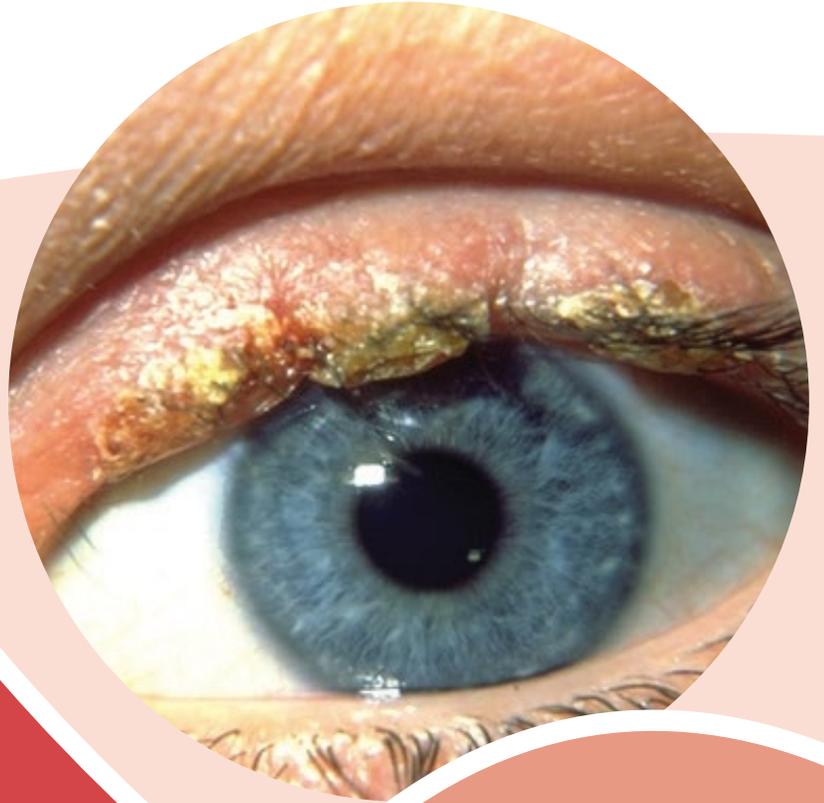AMERICAN ACADEMY
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Cornea 2023

What To See in 2023

Subspecialty Day | AAO 2023
San Francisco | Nov 4

Cornea 2023
What to See in 2023

Program Directors
Sonal S Tuli MD, Christina R Prescott MD PhD,
and Christopher S Sales MD

In conjunction with the Cornea Society

Cornea Society
Advancing the treatment of corneal disease

Moscone Center
San Francisco, California
Saturday, Nov. 4, 2023

Presented by:
The American Academy of Ophthalmology

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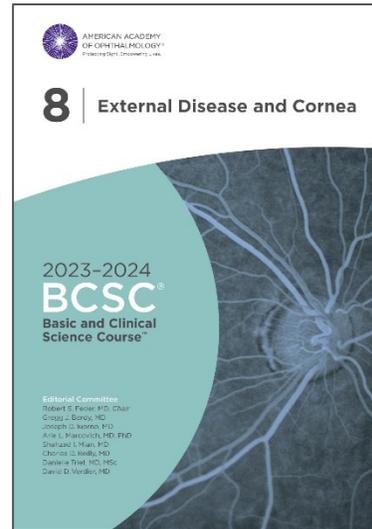
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Cornea 2023 Contents

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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.

Cornea Subspecialty Day Meeting 2023 Learning Objectives

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

- Understand how to use anterior segment imaging devices to assist with the diagnosis and management of corneal diseases
- Recognize ocular surface disorders that warrant surgical intervention and determine the ideal approach and timing of intervention
- Apply current best practices in the medical and surgical management of corneal infections and ocular surface inflammatory diseases
- Discuss common and complex keratoplasty techniques and alternative treatments in the management of corneal diseases

Cornea Subspecialty Day Meeting 2023 Target Audience

This program is for cornea specialists and comprehensive ophthalmologists with an interest in anterior segment diseases who are involved in the medical and surgical care of patients with corneal diseases.

