pigs in xenotransplantation. Decellularized porcine cornea (DPC) were approved to be used as a product clinically by the CFDA a few years ago. Up to now, more than 2000 patients have received xenotransplantation surgery, with positive outcomes in vision and repair. In this presentation, we will introduce the history of corneal xenotransplantation, the challenges we face today, and the future perspectives of this operation.

In These Unprecedented Times . . .

2021 Cornea Subspecialty Day

Darby D Miller MD MPH

The COVID-19 pandemic has impacted us in many ways, including our ability to effectively raise critical funds used to protect sight and empower lives. This objective requires active participation and commitment to advocacy from every ophthalmologist. Contributions to the following three critical funds are a part of that commitment:

- OPHTHPAC®
- Surgical Scope Fund (SSF)
- State Eye PAC

During AAO 2021 in New Orleans, invest in OPHTHPAC and Surgical Scope Fund at one of our two booths in the convention center or [online](#). You may also invest via phone by texting MDEYE to 41444 for OPHTHPAC and SCOPE to 51555 for the Surgical Scope Fund.

We also encourage you to stop by our booth in the Hall B Lobby to learn more about [OPHTHPAC Direct](#), a unique program that lets you decide who receives your political support.

Please help us in these unprecedented times to continue to protect quality patient eye care for everybody. Two Academy committees made up of your ophthalmology colleagues are working hard on your behalf to ensure this outcome. The OPHTHPAC Committee continues to identify Congressional Advocates in each state to maintain close relationships with federal legislators to advance ophthalmology and patient causes. The Surgical Scope Fund Committee is raising funds to be used to protect Surgery by Surgeons during scope battles at the state level.

Our mission of “protecting sight and empowering lives” requires robust funding of both OPHTHPAC and the Surgical Scope Fund. Each of us has a responsibility to ensure that these funds are strong so that ophthalmology continues to strive, especially in these unprecedented times.

OPHTHPAC®

OPHTHPAC represents the profession of ophthalmology to the U.S. Congress. OPHTHPAC’s most recent victories include the following:

Physician Relief

- ✓ Securing access to COVID-19 relief, including Provider Relief Funds and forgivable small business loans
- ✓ Pushing Congress to enact a provider-friendly “surprise” medical billing law

Medicare Payment

- ✓ Mitigating drastic Medicare cuts
- ✓ Obtaining a one-year moratorium extension on the 2% Medicare budget sequestration cut

Research & Relationships

- ✓ Increasing vision research funding by \$11.6 million
- ✓ Helping get three new physicians elected to Congress, including an ophthalmologist

However, facing ophthalmology’s federal issues is a continuous battle, and OPHTHPAC is always under pressure to ensure we have strong political connections in place to help protect ophthalmology, its members, and their patients.

The support OPHTHPAC receives from invested U.S. Academy members helps build the federal relationships that advance ophthalmology’s agenda on Capitol Hill. These relationships allow us to have a seat at the table with legislators willing to work on issues important to us and our patients. We also use these congressional relationships to help shape the rules and regulations being developed by federal health agencies.

Get engaged with OPHTHPAC and help strengthen ophthalmology’s voice on Capitol Hill as we address the following legislative and regulatory issues this year:

- Improving Medicare physician payments
- Fighting optometric scope expansion in the Veterans’ Health Administration
- Obtaining relief from prior authorization and step therapy requirements that delay patient care
- Seeking solutions for rising drug prices and access to drugs in shortage
- Ensuring fair reimbursements for Part B drugs

At the Academy’s annual Congressional Advocacy Day, the Academy and the Cornea Society ensure a strong presence of cornea specialists to support ophthalmology’s priorities. The Cornea Society also supports participation of young ophthalmologists via the Academy’s Advocacy Ambassador Program. Ophthalmologists visit members of Congress and their key health staff to discuss ophthalmology priorities as part of Congressional Advocacy Day. The Cornea Society remains a crucial partner with the Academy in its ongoing federal and state advocacy initiatives.

Surgical Scope Fund (SSF)

The Surgical Scope Fund (SSF) provides grants to state ophthalmology societies to support their efforts to protect patient safety from dangerous optometric surgery proposals. Since its inception, the Surgery by Surgeons campaign and the SSF, in partnership with state ophthalmology societies, has helped 41 state/territorial ophthalmology societies reject optometric scope-of-practice expansions into surgery.

If you already have made a SSF contribution, please go to safesurgerycoalition.org to see the impact of your gift.

Dollars from the SSF are critical to building complete, cutting-edge political campaigns, including media efforts (TV, radio, and social media), educating and building relationships with legislators, and educating the voting public to contact their legislators. These political campaigns help the SSF to protect patient safety by defeating optometry’s surgical initiatives.

Each of these endeavors is very expensive, and no one state has the critical resources to battle big optometry on their own. Ophthalmologists must join together and donate to the SSF and to fight for patient safety.

The Secretariat for State Affairs thanks the Cornea Society, who has joined state ophthalmology societies in the past in contributing to the SSF and has already contributed again in 2021. These ophthalmic organizations complete the necessary SSF support structure for the protection of our patients' sight.

State Eye PAC

It is increasingly important for all ophthalmologists to support their respective State Eye PACs because campaign contributions to legislators at the state level must come from individual ophthalmologists and cannot come from the Academy, OPHTHPAC, or the Surgical Scope Fund. The presence of a strong State Eye PAC providing financial support for campaign contributions and legislative education to elect ophthalmology-friendly candidates to the state legislature is critical, as scope-of-practice battles and many regulatory issues are all fought on the state level.

ACTION REQUESTED: Support ophthalmology's advocacy efforts

Academy Surgical Scope Fund contributions are used to support the infrastructure necessary in state legislative/regulatory battles and for public education. State PAC and OPHTHPAC contributions are necessary at the state and federal level, respectively, to help elect officials who will support the interests of our patients. Contributions to each of these three funds are necessary and help us protect sight and empower lives. Surgical Scope Fund contributions are completely confidential and may be made with corporate checks or credit cards. PAC contributions may be subject to reporting requirements.

Please respond to your Academy colleagues and be part of the community that contributes to OPHTHPAC, the Surgical Scope Fund, and your State Eye PAC. Please be part of the community that ensures ophthalmology has a strong voice in advocating for patients.

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Surgical Scope Fund	OPHTHPAC®	State Eye PAC
To protect patient safety by defeating optometric surgical scope-of-practice initiatives that threaten quality surgical care	Working across the political spectrum to advance ophthalmology and protect its members and patients at the federal level. Support for candidates for U.S. Congress.	Support for candidates for state House, Senate, and governor
Political grassroots activities, government relations, PR and media campaigns	Campaign contributions, legislative education	Campaign contributions, legislative education
No funds may be used for campaign contributions or PACs.		
Contributions: Unlimited.	Contributions: Limited to \$5,000	Contribution limits vary based on state regulations.
Individual, practice, corporate, and organization	Personal and corporate contributions are accepted.	
Contributions are 100% confidential.	Contributions \$200 and above are on the public record.	Contributions are on the public record depending upon state statutes.

No Zonule, No Problem!

Joanne Shen MD

- I. The Problem
 - A. What is the best method of IOL implantation when zonular and capsular support are not available?
 - B. 2020 Ophthalmic Technology Assessment
 - 1. 2002-2019 publications
 - 2. 734 citations yielded 45 retrospective articles, minimum 6 months follow-up
- II. The Solutions
 - A. Anterior chamber IOL (AC-IOL), 37 months of mean follow-up
 - B. Iris-clipped AC-IOL (standard and retropupillary fixation), 31 and 41 months of mean follow-up, respectively
 - C. Posterior chamber IOL (PC-IOL) sutured to iris (10-0 polypropylene [PP]), 42 months of mean follow-up
 - D. PC-IOL sutured to sclera (10-0 PP, 8-0 PP, CV-8 PFTE), 34, 36, and 11 months of mean follow-up, respectively
 - E. PC-IOL intrascleral haptic fixation without sutures (ie, “glued” or flanged haptic), 16 months of mean follow-up
- III. The Patient, the Surgeon, the OR

These factors influence the technique used:

 - A. Patient’s visual potential, tolerance for risk and repeat surgeries, age, and ability to follow up
 - B. Ocular abnormalities and risk for cystoid macular edema (CME), uveitis, glaucoma
 - C. Anterior segment vs. vitreoretinal surgeon and the role of pars plana vitrectomy?
 - D. Surgeon comfort with bimanual procedures and availability of microsurgical instrumentation and OR time
- IV. The Complications

Similar surgical technique cases were aggregated, and the weighted mean percentages were compared.

 - A. Pupillary capture
 - 1. Consider peripheral iridectomy to avoid this complication.
 - 2. Highest at 4% in PC-IOL intrascleral haptics
 - B. Lens tilt: highest at 2% in PC-IOL 10-0 PP sclera
 - C. Lens decentration: highest at 3% in PC-IOL 8-0 PP and 2% in AC-IOL, PC-IOL 10-0 PP sclera, and PC-IOL intrascleral haptics
 - D. Lens dislocation or haptic displacement
 - 1. Suture breakage can cause lens dislocation. Lens dislocation 4% for PC-IOL 10-0 PP sclera, 3% for iris-clipped AC-IOL, and 3% for PC-IOL 10-0 PP iris
 - 2. 3% haptic displacement for PC-IOL intrascleral haptics
 - E. External erosion of suture or haptic
 - 1. Patients need long-term follow-up.
 - 2. 3% suture erosion for PC-IOL 8-0 PP sclera, 2% for PC-IOL 10-0 PP
 - 3. 1% haptic erosion for PC-IOL intrascleral haptics
 - F. Wound leak
 - 1. Larger wounds may be more at risk for leak.
 - 2. Highest at 3% for iris-clipped AC-IOL
 - G. Chronic glaucoma

Highest at 13% in PC-IOL 8-0 PP sclera, followed by 7% in AC-IOL, 6% in PC-IOL 10-0 PP sclera
 - H. Chronic uveitis
 - 1. AC-IOL not advised
 - 2. 6% in AC-IOL and 4% in iris-clipped AC-IOL
 - 3. Lower at 1% in retropupillary iris-clipped AC-IOL and 2% in PC-IOL 10-0 PP sclera
 - I. Cystoid macular edema
 - 1. Most common complication
 - 2. PC-IOL 10-0 PP iris not advised
 - a. 16% risk of CME
 - b. 13% in PC-IOL 8-0 PP sclera
 - 3. 7% in AC-IOL, 5% in both PC-IOL 10-0 PP sclera and PC-IOL intrascleral haptics, and 4% in iris-clipped AC-IOL
 - J. Vitreous hemorrhage
 - 1. Usually self-limited
 - 2. Highest at 7% in PC-IOL CV-8 PFTE
 - K. Suprachoroidal hemorrhage
 - 1. Low percentages
 - 2. May be underreported due to the nature of retrospective reviews
 - L. Retinal break: low percentages
 - M. Retinal detachment: low percentages

- N. Endophthalmitis: highest at 2% in the PC-IOL 10-0 PP iris
- O. Risk of phototoxicity in cases with prolonged surgical time
- V. The Pipeline
 - A. NCT01547429 Artisan Aphakia Lens for the Correction of Aphakia (Secondary) in Adults
 - B. 300 eyes
 - C. December 2022 completion
- VI. The Conclusions
 - A. Surgeons resort to numerous methods to implant IOLs when zonular and capsular support are not available. The advantages and pitfalls of each technique are important to understand. These techniques continue to evolve since there is not a single best solution without risk of complications.
 - B. Newer techniques have shorter mean follow-up intervals.
 - C. Findings are based on retrospective data and must be interpreted with caution. However, percentages may help guide choices and patient conversations.
 - D. AC-IOL is associated with higher rates of glaucoma and anterior uveitis, but surprisingly with a typical risk of CME.
 - E. As expected, suturing to iris and clipping to the anterior iris are associated with higher risk of CME.
 - F. Due to potential erosion of sutures and haptics, patients must understand the need for follow-up exams.
 - G. PC-IOL 9-0 PP sclera studies are needed since none met criteria for OTA review.

Table 4: Weighted mean percentage of complications per intraocular lens technique

(Shen JF, Deng S, Hammersmith KM, Kuo AN, Li JY, Weikert MP, Shtein RM. Intraocular lens implantation in the absence of zonular support: an outcomes and safety update. *Ophthalmology*, September 2020, Vol 127, 1234-1258.)

Free article PDF for AAO members at <https://www.aao.org/ophthalmic-technology-assessment/intraocular-lens-implantation-in-absence-of-zonula>

Intraocular Lens Type	Suture (If Applicable)	Total No. of Eyes	Weighted Mean Follow-up (mos)	Pupillary Capture (%)	Lens Tilt (%)	Lens Decentration (%)	Lens Dislocation or Haptic Displacement (%)	External Erosion of Suture or Haptic (%)	
ACIOL	Angle	NA	311	37.4	2.2	NR	1.8	NR	NA*
ACIOL	Iris	NA - clipped	254	30.7	0.4	0*	NR	2.9	NA*
ACIOL	Iris (retropupillary)	NA - clipped	629	41.4	0.13	0*	0*	0.3	NA*
PCIOL	Iris	10-0 PP	639	42.1	NR	0*	0*	3.3	NA*
PCIOL	Sclera	10-0 PP	1163	33.9	2.4	1.6 [†]	1.6	3.5 [†]	2.4
PCIOL	Sclera	8-0 PP	30	36	0*	NR	3.3 [†]	NR	3.3 [†]
PCIOL	Sclera	CV-8 PFTE	85	10.8	0*	0*	0*	0*	NR
PCIOL	Sclera (intra-scleral)	NA	1331	15.6	3.5 [†]	0.1	2.3	2.9	0.7

Wound Leak (%)	Chronic Glaucoma (%)	Chronic Uveitis (%)	Cystoid Macular Edema (%)	Vitreous Hemorrhage (%)	Suprachoroidal Hemorrhage (%)	Retinal Break (%)	Retinal Detachment (%)	Endophthalmitis (%)
NR	6.8	5.6 [†]	7.3	2.2	NR	NR	0.9	0.6
2.7 [†]	0.4	3.5	4.2	1.2	NR	0.4	0.4	0*
0.1	1.2	1.0	2.8	0.3*	NR	NR	0.7	0.1
1.3	2.0	0.2	16.2 [†]	0.7	NR	NR	2.0	1.7 [†]
0.9	5.5	2.0	4.8	4.3 [†]	0.7 [†]	0.4	2.2	0.1
NR	13.2 [†]	0*	13.2	3.3	NR	NR	3.3 [†]	NR
NR	NR	0*	2*	7	0*	NR	0*	0*
0*	0.2	0.3	4.5	3.4	0*	NR	0.5	0.1

Abbreviations:

NA = not applicable

NR = not reported, which was counted as 0 which may underestimate risk

*Lowest percentage or not applicable for complication type

[†]Highest percentage for complication type

Figure 1. Table 4 from OTA article, reprinted with permission for ease of viewing.

Selected Readings

1. Shen JF, Deng S, Hammersmith KM, et al. Intraocular lens implantation in the absence of zonular support: an outcomes and safety update. *Ophthalmology* 2020; 127:1234-1258.
2. Kokame GT, Yanagihara RT, Shantha JG, Kaneko KN. Long-term outcome of pars plana vitrectomy and sutured scleral-fixated posterior chamber intraocular lens implantation or repositioning. *Am J Ophthalmol.* 2018; 189:10-16. [Retrospective review of 116 eyes with 2-year mean follow-up: single surgeon PC-IOL 10-0 PP sclera and includes discussion on suture breakage.]
3. Price MO, Price FW, Werner L, Berlie C, Mamalis N. Late dislocation of scleral-sutured posterior chamber intraocular lenses. *J Cataract Refract Surg.* 2005; 31:1320-1326. [Authors discuss diameter of 10-0 vs. 9-0 PP sutures.]
4. Parekh P, Green R, Stark WJ, Akpek EK. Subluxation of suture-fixated posterior chamber intraocular lenses: a clinicopathologic study. *Ophthalmology* 2007; 114:232-237. [Sharp edge of PC-IOL optic positioning holes may be associated with suture breakage.]
5. Chang D, ed. *Advanced IOL Fixation Techniques: Strategies for Compromised or Missing Capsular Support.* Slack Books; 2019. [This book includes many illustrations and videos for learning different techniques.]

The Cornea and Glaucoma Angle

Richard K Lee MD

- I. What is the angle?
 - A. Anatomy of the angle
 - B. Landmarks of the angle for glaucoma surgery
- II. What are the types of angle-based glaucoma surgeries?
 - A. Trabecular bypass
 - B. Trabecular ablation
 - C. Suprachoroidal drainage
 - D. Cyclophotocoagulation ciliary body destruction
- III. What are the mechanisms of action of these glaucoma angle surgeries to lower the IOP?
 - A. Trabecular meshwork/Schlemm canal
 - B. Suprachoroidal space
 - C. Aqueous humor production
- IV. Does angle-based glaucoma surgery affect the cornea?

Cataract Surgery in the Setting of Endothelial Dysfunction

Francis W Price Jr MD

Treatment of cataracts and endothelial dysfunction has changed significantly over the last 2 decades, improving our ability to provide consistent and reproducible refractive and visual outcomes.

Traditional teaching was that guttae did not affect vision, only corneal edema did. This teaching came from a time when penetrating keratoplasty (PK) was the only option to treat endothelial dysfunction, and in particular Fuchs dystrophy. The prolonged and unpredictable visual recovery with PK coupled with the drawback of perpetual wound weakness to trauma resulted in PK often being delayed until the cornea was extremely edematous and patients were legally blind.

In contrast, the significantly improved benefit-to-risk ratio with endothelial keratoplasty (EK) allows much earlier intervention, and it has now become evident that guttae can substantially degrade vision during daily living activities, even in the absence of significant corneal edema.¹

A recent report on 33,000 cataract procedures in Sweden found that patients with guttae substantially benefited from cataract surgery but had poorer visual results than those without guttae.² The authors suggested that transplant surgery should not be undertaken for at least 3 weeks after cataract surgery to see if postoperative corneal edema would resolve. As corneal surgeons with extensive experience treating Fuchs dystrophy, we disagree!

When EK was a new procedure, Fuchs dystrophy patients often had cataract surgery first, followed by EK as needed. However, studies showed that EK combined with cataract surgery had similar visual results and complication rates as staged procedures,^{3,4} and patients usually prefer a combined approach.

The refractive outcomes and uncorrected vision achieved when cataract surgery is combined with or staged before EK are far more predictable than with PK. However, the outcomes are significantly less predictable than those achieved with cataract surgery alone in patients without corneal problems because we are not yet able to accurately predict how resolution of corneal stromal and epithelial edema will affect the final manifest refraction.^{5,6}

Therefore, for patients who desire the best possible uncorrected visual acuity or a presbyopia-correcting IOL, we offer to stage Descemet membrane EK first, followed later by biometry imaging and cataract surgery, if the anterior chamber is sufficiently deep for EK without lens removal. Staging EK first produces significantly better refractive outcomes and uncorrected vision than combined procedures or cataract surgery first.⁶ We also offer EK combined with implantation of a light-adjustable lens, so that the IOL can be fine-tuned after corneal clearing. Additional adjustable lens options are in development but not yet approved in the United States.

References

1. Price FW Jr, Feng MT. Impact of corneal guttata on cataract surgery results. *J Cataract Refract Surg*. 2019; 45:1692.
2. Viberg A, Liv P, Behndig A, Lundström M, Byström B. The impact of corneal guttata on the results of cataract surgery. *J Cataract Refract Surg*. 2019; 45:803-809.
3. Terry MA, Shamie N, Chen ES, et al. Endothelial keratoplasty for Fuchs' dystrophy with cataract: complications and clinical results with the new triple procedure. *Ophthalmology* 2009; 116:631-639.
4. Chaurasia S, Price FW Jr, Gunderson L, Price MO. Descemet's membrane endothelial keratoplasty: clinical results of single versus triple procedures (combined with cataract surgery). *Ophthalmology* 2014; 121:454-458.
5. Schoenberg ED, Price FW Jr, Miller J, McKee Y, Price MO. Refractive outcomes of Descemet membrane endothelial keratoplasty triple procedures (combined with cataract surgery). *J Cataract Refract Surg*. 2015; 41:1182-1189.
6. Price MO, Pinkus D, Price FW Jr. Implantation of presbyopia-correcting intraocular lenses staged after Descemet membrane endothelial keratoplasty in patients with Fuchs dystrophy. *Cornea* 2020; 39(6):732-735.

Cataract Surgery Considerations in Abnormal Corneas

Kristin M Hammersmith MD

- I. Expectations of Cataract Surgery
- II. Abnormal corneas present challenges in pre-, intra-, and postop management of cataract surgery.
 - A. Lumps and bumps on the cornea
 1. Epithelial basement membrane degeneration/dystrophy
 2. Salzmann nodular degeneration
 3. Pterygia
 - B. Keratoconus
 - C. Herpes simplex keratitis
 - D. Endothelial dystrophy (covered in another lecture)
- III. Lumps and Bumps on the Cornea
 - A. Most important tools to detect and assess impact: Careful slit-lamp exam and topography
 - B. Epithelial basement membrane degeneration/dystrophy
 1. Most important is recognizing preoperatively and assessing impact.
 - a. Incidence in patients presenting for cataract surgery: 7.5%
 - b. Retroillumination and negative staining, anterior segment OCT
 2. Options for removal
 - a. Simple debridement
 - b. Diamond burr polishing
 - c. Phototherapeutic keratectomy
 3. Wait 2-3 months and ensure stable and regular topography.
 4. References
 - a. Tzelikis PF, Rapuano CJ, Hammersmith KM, et al. Diamond burr treatment of poor vision from anterior basement membrane dystrophy. *Am J Ophthalmol.* 2005; 140(2):308-310.
 - b. Ho VWM, Stanojcic N, O'Brart N, O'Brart D. [Refractive surprise after routine cataract surgery with multifocal IOLs attributable to corneal epithelial basement membrane dystrophy.](#) *J Cataract Refract Surg.* 2019; 45(5):685-689.
 - c. Goerlitz-Jessen MF, Gupta PK, Kim T. Impact of epithelial basement membrane dystrophy and Salzmann nodular degeneration on biometry measurements. *J Cataract Refract Surg.* 2019; 45(8):1119.
 - C. Salzmann nodular degeneration (SND)
 1. Patients with SND develop irregular corneal basal epithelium, a thinned or absent Bowman layer, and subepithelial hyalinized eosinophilic material that extends into the stroma.
 2. The elevated nodules seen in SND can cause peripheral corneal flattening and changes in tear-film distribution, which can result in astigmatic and other refractive changes. Biometric values acquired through corneal topography are impacted by the presence of SND, resulting in inaccurate IOL calculations, as high as 3.2 D in 1 study.
 3. Removal includes manual dissection, superficial keratectomy, diamond burr polishing, phototherapeutic keratectomy. Mitomycin C is used to prevent recurrence.
 4. Reference: Goerlitz-Jessen MF, Gupta PK, Kim T. Impact of epithelial basement membrane dystrophy and Salzmann nodular degeneration on biometry measurements. *J Cataract Refract Surg.* 2019; 45(8):1119-1123.
 - D. Pterygia
 1. Small vs. large
 2. Topography is helpful for extent and impact on astigmatism.
 3. When impactful, either by symptomatology or keratometry readings, remove pterygia with excision and conjunctival autograft.
 4. Wait 2-3 months until topography is stable prior to considering cataract surgery.
- IV. Keratoconus
 - A. Keratometry uses corneal index of refraction of 1.3375.
 1. This is based on the assumption that posterior cornea is 1.2 mm steeper than anterior corneal radius.
 2. Inaccurate for keratoconus and post-refractive patients

- B. Keratometry readings are difficult due to distortion, ectasia, fixation.
1. Steepest part of the cornea may be below visual axis.
 2. Clear corneal incision may have unpredictable effect on keratometry.
 3. RGP wearers need to be out of lenses for accurate keratometry.
- C. Which IOL formula?
1. Most formulas result in hyperopia.
 2. SRK/T yields best outcome of traditional formulas. Kane and Barrett True K later generation formulas
 3. The more severe the keratoconus, the less predictable any formula is.
- D. Which IOL?
1. Monofocal preferred by most
 2. Toric in select eyes; may affect contact lens wear postoperatively
- E. Intraoperative considerations
1. Peripheral cornea often very thin; consider scleral tunnel or aim for area with least thinning.
 2. Low threshold for suturing wound
 3. Consider capsular staining for best visualization
- F. References
1. Gazon N, Arriola V, et al. Intraocular lens power calculation in eyes with keratoconus. *J Cataract Refract Surg.* 2020; 46(5):778-783.
 2. Kane JX, Connell B, Yip H, et al. Accuracy of intraocular lens power formulas modified for patients with keratoconus. *Ophthalmology* 2020; 127(8):1037-1042.
 3. Ton Y, Barrett GD, Kleinmann G, Levy A, Assia EI. Toric intraocular lens power calculation in cataract patients with keratoconus. *J Cataract Refract Surg.* Epub ahead of print 2021 Mar 9. doi: 10.1097/j.jcrs.0000000000000638.
- V. Herpes Simplex Keratitis
- A. Cataracts are common given recurrent ocular inflammation and corticosteroid use.
- B. Intraoperatively, capsular staining, hooks or ring, and synechiolysis are common.
- C. Quiescence prior to cataract is important. Longer time to quiescence is associated with decreased rates of recurrence.
- D. Perioperative and postoperative antiviral prophylaxis are essential. No standard dosage regimen.
- E. References
1. Al-Ani HH, Lu LM, Meyer JJ, Niederer RL. Cataract surgery in herpes simplex virus ocular disease. *J Cataract Refract Surg.* Epub ahead of print 2021 Jul 12. doi: 10.1097/j.jcrs.0000000000000745.
 2. Kanclerz P, Alio JL. Ocular surgery after herpes simplex and herpes zoster keratitis. *Int Ophthalmol.* 2020; 40(12):3599-3612.

Global Consensus on Limbal Stem Cell Deficiency

Friedrich E Kruse MD

Limbal stem cell disease (LSCD) is a challenging problem in terms of both diagnosis and therapy. Thus members from the supranational cornea societies have met several times to reach agreement on the definition, classification, and diagnosis, as well as therapy of LSCD.

I. Definition of LSCD

LSCD is an ocular surface disease caused by a decrease in the population and/or function of corneal epithelial stem/progenitor cells; this decrease leads to the inability to sustain the normal homeostasis of the corneal epithelium.

The disease is characterized by conjunctivalization (ie, replacement of the normal corneal epithelium by conjunctival epithelium) and/or other signs of epithelial dysfunction, such as persistent or recurrent epithelial defects with or without neovascularization, ocular surface inflammation, and scarring. Frequent consequences are decreased vision and discomfort, leading to reduced health-related quality of life.

LSCD may present alone as a single entity or in association with abnormalities of other components of the ocular surface, such as the conjunctiva, meibomian glands, lacrimal glands, tears, corneal nerves, and immune system.

II. Partial vs. Total LSCD (see Figure 1)

Partial LSCD is characterized by incomplete conjunctivalization of the corneal surface and the presence of residual limbal and consequent corneal epithelial cells. *Total LSCD* is characterized by conjunctivalization of the entire corneal surface because of complete loss of corneal epithelial stem/progenitor cells.

III. Classification of LSCD

A. Acquired LSCD

1. Acquired nonimmune-mediated
 - a. Chemical injury
 - b. Thermal injury
 - c. Radiation injury
 - d. Contact lens wear
 - e. Multiple surgeries involving the limbus
 - f. Bullous keratopathy
 - g. Infectious ocular disease
 - h. Chronic lid disease
 - i. Severe blepharitis, rosacea
 - j. Trachoma
 - k. Tumors of the ocular surface
 - l. Severe pterygium
 - m. Drug-induced
 - n. Mitomycin C
 - o. 5-fluorouracil
 - p. Preservatives
 - q. Systemic chemotherapy and immunotherapy

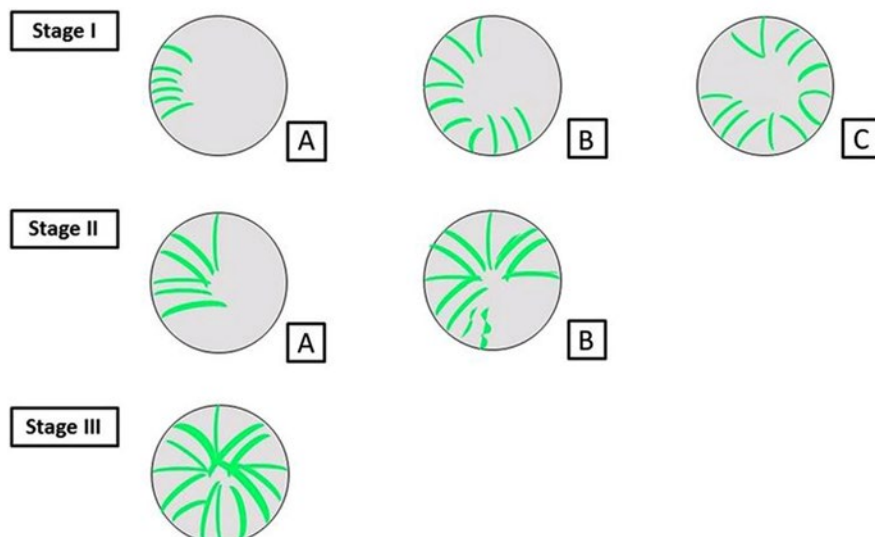


Figure 1. LSCD staging.

2. Acquired primary immune-mediated
 - a. Stevens-Johnson syndrome/toxic epidermal necrolysis
 - b. Mucous membrane pemphigoid
 - c. Allergic ocular surface disease
 - d. Vernal keratoconjunctivitis, graft-versus-host disease
 3. Idiopathic
- B. Hereditary LSCD
1. Congenital aniridia
 - a. Atopic keratoconjunctivitis
 2. Dyskeratosis congenita
 3. Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy/dysplasia
 4. Xeroderma pigmentosum
 5. Keratitis ichthyosis deafness syndrome
 6. Ectrodactyly-ectodermal dysplasia-clefting syndrome
 7. Lacrimo-auriculo-dental-digital syndrome
 8. Epidermolysis bullosa
- IV. Diagnosis of LSCD

Total LSCD is characterized by conjunctivalization of the entire corneal surface because of complete loss of corneal epithelial stem/progenitor cells. The presence of conjunctival epithelial cells (conjunctivalization) on the corneal surface and the absence of the corneal epithelium phenotype produces clinical signs of LSCD.

A. Delayed fluorescence staining at slit lamp

Slit lamp examination and fluorescein staining pattern could reveal signs of LSCD. Fluorescein staining of the ocular surface is a test that can differentiate between normal healthy corneal epithelium and abnormal pathologic epithelium. Under normal conditions, corneal epithelial cells on the surface are interconnected by tight junctions, which are impermeable to a large molecule such as fluorescein. By contrast, the conjunctival epithelium is characterized by relatively loose cell-cell contacts, resulting in a high permeability for fluorescein.

In LSCD, the epithelium on the corneal surface may be either conjunctival with neovascularization, a mixture of metaplastic corneal epithelial cells and conjunctival epithelial cells, or only conjunctival epithelial cells without neovascularization. Abnormal staining is observed 10 or more minutes after fluorescein instillation.

B. Cell sampling and application of dye or specific markers

Impression cytology or biopsy can be used to sample cells from the surface and to prove conjunctivalization of the corneal surface, both by conventional staining and by use of specific markers.

C. In vivo imaging

1. In vivo confocal microscopy (IVCM)

In vivo laser scanning confocal microscopy has emerged as a diagnostic tool for LSCD, in part because this method does not require the removal of corneal epithelial cells for the analyses. IVCM provides information about disease severity and can be used in both diagnosis and monitoring of LSCD. Corneal, conjunctival, and limbal epithelial cells can be distinguished on the basis of their different cell morphology. The absence of the corneal epithelium and/or the presence of conjunctival cells on the cornea is diagnostic of LSCD. Goblet cells can be detected by IVCM.

2. Anterior segment OCT (AS-OCT)

AS-OCT has emerged as an alternative imaging technique for LSCD, allowing for both noninvasive imaging of the ocular surface, including the limbus, and a larger field of view at the expense of resolution. Although AS-OCT does not offer the same degree of resolution at the cellular level as IVCM does, AS-OCT may prove useful in measuring epithelial thickness and pannus depth, assessing palisades of Vogt, limbal crypts, and the clear transition between the hyporeflexive corneal epithelium and hyperreflective conjunctival epithelium in the limbal region.

V. Staging

LSCD can be categorized into 3 stages based on the extent of corneal and limbal involvement detected by clinical examination, as illustrated in Figure 1. Staging of LSCD is important to guide therapeutic recommendations and surgical planning. The most important factors to be considered are whether the visual axis or central 5 mm of cornea is affected (stages II and III) and whether more than 50% of the LSCs are intact. The final stage (stage III) involves total LSCD, where the whole corneal surface is affected. Abnormalities of other components of the ocular surface, such as the conjunctiva, meibomian glands, lacrimal glands, tears, corneal nerves, and immune system, are important in the management of LSCD and will be addressed in a separate document on the global consensus of the treatment of LSCD.

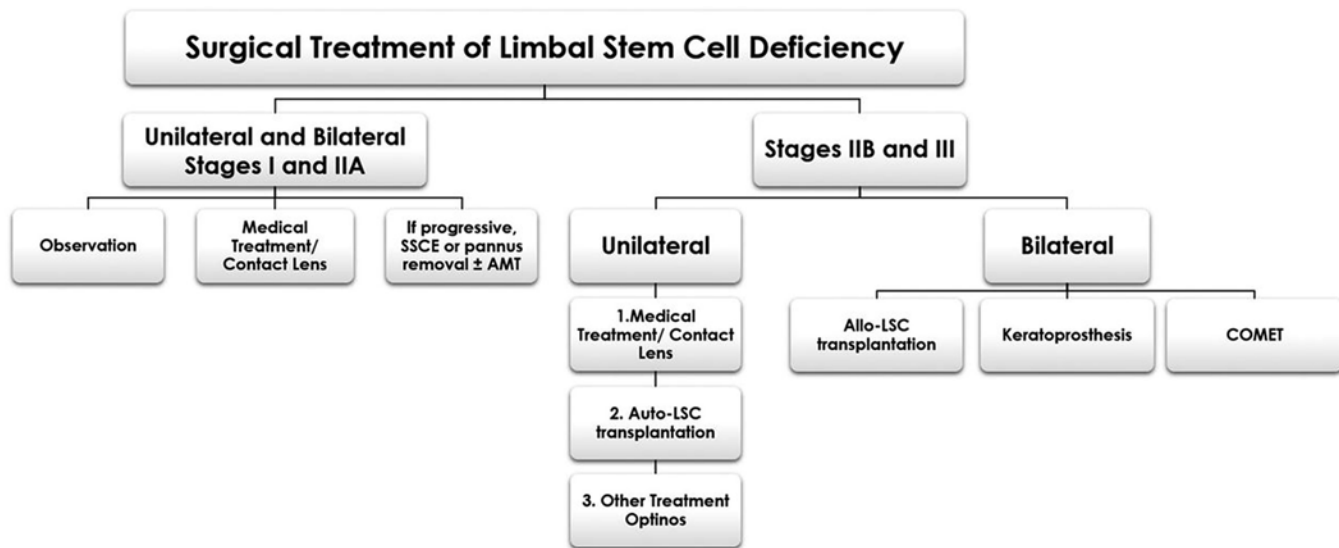


Figure 2

VI. Therapy

Treatment of LSCD is challenging and should be selected according to the stage of the disease (Figure 2). There is no medical treatment to replenish absent or lost stem cells. However, LSCD is often complicated by ocular comorbidities that impair function of residual stem cells. Thus treatment of comorbidities may significantly improve LSCD by optimizing the ocular surface by a comprehensive step-by-step approach including the following:

- Eyelid and conjunctival reconstruction, possibly including lysis of symblephara or tarsorrhaphy
- Anti-inflammatory treatment to eliminate toxic effects as well as nerve damage by systemic immune modulators, and/or topical cyclosporine, tacrolimus, lifitegrast, or steroids
- Optimization of the tear film by preservative-free lubrication, punctal occlusion, and blood-based eye drops such as autologous serum, as well as comprehensive treatment of meibomian gland disease
- Optimization of the ocular surface epithelium with retinoid acid, nerve growth factor, and therapeutic contact lenses

The selection of the best form of surgical treatment should be selected on the basis of the stage of the disease and laterality (see Figures 1 and 2), and the reader is referred to the consensus report by Deng et al for details.¹

For unilateral or bilateral stages I and IIA, residual LSCs can be used to repopulate areas in which conjunctivalized epithelium has been removed by sequential sectorial conjunctival epitheliectomy or by transplantation of amniotic membrane.

Surgical treatment for stages IIB and II depends on laterality and is summarized in Figure 2.

For unilateral LSCD stages IIB and III, autologous limbal transplantation has been described either by conjunctival limbal autograft (CLAU), ex vivo cultivated LSCs, or more recently by the simple limbal epithelial transplantation (SLET).

Advanced stages of bilateral LSCD are among the most challenging diseases in ophthalmology. Allogenic CLAU either alone or in the context of a comprehensive ocular surface reconstruction (Cincinnati procedure) can be performed with subsequent immunosuppression. Alternatively, grafts composed of ex vivo expanded allogenic LSCs or cultivated oral mucosa (COMET) have been used. Keratoprosthesis—namely, Boston KPro—eliminates the risk associated with systemic immunosuppression and has proven to be a valuable alternative to tissue-based strategies to treat advanced stages of LSCD.

Selected Readings

1. Deng SX, Kruse F, Gomes JAP, et al; the International Limbal Stem Cell Deficiency Working Group. Global consensus on the management of limbal stem cell deficiency. *Cornea* 2020; 39:1291-1302.
2. Biber JM, Skeens HM, Neff KD, et al. The Cincinnati procedure: technique and outcomes of combined living-related conjunctival limbal allografts and keratolimbal allografts in severe ocular surface failure. *Cornea* 2011; 30:765-771.
3. Deng SX, Borderie V, Chan CC, et al. Global consensus on definition, classification, diagnosis, and staging of limbal stem cell deficiency. *Cornea* 2019; 38:364-375.
4. Dua HS. Sequential sector conjunctival epitheliectomy (SSCE). In: Holland EJ, Mannis MJ, eds. *Ocular Surface Disease: Medical and Surgical Management*. New York, NY: Springer; 2002:168-174.

5. Kenyon KR, Tseng SC. Limbal autograft transplantation for ocular surface disorders. *Ophthalmology* 1989; 96:709-722; discussion, 722-723.
6. Le Q, Xu J, Deng SX. The diagnosis of limbal stem cell deficiency. *Ocul Surf*. 2018; 16:58-69.
7. Le Q, Yang Y, Deng SX, et al. Correlation between the existence of the palisades of Vogt and limbal epithelial thickness in limbal stem cell deficiency. *Clin Exp Ophthalmol*. 2017; 45:224-231.
8. Nishida K, Yamato M, Hayashida Y, et al. Corneal reconstruction with tissue-engineered cell sheets composed of autologous oral mucosal epithelium. *N Engl J Med*. 2004; 351:1187-1196.
9. Rama P, Matuska S, Paganoni G, et al. Limbal stem-cell therapy and long-term corneal regeneration. *N Engl J Med*. 2010; 363:147-155.
10. Sangwan VS, Basu S, MacNeil S, et al. Simple limbal epithelial transplantation (SLET): a novel surgical technique for the treatment of unilateral limbal stem cell deficiency. *Br J Ophthalmol*. 2012; 96:931-934.
11. Sejpal K, Yu F, Aldave AJ. The Boston keratoprosthesis in the management of corneal limbal stem cell deficiency. *Cornea* 2011; 30:1187-1194.

Pterygium Surgery Complications and Management

Allan R Slomovic MD FRCSC MSc

Complications associated with pterygium surgery are uncommon but can occur preoperatively (ie, in the planning stages), intraoperatively, and postoperatively. This talk will focus on the major complications that can occur during any of these 3 phases of the surgery and will address management principles.

I. Preoperative Complications

Potential complications are best avoided by careful preoperative planning. In this section, we will discuss the following 2 scenarios:

A. Pterygium and cataract

It is important to understand the effect that a pterygium has on corneal topography and higher-order aberrations (HOAs). Pterygia result in flattening of the cornea in the area of the pterygium, resulting in with-the-rule astigmatism. They also will result in an increase in HOAs. Both of these factors are significantly improved after successful pterygium surgery. Examples will be given.

Take-home message: When faced with a patient with both a pterygium and a cataract, the appropriate management is to perform a pterygium excision with a conjunctival autograft first and then wait until keratometry and corneal topography are stable, usually 2-3 months, before proceeding with biometry and cataract surgery. This is especially relevant with new technology IOLs.

B. Misdiagnosis: The 3 most common mistakes in this category:

1. Ocular surface squamous neoplasia (OSSN):

OSSN can masquerade as a primary pterygium. The rate of OSSN has been reported to be as high as 10% of pterygium specimens.

Take-home message: This rate of unsuspected OSSN suggests that all pterygium specimens should be submitted for histopathologic examination.^{1,2}

2. Pseudopterygia:

There frequently is significant corneal thinning under the area of the pseudopterygium, as may occur in Terrien marginal corneal degeneration or from prior mechanical or chemical trauma. Removal of the pterygium in these cases may result in progressive corneal thinning and even perforation. Careful history, slit-lamp examination, and preoperative corneal OCT may help to identify these patients preoperatively.³

3. Unsuspected recurrent pterygium:

Recurrent pterygium is frequently more aggressive and associated with a higher incidence of recurrence. Patients may forget that they had prior surgery. Meticulous attention to ocular history and careful slit-lamp exam often reveals signs of prior surgery. We have reported excellent outcomes on recurrent pterygium using a combination of mitomycin C 0.02% for 2 minutes combined with a conjunctival autograft, using tissue glue to adhere the conjunctival autograft. Our recurrence rate was 3.5%.⁴

II. Intraoperative Complications

The most common complications:

A. Inadvertently cutting the medial rectus muscle:

This is more likely to occur in recurrent pterygium surgery where there is significantly more scar tissue and can result in excess bleeding, and if the muscle is transected this can result in postoperative diplopia, requiring further surgery to reattach the muscle.

Take-home message: Understanding that the medial rectus muscle inserts 5.5 mm from the limbus and identifying the muscle with a muscle hook intraoperatively, especially where there is significant scar tissue, will help to prevent this complication.⁵

B. Removing more of the pterygium than expected:

Once the pterygium and the subconjunctival scar tissue have been removed, the area of the bare scleral bed is frequently larger than expected. This is especially true in fleshy, thick pterygia, where there is significant subconjunctival connective tissue. Complications here also include excision of the caruncular tissue, which can result in significant scarring.

Take-home message: Mark the conjunctival area of the pterygium to be excised prior to the start of the surgery when all the landmarks are clearly visible and can be easily identified. This is especially useful for ophthalmologists just starting to perform pterygium surgery.

C. Inadequately sized conjunctival autografts and inadvertently turning the conjunctival autograft upside-down:

Prior to dissecting the conjunctival autograft, the bare scleral bed should be measured with calipers. Using these measurements, the appropriately sized conjunctival autograft should be marked with a

surgical marking pen. We have shown that superior and inferior grafts (for those patients with a history of glaucoma who might require future glaucoma surgery) are equally effective.

Take-home message: We recommend marking the conjunctival graft with a surgical marking pen and, when dissecting the graft, staying outside (and including within the graft) the surgical markings. The free conjunctival graft can easily become inverted during surgery. However, having these markings on the graft allows the surgeon to determine the graft's orientation. Also, including the markings allows for a slightly larger graft to cover the bare sclera.

III. Postoperative Complications

A. Recurrence:

Recurrence of the pterygium following excision is the most common postoperative complication. The gold standard for 2021 is a pterygium excision with a conjunctival autotransplant, with recurrence rates in the range of 3% to 10%. We and others have shown that the use of fibrin glue to adhere the conjunctival autograft reduces surgical time and the patient's experience of pain and is also associated with less postoperative inflammation. Reduced postoperative inflammation may be associated with a reduced recurrence rate.^{6,7}

Recurrent pterygium is frequently more aggressive than primary pterygia and has a higher recurrence rate. We have shown that pterygium excision with a conjunctival autograft and mitomycin C 0.02% for 2 minutes placed under the excised conjunctival portion of the pterygium was a safe and effective means for treating recurrent pterygium, with a recurrence rate of only 3.5%. However, we also showed that the use of mitomycin C 0.02%, even when placed under the conjunctiva, was still associated with a 4% reduction of endothelial cells at 3 months postoperatively ($P = .08$) when compared with a control group that did not use mitomycin C.⁸ We also showed that for recurrent pterygium or double-headed pterygium, simple limbal epithelial transplantation can also be an effective surgical procedure.⁹

B. Slippage:

A possible complication that can occur following the use of fibrin glue to adhere the conjunctival autograft is slippage of the graft, despite informing the patient not to rub the eye postoperatively. We have shown that this can be effectively repaired by bringing the patient back to the treatment room and unravelling the conjunctival autograft on top of a bed of fibrin glue. However, in this situation anchoring sutures to keep the graft in place should be considered.¹⁰

C. Other, less frequent complications that can occur postoperatively

1. An avascular graft: These grafts should be removed, as they may serve as a nidus for postoperative infection.
2. Dellen formation may also occur and is more common with postoperative chemosis. Dellen formation can be managed by either copious lubrication or patching.
3. Pyogenic granulomas may form in the area where the conjunctival graft has been harvested. These granulomas are a sign of inflammation and should be managed by frequent topical steroid application and in some instances may need to be surgically excised along with the steroid treatment.

In summary, complications associated with pterygium surgery are uncommon and may be divided into preoperative planning considerations and complications that can occur intraoperatively or postoperatively. Careful attention to the management principles discussed above will lead to excellent functional and cosmetic results.

References

1. Hirst LW, Axelsen RA, Schwab I. Pterygium and associated ocular surface squamous neoplasia. *Arch Ophthalmol.* 2009; 127(1):31-32.
2. Yeung SN, Kim P, Lichtinger A, et al. Incidence of ocular surface squamous neoplasia in pterygium specimens: an 8-year survey. *Br J Ophthalmol.* 2011; 95(4):592.
3. Chan AT, Ulate R, Goldich Y, Rootman DS, Chan CC. Terrien marginal degeneration: clinical characteristics and outcomes. *Am J Ophthalmol.* 2015; 160(5):867-872.e1.
4. Shehadeh-Mashor R, Srinivasan S, Boimer C, Lee K, Tomkins O, Slomovic AR. Management of recurrent pterygium with intraoperative mitomycin C and conjunctival autograft with fibrin glue. *Am J Ophthalmol.* 2011; 152(5):730-732.
5. Sen P, Kumar A, Jain E, Mohan A. Slipped medial rectus muscle with stretched scar after pterygium surgery. *J Pediatr Ophthalmol Strabismus.* 2019; 56:e34-e37.
6. Srinivasan S, Dollin M, McAllum P, Berger Y, Rootman DS, Slomovic AR. Fibrin glue versus sutures for attaching the conjunctival autograft in pterygium surgery: a prospective observer masked clinical trial. *Br J Ophthalmol.* 2009; 93(2):215-218.
7. Ratnalingam V, Eu AL, Ng GL, Taharin R, John E. Fibrin adhesive is better than sutures in pterygium surgery. *Cornea* 2010; 29(5):485-489.
8. Bahar I, Kaiserman I, Lange AP, et al. The effect of mitomycin C on corneal endothelium in pterygium surgery. *Am J Ophthalmol.* 2009; 147(3):447-452.e1.
9. Trinh T, Mimouni M, Mednick Z, et al. Outcomes of ipsilateral simple limbal epithelial transplantation, tenonectomy, mitomycin and amniotic membrane transplantation for treatment of recurrent pterygium. *Cornea* 2021; 40(1):43-47.
10. Srinivasan S, Slomovic AR. Eye rubbing causing conjunctival graft dehiscence following pterygium surgery with fibrin glue. *Eye (Lond).* 2007; 21(6):865-867.

Management of Autoimmune-Mediated Keratolysis

Kimberly C Sippel MD

I. Background

A. First, a set of definitions:

1. *Persistent epithelial defect (PED)* = an epithelial defect in which epithelialization is not progressing at a normal rate.
2. *Sterile corneal ulcer* = a PED with associated loss of stromal corneal tissue (and no evidence of infection).
3. *Corneal thinning without an epithelial defect* (eg, dellen, healed corneal ulcer) = no epithelial defect present.

B. Both a PED and a corneal ulcer require urgent attention.

In the absence of corneal epithelium, proteases in the tear film have access to the stroma; *keratolysis* (“melting”) then occurs, which can ultimately lead to perforation. The goal is to attain epithelialization of the defect; keratolysis will usually cease at that point.

II. How do autoimmune diseases → keratolysis?

A. By direct autoimmune-mediated means.

For example, the vasculitis-associated autoimmune conditions (rheumatoid arthritis, granulomatosis with polyangiitis [Wegener’s], relapsing polychondritis, etc.) may lead to peripheral ulcerative keratitis through immune complex deposition at the limbus and subsequent production of proteolytic enzymes, etc.

B. By indirect means.

For example, if an autoimmune condition results in limbal stem cell destruction (eg, Stevens-Johnson syndrome) and/or end-stage dry eye (eg, graft-versus-host disease), PEDs may ensue. Proteolytic enzymes in the tear film then have access to the stromal tissue, with keratolysis and sterile ulcer formation ensuing.

A systematic approach to treatment is needed.

III. First, infection needs to be ruled out.

A. An *infiltrate* is typically evident in infectious situations.

1. However, this is not always the case. Herpetic keratitis and *Acanthamoeba* keratitis may present without an obvious infiltrate.
2. Beware of fungal colonization/ keratitis. This is common in patients treated with long-term topical corticosteroids and topical antibiotics, the

latter serving to alter the normal ocular surface flora. Fungal colonization/keratitis may manifest simply as chalky deposits on the corneal surface in a fairly uninflamed eye.

B. Even if there is no evidence of infection, prophylactic antibiotic coverage is needed in the case of a PED/sterile ulcer.

IV. Second, treat any associated active autoimmune condition aggressively. This is *critical*.

A. The autoimmune process needs to be brought under optimal control as quickly as possible before much headway can be made in achieving control of the keratolytic process.

B. Good communication with a rheumatologist is key! A patient may appear to the rheumatologist to be well controlled, yet if autoimmune-mediated keratolysis is present, the rheumatologist needs to be informed that the condition is not under optimal control and that higher levels of immunomodulatory treatment are needed.

C. Be aware that most immunomodulatory agents take weeks to start working. The patient may therefore initially need to be treated with oral prednisone or intravenous methylprednisolone to bring about quick control, which will buy time until other, more long-term agents have become fully active.

V. First-Line Medical Interventions (applicable to all PEDs and corneal ulcers, whether autoimmune-related or not)

A. Address ocular surface desiccation: exogenous lubrication (including gels and ointments), punctal plugs, topical cyclosporine, autologous serum tears, etc.

B. Address blepharitis/meibomian gland dysfunction: warm compresses/lid hygiene, oral doxycycline or minocycline, Demodex treatment, etc.

C. Address medicamentosa: Minimize use of preserved medications.

D. Avoid use of topical nonsteroidal anti-inflammatory medications (NSAIDs): Most NSAIDs have been linked to the risk of keratolysis.

E. Consider oral ascorbate supplementation: Vitamin C is a cofactor in collagen synthesis.

F. Consider oral or topical metalloproteinase inhibitors (eg, oral doxycycline).

G. Fox shield (to minimize inadvertent eye rubbing)

H. Judicious use of a mild topical corticosteroid: Inflammation has a negative effect on the epithelialization process, and hence a mild topical steroid may have a positive effect in this regard. However, exercise caution since steroids have a negative effect on collagen synthesis and hence may exacerbate the keratolytic process.

1. Recommend starting with a low-potency steroid such as loteprednol and monitor very closely.
2. Do not use if marked thinning/descemetocoele is present.

I. Address, as best as possible, mechanical trauma from diseased eyelids (eg, misdirected eyelashes, keratinized lid margins, tarsal conjunctival scarring).

1. Misdirected lashes may be removed by forceps or electroepilation.
2. Keratinized lid margins and tarsal conjunctival scarring may require significantly more involved surgical interventions, such as mucous membrane grafting.

VI. Second-Tier Interventions

A. Bandage contact lens (BCL):

BCLs are highly effective in treating PEDs/sterile ulcers, but they do require some tear production to remain hydrated and fairly normal eyelid and conjunctival anatomy to remain in position. Large-diameter BCLs (eg, Kontur lenses, Kontur Kontakt Lens; Hercules, CA) are often useful. Only a subset of contact lenses are FDA approved for use as BCLs, but many are used off-label for this purpose.

B. Lateral tarsorrhaphy:

The extent of the lateral tarsorrhaphy is determined by the degree of corneal coverage needed. A lateral tarsorrhaphy can be performed utilizing sutures or cyanoacrylate glue (in which the eyelashes are glued together). Botulinum toxin can also be used to effect temporary lid closure. The technique of using tape to “splint” the upper eyelid will be presented.

VII. Third-Tier Interventions

A. Amniotic membrane:

Amniotic membrane is believed to facilitate epithelialization and decrease inflammation. It has minimal tectonic strength and should be considered a “biological” dressing, not a corneal stromal substitute.

1. Both cryopreserved and dehydrated versions are available. Cryopreserved amniotic membrane needs to be stored refrigerated or frozen, while dehydrated can be stored at room temperature.
2. Certain amniotic membrane products are designed to be readily placed in the office. This includes the Prokera device (BioTissue; Miami FL), which consists of a sheet of cryopreserved amniotic membrane mounted in a symblepha-

ron-style ring, and placement is akin to that of a BCL. Fluorescein to assess for an epithelial device can be used without removal of the device. Discs of dehydrated amniotic membrane (eg, AmbioDisk, Katena; Parsippany, NJ) can also be placed in the office; they are rehydrated, placed on the cornea, and then covered with a BCL.

3. Sheets of amniotic membrane—again available in a cryopreserved version (Amniograft, BioTissue), as well as a dehydrated version (eg, Ambio2 and Ambio5, Katena)—are used when large areas of the ocular surface need to be covered. Sutures are usually used to secure the amniotic membrane; use of fibrin sealants (Tisseel, Baxter or Vistaseal, Ethicon/ J&J; Bridgewater, NJ) has also been described (off-label for ophthalmic use), although it should be noted that fibrin sealants do not adhere well to areas of intact corneal or conjunctival epithelium. Sutured or glued amniotic membrane will still usually need to be covered by a BCL (or a generous lateral tarsorrhaphy) to properly stay in place.

One indication for use of amniotic membrane is acute Stevens-Johnson syndrome/toxic epidermal necrolysis, the hallmark of which is the extensive sloughing of the conjunctival and corneal epithelium.

B. Continuous wear of a scleral lens:

Specialized rigid gas-permeable scleral lenses that have a reservoir of fluid under the lens to provide the corneal surface with a “liquid BCL” and, unlike standard BCLs, can be used when the ocular surface is markedly desiccated or the corneal curvature is highly ectatic. These lenses are FDA approved only for day-time use, but they can be used “off-label” 24-hours per day to heal a PED/sterile corneal ulcer. (Note: The reservoir still needs to be changed daily.) Examples of this type of lens include the BostonSight PROSE device (Boston Foundation for Sight; Needham MA).

C. Other:

1. In cases in which a neurotrophic (decreased corneal sensation) component is present, consideration may be given to nerve growth factor treatment (cenegermin, Oxervate, Dompé; Milan, Italy).
2. Bevacizumab (Avastin, Genentech; South San Francisco, CA) has been used in an off-label fashion to treat corneal neovascularization, since corneal blood vessels are a source of inflammatory cells and mediators. However, bevacizumab treatment itself has been associated with development of PEDs and keratolysis, and therefore use must be approached with care in this setting.

3. Conjunctival recession/resection in the setting of, specifically, peripheral ulcerative keratitis has been used to removed inflamed conjunctiva with its associated blood vessels and inflammatory cells and mediators away from the area of keratolysis, and it is still used in select circumstances. However, appropriate systemic immunomodulatory treatment is currently deemed to be the mainstay for achieving optimal control of autoimmune-mediated inflammation.
4. Limbal stem cell deficiency is diagnosed on the basis of clinical history, slit lamp appearance (delayed fluorescein staining in a “whorl-like” pattern), and impression cytology (which assesses for presence of goblet cells suggestive of the presence of conjunctival epithelium instead of corneal epithelium on the cornea). If several clock hours of limbal stem cell function are present, the cornea will still be able to epithelialize properly. However, if complete destruction of all limbal stem cells has occurred, limbal stem cell transplantation is needed.

Bilateral total limbal stem cell deficiency requires limbal stem cell *allografting* (ie, from a living donor or eye bank tissue), as opposed to *autografting* (ie, from one eye to the other in the same patient). This in turn requires systemic immunosuppression, given the high risk of rejection of a limbal stem cell allograft.

VIII. Treatment of Micro- and Macroperforations

- A. If the perforation is a pinpoint, it may heal spontaneously with the use of:
 1. Topical aqueous suppressants (such as timolol)
 2. A tight-fitting BCL
 3. Pressure patching
 4. Withdrawal of topical corticosteroid drops
- B. Microperforation
 1. Topical corticosteroids need to immediately be placed on hold.
 2. Application of a cyanoacrylate-based glue constitutes the classic treatment. Only descemetocelles or microperforations (<1 mm) lend themselves to use of cyanoacrylate-based glue. Cyanoacrylate-based glue requires a dry bed (otherwise it polymerizes too quickly), and a large perforation will leak aqueous at too rapid a rate. Circular pieces of plastic drape fashioned with the use of skin biopsy punches can be used to facilitate application (see also Selected Readings). A BCL (typically a thicker lens such as a Kontur lens) is applied after glue application since the glue is very rough and cannot be tolerated/will dislodge if not covered. The cyanoacrylate-based glue eventually sloughs, often leaving behind a thin and irregular, but tectonically stable, cornea. However, in the case of a central corneal perforation, a penetrating keratoplasty

may be needed at a later time to effect visual rehabilitation.

Currently the only cyanoacrylate-based glues available in the United States are FDA approved only for dermatologic use (eg, Dermabond, Ethicon/J&J; Bridgewater, NJ); hence, use of cyanoacrylate glue is considered off-label for ophthalmic purposes.

3. Amniotic membrane application (applied as multiple layers or in a pleated fashion) has also been described in the setting of descemetocelles or microperforations (see Selected Readings for technique). However, again, amniotic membrane itself only offers minimal tectonic strength.

C. Macroperforation

1. Treated with patch or full-size penetrating keratoplasty. Lamellar (partial-thickness) grafting is also an option, but can be more technically challenging.
 - a. Patch grafting is performed using smaller trephines; most trephines, such as the Beaver trephine blades (Beaver-Visitec; Waltham, MA), are available in sizes as small as 4 mm.
 - b. If the far periphery and/or limbus is involved, a full-thickness or lamellar graft hand-fashioned into the shape of a crescent may be used (see Selected Readings).
2. In addition to fresh corneal tissue, irradiated corneal tissue is now also an option. Irradiated corneal tissue does not possess viable endothelial cells, but it can be used for tectonic purposes. It is available as full-thickness but also as split-thickness tissue, as well as in different shapes. It can be stored at room temperature for 2 years and does not require reconstitution (in contrast to glycerin-preserved corneal tissue).

Irradiated corneal tissue available in the United States includes VisionGraft (CorneaGen; Seattle, WA) and Halo Sterile Allografts (Eversight; Ann Harbor, MI).

Selected Readings

1. Ciralsky JB, Chapman KO, Rosenblatt MI, et al. Treatment of refractory persistent corneal epithelial defects: a standardized approach using continuous wear PROSE Therapy. *Ocul Immunol Inflamm.* 2015; 23:219.
2. Deshmukh R, Stevenson LJ, Vajpayee RB. Techniques of non-circular corneal transplantation. *Curr Opin Ophthalmol.* 2020; 31:293.
3. Gandhewar J, Savant V, Prydal J, Dua H. Double drape tectonic patch with cyanoacrylate glue in the management of corneal perforation with iris incarceration. *Cornea* 2013; 32:e137.
4. Gregory DG. New grading system and treatment guidelines for the acute ocular manifestations of Stevens-Johnson syndrome. *Ophthalmology* 2016; 123:1653.

5. Holland EJ. Management of limbal stem cell deficiency: a historical perspective, past, present, and future. *Cornea* 2015; 10:S9-15.
6. Jhanji V, Young AL, Mehta JS, et al. Management of corneal perforation. *Surv Ophthalmol*. 2011; 56:522.
7. Ma KN, Thanos A, Chodosh J. A novel technique of amniotic membrane transplantation in patients with acute Stevens-Johnson syndrome. *Ocular Surf*. 2016; 14:31.
8. Namba H, Narumi M, Nishi K, et al. "Pleats fold" technique of amniotic membrane transplantation for management of corneal perforations. *Cornea* 2014; 33:653.
9. Tuli SS, Schultz GS, Downer DM. Science and strategy for preventing and managing corneal ulceration. *Ocul Surf*. 2007; 4:23.
10. Utine CA, Tzu JH, Akpek EK. Lamellar keratoplasty using gamma-irradiated corneal lenticules. *Am J Ophthalmol*. 2011; 151:170.

Forniceal and Conjunctival Reconstruction

Clara C Chan MD

- I. Why is the conjunctiva important?
 - A. Allows for monitoring of inflammation
 - B. Hallmark of the tissue is presence of goblet cells that form mucin layer of tear film.
- II. Sequelae of Conjunctival Deficiency
 - A. Decrease in goblet cell density and mucin deficiency
 - B. Symblephara formation
 - C. Shortening/loss of fornices
 - D. Limbal stem cell deficiency
 - E. Squamous metaplasia
 - F. Surface keratinization (end stage)
- III. Etiologies for Conjunctival Deficiency
 - A. Inflammation: atopy, rosacea, post-peripheral ulcerative keratitis, Stevens-Johnson syndrome (SJS), graft versus host disease, mucous membrane pemphigoid, glaucoma drop toxicity
 - B. Trauma: chemical, thermal injury, iatrogenic (mitomycin C), radiation, large ocular surface squamous neoplasia resection
 - C. Postinfectious scarring (trachoma)
- IV. Step 1 in the Stepwise Approach to Ocular Surface Reconstruction¹
 - A. Tip: Place fresh frozen amnion across all ocular mucosal surfaces asap after chemical/thermal injury, SJS to prevent conjunctival scarring, symblepharon, fornix shortening, lid margin keratinization.
 - B. Technique video (<https://www.youtube.com/watch?v=iYLiiSKqGU> – starting at 55:45)
 - C. Materials for conjunctival and fornix reconstruction
 1. Conjunctival autograft
 2. Amniotic membrane (fresh frozen, dehydrated, cryopreserved)
 3. Buccal (inner cheek)/labial (lip) mucosa
 4. Conjunctival allograft (living donor)
 5. Keratolimbal allograft (deceased donor)
 - D. Video links:
 1. Technique to recover buccal mucosa: <https://webeye.ophth.uiowa.edu/eyeforum/video/plastics/2/Mucous-membrane-harvest.htm>
 2. Technique to recover labial mucosa for lid margin reconstruction: <https://youtu.be/Rq108WCLyDo> (starting at 19:50)

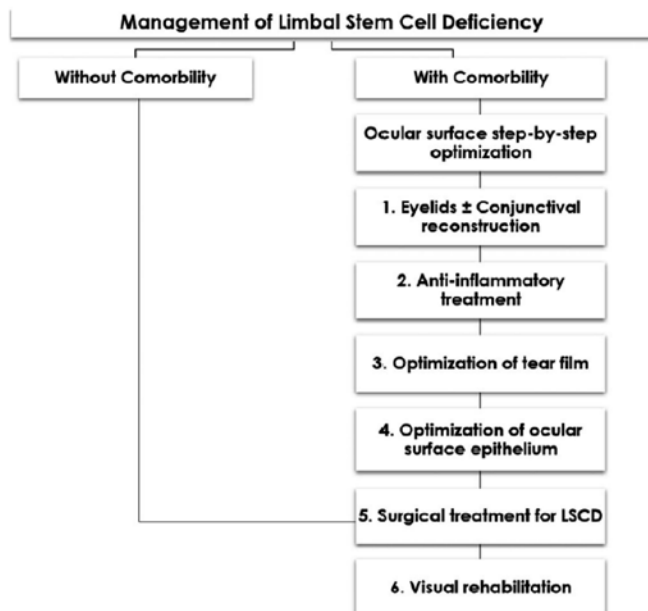


Figure 1. Steps for the optimization of the ocular surface before surgical treatment of LSCD.

Reference and Selected Readings

1. Deng SX, Kruse F, Gomes JAP, et al.; International Limbal Stem Cell Deficiency Working Group. Global consensus on the management of limbal stem cell deficiency. *Cornea* 2020; 39(10):1291-1302.
2. Biber JM, Skeens HM, Neff KD, Holland EJ. The Cincinnati procedure: technique and outcomes of combined living-related conjunctival limbal allografts and keratolimbal allografts in severe ocular surface failure. *Cornea* 2011; 30(7):765-771.
3. Chan CC, Biber JM, Holland EJ. The modified Cincinnati procedure: combined conjunctival limbal autografts and keratolimbal allografts for severe unilateral ocular surface failure. *Cornea* 2012; 31(11):1264-1272.
4. Farid M, Lee N. Ocular surface reconstruction with keratolimbal allograft for the treatment of severe or recurrent symblepharon. *Cornea* 2015; 34(6):632-636.
5. Einan-Lifshitz A, Belkin A, Mathew D, et al. Repair of exposed Ahmed Glaucoma Valve tubes: long-term outcomes. *J Glaucoma*. 2018; 27(6):532-536.
6. Ziai S, Rootman DS, Slomovic AR, Chan CC. Oral buccal mucous membrane allograft with a corneal lamellar graft for the repair of Boston type 1 keratoprosthesis stromal melts. *Cornea* 2013; 32(11):1516-1519.
7. Nordlund ML, Holland EJ, Kersten RC. Ocular surface reconstruction in a patient with complete ankyloblepharon resulting from Stevens-Johnson syndrome. *Arch Ophthalmol*. 2004; 122(6):934-935.

Case Presentation: Difficult Ocular Surface Reconstruction

The Battle Is Not Lost . . . Yet!

Swapna Shanbhag MBBS

A case of a patient who underwent surgical interventions both in the acute and the chronic phases of ocular chemical burn will be presented. A young child presented with an acute unilateral ocular chemical burn with cement particles in the eye. An amniotic membrane transplantation with removal of all foreign body particles from the ocular surface was performed. Over the course of the next 2 months, the patient developed total limbal stem cell deficiency (LSCD) with symblepharon in 2 quadrants in the operated eye. An ocular surface reconstruction was planned 3 months after the acute burn to reduce the risk of amblyopia. Simple limbal epithelial transplantation (SLET) with simultaneous conjunctival autografts was performed. The limbal biopsy and the conjunctival grafts were harvested from the contralateral healthy eye. At 2 years of follow-up post the ocular surface reconstruction, the patient's BCVA was 20/30, with a completely epithelized ocular surface with a clear cornea and no recurrence of symblepharon. The contralateral eye was healthy, and no iatrogenic LSCD was noted.

SLET, a form of limbal stem cell transplantation, is a safe and effective surgical procedure for addressing total LSCD. Addressing symblephara simultaneously during limbal stem cell transplantation reduces the need for multiple surgical interventions and aids in faster visual rehabilitation.

Selected Readings

1. Sangwan VS, Basu S, MacNeil S, Balasubramanian D. Simple limbal epithelial transplantation (SLET): a novel surgical technique for the treatment of unilateral limbal stem cell deficiency. *Br J Ophthalmol*. 2012; 96:931-934.
2. Basu S, Sureka SP, Shanbhag SS, Kethiri AR, Singh V, Sangwan VS. Simple limbal epithelial transplantation: long-term clinical outcomes in 125 cases of unilateral chronic ocular surface burns. *Ophthalmology* 2016; 123:1000-1010.
3. Shanbhag SS, Nikpoor N, Rao Donthineni P, Singh V, Chodosh J, Basu S. Autologous limbal stem cell transplantation: a systematic review of clinical outcomes with different surgical techniques. *Br J Ophthalmol*. 2020; 104:247-253.
4. Shanbhag SS, Patel CN, Goyal R, Donthineni PR, Singh V, Basu S. Simple limbal epithelial transplantation (SLET): review of indications, surgical technique, mechanism, outcomes, limitations, and impact. *Indian J Ophthalmol*. 2019; 67:1265-1277.
5. Thokala P, Singh A, Singh VK, et al. Economic, clinical and social impact of simple limbal epithelial transplantation for limbal stem cell deficiency. *Br J Ophthalmol*. Epub ahead of print 2021 Mar 9. doi: 10.1136/bjophthalmol-2020-318642.

Therapeutic Scleral Contact Lenses

Alejandro Navas MD, Norma Morales Flores, MD, Omar Santana-Cruz OD, Eduardo J Polanía-Baron MD, Natalia Quiroz-Casian MD, and Enrique O Graue-Hernández MD MSc

- I. History
 - II. Materials
 - III. Fitting
 - IV. Advantages and Disadvantages
 - V. Indications
 - A. Vision improvement
 - 1. Corneal ectasias
 - 2. Post–penetrating keratoplasty
 - 3. Post–refractive surgery
 - B. Ocular surface protection
 - 1. Stevens-Johnson syndrome
 - 2. Cicatrizing ocular pemphigoid
 - 3. Chemical burns
 - 4. Acne rosacea
 - 5. Sjögren syndrome
 - 6. Nonspecific dry eye
 - C. Cosmetics
 - 1. Ptosis
 - 2. Painted scleral lenses
 - VI. Novel Uses
 - A. Drug delivery
 - B. Crosslinking
 - C. Keratitis
 - VII. Future Directions
 - A. Reservoir
 - B. Technological advances
7. Exposure keratitis
8. Epithelial defects
9. Neurotrophic keratitis
10. Corneal dystrophies
11. Others

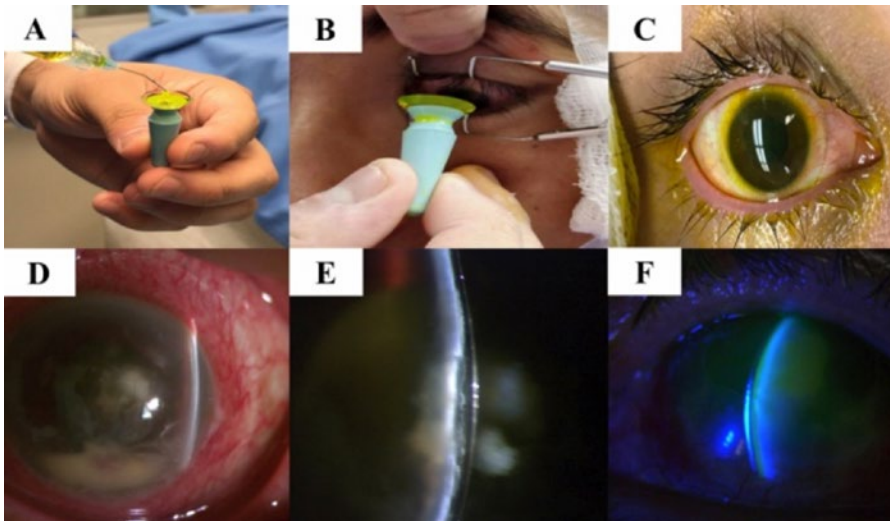


Figure 1. (A) Riboflavin into the scleral lens. (B) Scleral lens fitting. (C) Scleral lens for impregnation previous corneal collagen crosslinking. (D) Scleral support evidence as a reservoir for antibiotic in infectious keratitis. (E) Slit-lamp photograph showing around 300-micron vault, filled with antibiotic. (F) Fluorescein staining showing fluid reservoir.

Selected Readings

1. Pullum K, Buckley R. Therapeutic and ocular surface indications for scleral contact lenses. *Ocul Surf*. 2007; 5(1):40-49.
2. Dimit R, Gire A, Pflugfelder SC, Bergmanson JPG. Patient ocular conditions and clinical outcomes using a PROSE scleral device. *Cont Lens Anterior Eye*. 2013; 36(4):159-163.
3. Vincent SJ, Fadel D. Optical considerations for scleral contact lenses: a review. *Cont Lens Anterior Eye*. 2019; 42(6):598-613.
4. Rosenthal P, Cotter JM, Baum J. Treatment of persistent corneal epithelial defect with extended wear of a fluid-ventilated gas-permeable scleral contact lens. *Am J Ophthalmol*. 2000; 130(1):33-41.
5. Katsoulos K, Livir Rallatos G, Mavrikakis I. Scleral contact lenses for the management of complicated ptosis. *Orbit* 2018; 37(3):201-207.
6. Schornack MM, Pyle J, Patel SV. Scleral lenses in the management of ocular surface disease. *Ophthalmology* 2014; 121(7):1398-1405.
7. Harthan JS, Shorter E. Therapeutic uses of scleral contact lenses for ocular surface disease: patient selection and special considerations. *Clin Optom (Auckl)*. 2018; 10:65-74.
8. Lim L, Lim EW. Therapeutic contact lenses in the treatment of corneal and ocular surface diseases—a review. *Asia-Pac J Ophthalmol*. 2020; 9(6):524-532.
9. Polania-Baron EJ, Santana-Cruz O, Lichtinger A, Graue-Hernandez EO, Navas A. Treatment of severe infectious keratitis with scleral contact lenses as a reservoir of moxifloxacin 0.5. *Cornea* 2021; 40(7):831-836.

Smite the Mite! Novel Blepharitis Treatments

Christine Shieh MD

I. Introduction

Blepharitis is characterized by eyelid margin inflammation. While there are different classification systems, blepharitis is popularly defined by anatomic location.¹

A. Anterior blepharitis affects eyelid skin, base of eyelashes, eyelash follicles.¹ Often further subclassified into:

1. Staphylococcal¹

- a. Signs: scaling, crusting, and erythema of eyelid margin with collarettes
- b. May involve acute exacerbations that lead to ulcerative blepharitis and corneal involvement (eg, marginal infiltrates, cornea neovascularization)

2. Seborrheic¹

- a. Signs: greasy scaling of anterior eyelid
- b. Association with seborrheic dermatitis of the eyebrows and scalp

B. Posterior blepharitis² affects meibomian glands (ie, meibomian gland dysfunction). Association: rosacea or seborrheic dermatitis¹

C. Associated conditions (not classified by anatomic location)

1. Demodex: associated with anterior and posterior blepharitis

- a. *Demodex folliculorum*: Found primarily in lash follicles
- b. *Demodex brevis*: Found mainly in the sebaceous and meibomian glands of the lids

2. Blepharo(kerato)conjunctivitis

- a. Inflammation of the eyelids, conjunctiva, ± cornea
- b. Also known as: staphylococcal marginal keratitis, phlyctenular keratoconjunctivitis, ocular rosacea
- c. Underrecognized in children, in whom chronic recurring keratitis can present asymmetrically; may result in vision loss
- d. Association: history of styes/chalazion, rosacea

II. Overview of Treatments

Includes off-label treatments. List below may not be completely comprehensive.

A. Lid hygiene: Targets anterior blepharitis

1. Patient performs at home: A plethora of eyelid wipes/cleaners are available.³ Specific notes:

- a. Solutions/wipes with hypochlorous acid have an antimicrobial effect.
- b. *Demodex* eradication historically has involved the application of products containing tea tree oil or its major acaricidal component, terpinen-4-ol.⁴ There is some uncertainty as to the effectiveness of different concentrations for the short-term treatment of *Demodex* blepharitis, with a need for studies with longer-term follow-up.^{4,5}
- c. NuLids (NuSight Medical): an oscillating hand-held device used to remove eyelash debris (mechanical microblepharoexfoliation)

2. Commercial/in-office treatments

- a. Various cleansing gels (eg, I-Lid 'N Lash Pro [I-MED Pharma] cleansing gel with 20% tea tree oil)
- b. BlephEx (Blephex, distributed in the U.S. by Alcon): rotating micro sponge device used to remove eyelash debris (mechanical microblepharoexfoliation)

B. Thermal therapy: targets posterior blepharitis²

1. Patient performs at home: lid massage and warm compresses/various eye masks (too many to enumerate)

2. Commercial/in-office treatments

- a. LipiFlow (Johnson & Johnson): automated device that heats and expresses anterior and posterior eyelids
- b. Tear Care (Sight Sciences): automated heat treatment to anterior eyelid, followed by manual expression using trademarked forceps/squeezers
- c. iLux (Alcon): manually applied device that heats and expresses anterior and posterior eyelids
- d. MiBoFlo (MiBo medical group): manually applied heat to the anterior eyelid (over closed eyelids)
- e. OCuSOFT Thermal 1-Touch (OCuSOFT): heating device placed over anterior eyelid (over closed eyelids)

- C. Intraductal meibomian gland probing (in-office treatment)
1. Targets posterior blepharitis^{1,2}
 2. Maskin probe (Katena products): cannula used to probe anesthetized plugged meibomian gland orifices

D. Pharmaceutical

1. Topical antibiotics/antiparasitic agents (to eyelid margin or ocular surface)
 - a. Antibiotics (eg, bacitracin, erythromycin) to decrease bacterial load¹
 - i. Azithromycin also used to treat posterior blepharitis²
 - ii. Minocycline (Hovione): ophthalmic ointment formulation (in clinical trials)
 - b. Antibiotic-steroid ointments (eg, Tobradex, Polydex)¹
 - c. Ivermectin⁵
 - d. Metronidazole⁵
 - e. TP-03 (Tarsus Pharmaceuticals): ophthalmic formulation of lotilaner, an antiparasitic agent, used to treat *Demodex* blepharitis (in clinical trials)
2. Topical anti-inflammatory agents
 - a. Steroids: Goal is to use minimal effective dose/duration to limit adverse effects.¹
 - b. Cyclosporine¹ (eg, Restasis, Cequa), lifitegrast (ie, Xiidra)
 - c. Tacrolimus ointment has been used for refractory posterior blepharitis.⁶
3. Oral antibiotics/antiparasitic agents
 - a. Antibiotics (eg, doxycycline, minocycline, erythromycin, azithromycin). Dosing and treatment regimens vary in children and adults.^{7,8}
 - b. Ivermectin⁵
 - c. Metronidazole⁵
4. Oral supplements

There is conflicting data from recent studies on the results of omega-3 and omega-6 fatty acid supplementation.² A 2018 prospective, multicenter, double-blind clinical trial funded by NEI/NIH did not find a benefit to omega-3 supplementation.⁹ A 2019 Cochrane review suggested that omega-3 supplementation may be beneficial, but the evidence is inconsistent.¹⁰

- E. Other exploratory modalities in the peer-reviewed literature

1. Blepharitis associated with *Demodex*: manuka honey microemulsion eye cream, okra eyelid patch, periocular castor oil, pilocarpine gel,⁵ camphorated oil, permethrin, povidone-iodine
2. Posterior blepharitis: hormone therapy,² topical androgens/testosterone²
3. Blepharitis associated with atopic dermatitis: 0.5% delgocitinib ointment

References

Keeping to the limit of no more than 10 references necessitated citing mostly meta-analyses and review articles.

1. Amescua G, Akpek EK, Farid M, et al. Blepharitis Preferred Practice Pattern®. *Ophthalmology* 2019; 126(1):56-93.
2. Sabeti S, Kheirikhah A, Yin J, Dana R. Management of meibomian gland dysfunction: a review. *Surv Ophthalmol.* 2020; 65(2):205-217.
3. Bitton E, Ngo W, Dupont P. Eyelid hygiene products: a scoping review. *Cont Lens Anterior Eye.* 2019; 42(6):591-597.
4. Savla K, Le JT, Pucker AD. Tea tree oil for Demodex blepharitis. *Cochrane Database Syst Rev.* 2020; 6(6):CD013333.
5. Navel V, Mulliez A, Benoist d'Azy C, et al. Efficacy of treatments for Demodex blepharitis: a systematic review and meta-analysis. *Ocul Surf.* 2019; 17(4):655-669.
6. Sakassegawa-Naves FE, Ricci HMM, Moscovici BK, et al. Tacrolimus ointment for refractory posterior blepharitis. *Curr Eye Res.* 2017; 42(11):1440-1444.
7. Wladis EJ, Bradley EA, Bilyk JR, Yen MT, Mawn LA. Oral antibiotics for meibomian gland-related ocular surface disease: a report by the American Academy of Ophthalmology. *Ophthalmology* 2016; 123(3):492-496.
8. O'Gallagher M, Banteka M, Bunce C, Larkin F, Tuft S, Dahmann-Noor A. Systemic treatment for blepharokeratoconjunctivitis in children. *Cochrane Database Syst Rev.* 2016; (5):CD011750.
9. Asbell PA, Maguire MG, Pistilli M, et al. N-3 fatty acid supplementation for the treatment of dry eye disease. *New Engl J Med.* 2018; 378(18):1681-1690.
10. Downie LE, Ng SM, Lindsley KB, Akpek EK. Omega-3 and omega-6 polyunsaturated fatty acids for dry eye disease. *Cochrane Database Syst Rev.* 2019; 12(12):CD011016.

Fight the Blight With Light: Lasers for Blepharitis

Vatinee Y Bunya MD

- I. Treatment Options
 - A. Intense pulsed light (IPL)
 1. Clinical evidence
 2. Contraindications
 - a. Darker pigmented skin (Fitzpatrick skin type 4 or below)
 - b. Possible depigmentation
 3. Possible side effects (rare with proper precautions): iritis, iris atrophy, posterior synechiae, chronic eye pain, light sensitivity
 - B. Thermal pulsation
 1. Vectored thermal pulsation (LipiFlow)
 - a. Clinical evidence
 - b. Contraindications
 - i. Ocular injury within past 3 months
 - ii. Herpes infection of eye/eyelid within past 3 months
 - iii. Active ocular infection
 - iv. Ocular inflammation within past 3 months
 - v. Eyelid abnormalities that affect lid function
 - vi. Ocular surface abnormality that may compromise corneal integrity
 - c. Possible side effects
 - i. Eyelid/eye pain requiring discontinuation of procedure
 - ii. Eyelid irritation/inflammation
 - iii. Ocular surface irritation/inflammation
 - iv. Ocular symptoms (burning, stinging, tearing, itching, redness, foreign body sensation, sensitivity to light)
 - d. Potential serious adverse events (unlikely with safety precautions)
 - i. Thermal injury to eyelid or eye
 - ii. Physical pressure-induced injury to eyelid
 - iii. Ocular surface infection
 2. Meibomian gland dysfunction thermal pulsation system (iLux)
 - a. Clinical evidence
 - b. Contraindications
 - i. Pupils pharmaceutically dilated
 - ii. Ocular surgery within prior 12 months
 - iii. Ocular injury, trauma, chemical burns, limbal stem cell deficiency within 3 months
 - iv. Active herpes infection of eye/eyelid within past 3 months
 - v. Cicatricial lid margin disease
 - vi. Active ocular infection
 - vii. Ocular inflammation within past 3 months
 - viii. Ocular surface abnormality that may compromise corneal integrity
 - ix. Lid abnormalities that affect lid function
 - x. Permanent makeup or tattoos on eyelids
 - c. Potential side effects
 - i. Eyelid/eye pain requiring stopping procedure
 - ii. Eyelid irritation/inflammation
 - iii. Eye irritation or inflammation (corneal abrasion, conjunctival injection/edema)
 - iv. Temporary redness of skin
 - v. Eye symptoms (burning, stinging, tearing, itching, discharge, redness, foreign body sensation, sensitivity to light)
 - C. Devices to warm eyelids
 1. MiBo Thermoflo
 2. eyeXpress
 3. TearCare
 - D. Devices to clean eyelids
 1. Blephex
 2. Nulids
- II. Comparison of Treatments
- III. Newer Treatment
 - A. Quantum molecular resonance (Rexon-Eye): high-frequency electrotherapy device

Selected Readings

1. Blackie CA, Coleman CA, Holland EJ. The sustained effect (12 months) of a single-dose vectored thermal pulsation procedure for meibomian gland dysfunction and evaporative dry eye. *Clin Ophthalmol*. 2016; 10:1385-1396.
2. Craig JP, Chen YH, Turnbull PR. Prospective trial of intense pulsed light for the treatment of meibomian gland dysfunction. *Invest Ophthalmol Vis Sci*. 2015; 56(3):1965-1970.
3. Tauber J, Owen J, Bloomenstein M, Hovanesian J, Bullimore MA. Comparison of the iLUX and the LipiFlow for the treatment of meibomian gland dysfunction and symptoms: a randomized clinical trial. *Clin Ophthalmol*. 2020; 14:405-418.
4. Xue AL, Wang MTM, Ormonde SE, Craig JP. Randomised double-masked placebo-controlled trial of the cumulative treatment efficacy profile of intense pulsed light therapy for meibomian gland dysfunction. *Ocul Surf*. 2020; 18(2):286-297.
5. Zhao Y, Veerappan A, Yeo S, et al.; Collaborative Research Initiative for Meibomian gland dysfunction (CORIM). Clinical trial of thermal pulsation (LipiFlow) in meibomian gland dysfunction with pretreatment meibography. *Eye Contact Lens*. 2016; 42(6):339-346.

Emerging Treatments for Dry Eye Disease

Amy Lin MD

I. Introduction

Many existing therapies and potential new therapies in pipeline

II. Anticipated FDA Approval in 2021

OC-01 (varenicline) nasal spray (Oyster Point Pharma)

- A. Highly selective cholinergic agonist as a multidose preservative-free nasal spray to treat signs and symptoms of dry eyes
- B. Activates trigeminal parasympathetic pathway in nasal cavity to stimulate natural tear film production
- C. Phase 2b (ONSET-1) and Phase 3 (ONSET-2) trials improved Schirmer score (primary endpoint), as well as symptomatic eye dryness score (secondary endpoints) starting as early as Day 14 (ONSET-1) or Day 28 (ONSET-1).

III. Other Potential Therapies in Pipeline

- A. Phase 2 clinical trial under way for mycophenolate sodium and betamethasone sodium phosphate in Klarity vehicle (SURF-100), by Surface Ophthalmics. First-ever head-to-head study in chronic dry eye disease, including study arms comparing lifitegrast 5% (Xiidra) and cyclosporine 0.05% (Restasis), with primary endpoint of symptom improvement at Day 84.
- B. Progesterone gel (Pro-ocular) applied b.i.d. to forehead, by SIFI
 1. Activates neural pathway stimulating lacrimal and meibomian gland function
 2. Phase 2 study with tear film production with no adverse events
 3. Results of another Phase 2 study (ProGIFT trial) comparing 1% and 0.5% are pending.

C. Topical anti-TNF α antibody (OCS-02), by Oculis

1. Phase 2 study demonstrated effectiveness in relieving severe ocular discomfort ($P = .041$).¹
 - a. Pharmacogenetics study showed more dramatic effect in dry eye patients with a specific biomarker ($P < .0001$).
 - b. The next clinical study will aim to validate the role of OCS-02 as an anti-inflammatory treatment in patients with this biomarker, which could enable the drug to be the first personalized treatment for this indication.
 2. OCS-02 also has positive data in acute anterior uveitis.
- ## D. Phase 3 trial (GOBI trial) for topical perfluorohexyloctane (NOV03): Bausch + Lomb and Novaliq
1. Novel mechanism for dry eye disease caused by meibomian gland function: preservative free and water free, based on patented EyeSol technology
 2. Improvement in corneal fluorescein staining and subjective dryness score from baseline at Day 15 with continued results at Day 57

Reference

1. Perez VL. Variant in the TBFRI gene associated with response to topical anti-TNF α antibody fragment OCS-02 in patients with dry eye disease. *Invest Ophthalmol Vis Sci.* 62(8):921.

Ocular Neuropathic Pain

Shruti Aggarwal MBBS

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Case Presentation: Not Your Typical Dry Eye

Stephen C Pflugfelder MD

The patient is an 80-year-old woman with a history of ECCE/IOL 30 years ago and chronic glaucoma treated with multidose timolol/dorzolamide and latanoprost. She was referred with bilateral diffuse corneal epitheliopathy and central recurrent epithelial defects. The epithelial defects healed with therapeutic contacts and self-retained amniotic membrane, but recurred. Moderate stromal haze was noted. Tear production was reduced, and corneal sensitivity was absent in both eyes. Lid margin cornification was noted. Diagnostic workup was performed, and treatment was instituted that resulted in durable epithelial healing, decreased stromal haze, and improved vision. Diagnostic and treatment decision making and disease pathogenesis will be discussed.¹⁻³

References

1. Dua HS, Said DG, Messmer EM, et al. Neurotrophic keratopathy. *Prog Retin Eye Res.* 2018; 66:107-131.
2. Pflugfelder SC, Massaro-Giordano M, Perez VL, et al. Topical recombinant human nerve growth factor (cenegermin) for neurotrophic keratopathy: a multicenter randomized vehicle-controlled pivotal trial. *Ophthalmology* 2020; 127(1):14-26.
3. Alam J, Yu Z, de Paiva CS, Pflugfelder SC. Retinoid regulation of ocular surface innate inflammation. *Int J Mol Sci.* 2021; 22(3):1092.

Medical Treatment of Fuchs Endothelial Corneal Dystrophy

Kathryn Colby MD PhD

Fuchs endothelial corneal dystrophy (FECD) affects up to 4% of patients in the United States. This disease is the most common indication for corneal transplantation, accounting for approximately one-third of the cornea transplants done nationwide. Surgical management of FECD has seen tremendous advances in the last 25 years and now includes various forms of endothelial keratoplasty (EK)—including Descemet membrane EK and Descemet-stripping automated EK—and more recently, nongraft techniques including Descemet stripping only (DSO) EK.^{1,2} Cultured corneal endothelial cells for injection are under investigation and show promise as a treatment for all forms of endothelial dysfunction.³

Described over 100 years ago, FECD remains an enigmatic disease. Multiple different mechanisms have been suggested to play a role in its pathophysiology, including oxidative stress, mitochondrial dysfunction, unfolded protein response, and endothelial-mesenchymal transition.⁴ Despite the numerous genetic mutations that have been associated with FECD, the disease has only 1 clinical phenotype (although age of onset can vary with genotype). The vast majority of FECD patients in the United States manifest a trinucleotide repeat expansion in the *TCF4* gene.⁵ How repeat expansion causes the cellular changes responsible for FECD is not yet understood, although several possible mechanisms have been suggested.⁶

A better understanding of which of the putative pathways are actually responsible for FECD is an essential first step for developing effective medical therapy. Many genotypes produce the same clinical phenotype, suggesting that there is a “final common pathway” that results in FECD. Several lines of evidence suggest that the mitochondria may be this final common pathway, as shown in Figure 1.

Rho kinase (ROCK) inhibition has emerged as a possible medical therapy for FECD. Ripasudil, a topical ROCK inhibitor, “rescued” 2 slow-to-clear DSO patients,⁸ increased final endothelial cell count, and sped time to clearance after DSO.⁹ A recent clinical trial showed a reduction of corneal thickness in Fuchs patients treated with netarsudil, a ROCK inhibitor approved in the United States as a glaucoma therapy.¹⁰ Laboratory evidence suggests that ripasudil may help restore endothelial pump function, among other effects.¹¹

This talk will review what is known about FECD pathophysiology and discuss possible strategies for future medical therapies.

References

- Blitzer A, Colby K. Update on the surgical management of Fuchs endothelial corneal dystrophy. *Ophthalmol Ther*. 2020; 9:757-765.
- Borkar DS, Veldman P, Colby KA. Treatment of Fuchs endothelial dystrophy by Descemet stripping without endothelial keratoplasty. *Cornea* 2016; 35:1267-1273.
- Kinoshita S, Koizumi N, Ueno M, et al. Injection of cultured cells with a ROCK inhibitor for bullous keratopathy. *N Engl J Med*. 2018; 378:995-1003.
- Sarnicola C, Farooq A, Colby KA. Fuchs endothelial corneal dystrophy: update on pathogenesis and future directions. *Eye Contact Lens*. 2019; 45:1-10.
- Wieben ED, Aleff RA, Tosakulwong N, et al. A common trinucleotide repeat expansion within the transcription factor 4 (*TCF4*, *E2-2*) gene predicts Fuchs corneal dystrophy. *PLoS One*. 2012; 7:e49083.

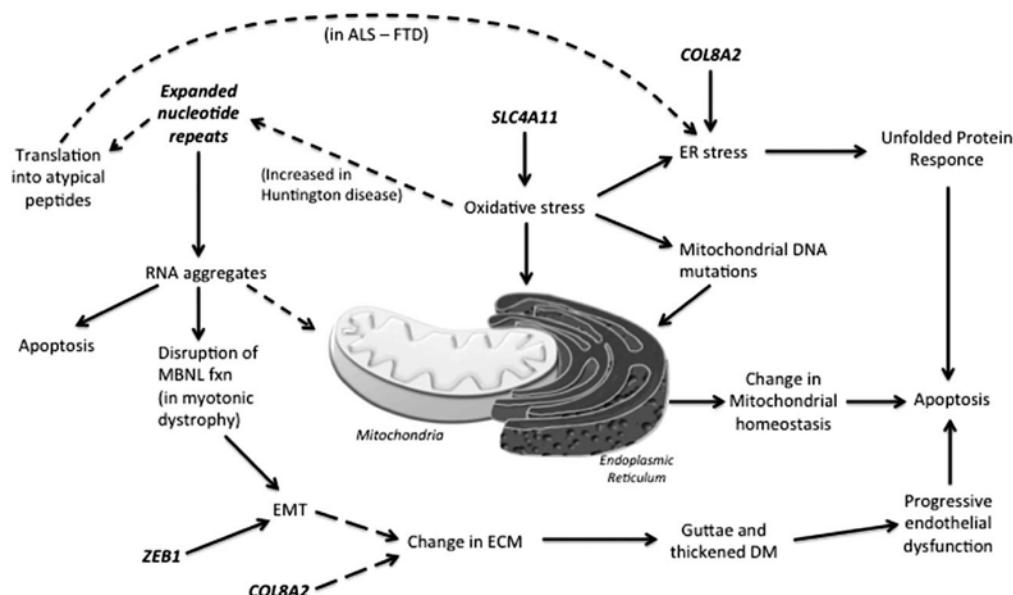


Figure 1. Working theory of FECD pathogenesis. Source: Sarnicola C, Farooq A, Colby KA. Fuchs endothelial corneal dystrophy: update on pathogenesis and future directions. *Eye Contact Lens*. 2019; 45:1-10 (open access).

6. Fautsch MP, Wieben ED, Baratz KH, et al. TCF4-mediated Fuchs endothelial corneal dystrophy: insights into a common trinucleotide repeat-associated disease. *Prog Retin Eye Res.* 2021; 81:100883.
7. Kinoshita S, Colby K, Kruse F. A close look at the clinical efficacy of rho-associated kinase inhibitor eye drops for Fuchs endothelial corneal dystrophy. *Cornea.* Epub ahead of print 2021 Febr 4. doi: 10.1097/ICO.0000000000002642.
8. Moloney G, Petsoglou C, Ball M, et al. Descemetorhexis without grafting for Fuchs endothelial dystrophy-supplementation with topical ripasudil. *Cornea* 2017; 36:642-648.
9. Macsai MS, Shiloach M. Use of topical rho kinase inhibitors in the treatment of Fuchs dystrophy after Descemet stripping only. *Cornea* 2019; 38:529-534.
10. Price MO, Price FW Jr. Randomized, double-masked, pilot study of netarsudil 0.02% ophthalmic solution for treatment of corneal edema in Fuchs dystrophy. *Am J Ophthalmol.* 2021; 227:100-105.
11. Schlötzer-Schrehardt U, Zenkel M, Strunz M, et al. Potential functional restoration of corneal endothelial cells in Fuchs endothelial corneal dystrophy by ROCK Inhibitor (ripasudil). *Am J Ophthalmol.* 2021; 224:185-199.

Clearing the Cornea With Stem Cells

Sayan Basu MBBS MS

Introduction and Background

Corneal scarring is one of the leading causes of blindness, particularly in the developing world.¹ Corneal transplantation is presently the only definitive cure, but the gap between demand of donor corneal tissue and supply is also ironically most acute in developing countries, where the need is the greatest.² The need for trained and skilled corneal surgeons and a network of eye banks and ophthalmologists experienced enough to deal with postoperative problems further limits the scope of corneal transplantation as a sustainable solution for the burden of morbidity caused by corneal blindness. Lastly, the major causes of corneal blindness in developing countries like India are those that have moderate to poor prognosis for long-term survival of corneal grafts.³

So along with training more corneal surgeons, improving the eye banking network and the global supply chain of donor tissue, attention also needs to be paid to developing alternative therapies that can address the limitations of corneal transplantation. One promising approach is the use of stem cells, particularly mesenchymal stem cells (MSCs), for the treatment of corneal scarring. In addition to the bone marrow, adipose tissue, and dental pulp, MSCs are also located in the corneal limbus.⁴ These limbal-derived MSCs (LMSCs) are capable of transdifferentiating into corneal keratocytes, and they produce normal corneal extracellular matrix in vitro and modulate scarless corneal wound healing in vivo.⁵ The LMSCs are easily accessible to ophthalmologists and can be isolated by obtaining tiny limbal biopsies from either living donors or from cadaveric corneal-scleral rims from eye banks.⁵ These cells can be applied on the surface of the cornea using a minimally invasive approach and could obviate the need for long-term medications, follow-ups, or suture management.⁵

Progress So Far and Future Directions

Preclinical studies have demonstrated the ability of these cells to have significant regenerative potential to prevent and modulate corneal scarring.⁵ A pilot human clinical trial has shown greater efficacy in preventing scarring when applied in acute conditions such as burns and ulcers than existing quiescent scars.^{6,7} The method of application is simple and sutureless, mixing the cells in one of the components of fibrin glue. The LMSCs can be transported at room temperature by alginate encapsulation over 3-5 days without loss of cell viability or characterization.⁸ This opens the possibility of safe transportation over long distances without requiring a cold-chain, which can be especially useful in the resource-limited settings of developing countries.⁸ Recent research has focused on incorporating the cells in ECM constructs as corneal substitutes.^{9,10} This can have potential applications as stromal lenticules in keratorefractive procedures for correcting refractive errors or volume replacement

as a treatment of keratoconus, in addition to their regenerative applications in corneal wounds. The term “limbal stem cells” has traditionally been used to refer to the epithelial stem cells located within the palisades of Vogt, but with the advent and clinical translation of LMSCs, this term needs to be qualified by referring to the cell type, epithelial or mesenchymal.¹¹

References

1. Flaxman SR, Bourne RRA, Resnikoff S, et al.; Vision Loss Expert Group of the Global Burden of Disease Study. Global causes of blindness and distance vision impairment 1990-2020: a systematic review and meta-analysis. *Lancet Glob Health*. 2017; 5(12):e1221-e1234.
2. Gain P, Jullienne R, He Z, et al. Global survey of corneal transplantation and eye banking. *JAMA Ophthalmol*. 2016; 134(2):167-173.
3. Das AV, Basu S. Indications and prognosis for keratoplasty in eyes with severe visual impairment and blindness due to corneal disease in India. *Br J Ophthalmol*. 2021; 105(1):17-21.
4. Du Y, Funderburgh ML, Mann MM, SundarRaj N, Funderburgh JL. Multipotent stem cells in human corneal stroma. *Stem Cells* 2005; 23(9):1266-1275.
5. Basu S, Hertszenberg AJ, Funderburgh ML, et al. Human limbal biopsy-derived stromal stem cells prevent corneal scarring. *Sci Transl Med*. 2014; 6(266):266ra172.
6. Basu S, Damala M, Singh V. Limbal stromal stem cell therapy for acute and chronic superficial corneal pathologies: early clinical outcomes of the Funderburgh technique. *Invest Ophthalmol Vis Sci*. 2017; 58(8):3371.
7. Basu S, Damala M, Tavakkoli F, Mitragotri N, Singh V. Human limbus-derived mesenchymal/stromal stem cell therapy for superficial corneal pathologies: two-year outcomes. *Invest Ophthalmol Vis Sci*. 2019; 60(9):4146-4146.
8. Damala M, Swioklo S, Koduri MA, et al. Encapsulation of human limbus-derived stromal/mesenchymal stem cells for biological preservation and transportation in extreme Indian conditions for clinical use. *Sci Rep*. 2019; 9(1):16950.
9. Chameettachal S, Prasad D, Parekh Y, et al. Prevention of corneal myofibroblastic differentiation in vitro using a biomimetic ECM hydrogel for corneal tissue regeneration. *ACS Applied Bio Materials*. 2021; 4(1):533-544.
10. Chandru A, Agrawal P, Ojha SK, et al. Human cadaveric donor cornea derived extra cellular matrix microparticles for minimally invasive healing/regeneration of corneal wounds. *Biomolecules* 2021; 11(4):532.
11. Shukla S, Shanbhag SS, Tavakkoli F, Varma S, Singh V, Basu S. Limbal epithelial and mesenchymal stem cell therapy for corneal regeneration. *Curr Eye Res*. 2020; 45(3):265-277.

New Treatments for Neurotrophic Keratitis

Simon Fung MD MA(Oxon) FRCOphth

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References

1. Soifer M, Starr CE, Mousa HM, et al. Neurotrophic keratopathy: current perspectives. *Curr Ophthalmol Rep.* 2020; 8:29-35.
2. Dua HS, Said DG, Messmer EM, et al. Neurotrophic keratopathy. *Prog Retin Eye Res.* 2018; 66:107-131.
3. Pflugfelder SC, Massaro-Giordano M, Perez VL, et al. Topical recombinant human nerve growth factor (cenergeermin) for neurotrophic keratopathy: a multicenter randomized vehicle-controlled pivotal trial. *Ophthalmology* 2020; 127:14-26.
4. Bonini S, Lambiase A, Rama P, et al. Phase II randomized, double-masked, vehicle-controlled trial of recombinant human nerve growth factor for neurotrophic keratitis. *Ophthalmology* 2018; 125:1332-1343.
5. Catapano J, Fung SSM, Halliday W, et al. Treatment of neurotrophic keratopathy with minimally invasive corneal neurotization: long-term clinical outcomes and evidence of corneal reinnervation. *Br J Ophthalmol.* 2019; 103:1724-1731.
6. Fung SSM, Catapano J, Elbaz U, et al. In vivo confocal microscopy reveals corneal reinnervation after treatment of neurotrophic keratopathy with corneal neurotization. *Cornea* 2018; 37:109-112.

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 Bausch + Lomb: C
 CorneaGen: L
 Dompé: C
 EyeVance: C
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 Johnson & Johnson: C
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