Teaching at a Live Activity

Teaching an instruction course 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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Saturday Subspecialty Day Activity: Cornea, Oculofacial Plastic Surgery, and Retina (Day 2)
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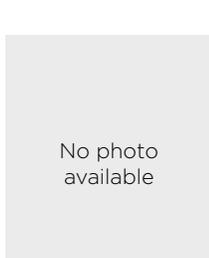
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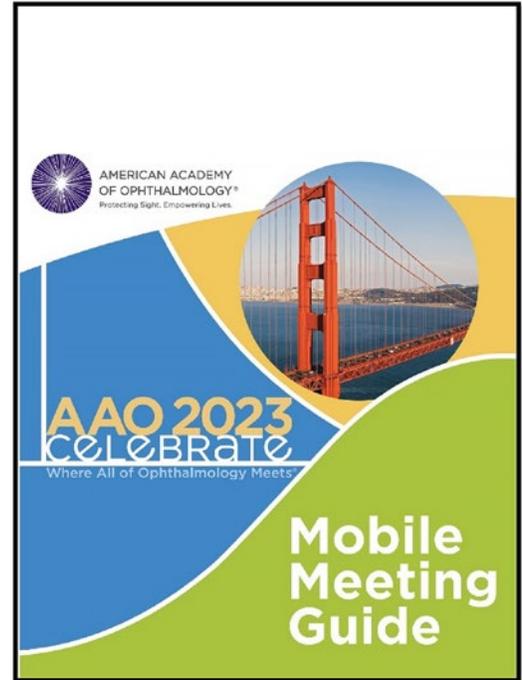To ask the moderator a question during the meeting, follow the directions below.

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Cornea Subspecialty Day 2023: What to See in 2023

SATURDAY, NOV. 4

7:00 AM	CONTINENTAL BREAKFAST	
8:00 AM	Welcome and Introductions	Sonal S Tuli MD Christina R Prescott MD PhD Christopher S Sales MD

Section I: **Keratoplasty**

Moderators: Christina R Prescott MD PhD, Christopher S Sales MD, and Sonal S Tuli MD

8:02 AM	Introduction	Christina R Prescott MD PhD	
8:04 AM	DSEK: When DMEK Just Won't Do	Jodhbir S Mehta MBBS PhD	1
8:13 AM	Descemet Membrane Endothelial Keratoplasty: Pushing Limits	Gregory Moloney MD	2
8:22 AM	Saving a Deep Anterior Lamellar Keratoplasty	Caterina Sarnicola MD	3
8:31 AM	Customized Patch Grafts . . . Fitting the Puzzle Together	Sunita Chaurasia MD	5
8:40 AM	Complex Corneal Transplants	Maria S Cortina MD	6
8:49 AM	Management of Graft Complications	Ashiyana Nariani MD MPH	8
8:58 AM	Discussion		

Section II: **Keratoplasty Alternatives**

Moderators: Christopher S Sales MD, Christina R Prescott MD PhD, and Sonal S Tuli MD

9:13 AM	Introduction	Christopher S Sales MD	
9:15 AM	Descemet Stripping Only: No Graft, No Problem!	Kathryn A Colby MD PhD	9
9:24 AM	Endothelial Cell Injection Therapy	Friedrich E Kruse MD	10
9:33 AM	Lamellar Keratectomy	Sumitra S Khandelwal MD	12
9:42 AM	Corneal Inlays and Onlays	Viridiana Kocaba MD PhD	13
9:51 AM	What's New in Artificial Corneas	Esen K Akpek MD	21
10:00 AM	Discussion		
10:15 AM	United for Sight: A Vision for Effective Advocacy	Lee A Snyder MD	22
10:20 AM	REFRESHMENT BREAK		

Section III: **Keratitis**

Moderators: Sonal S Tuli MD, Christina R Prescott MD PhD, and Christopher S Sales MD

10:50 AM	Introduction	Sonal S Tuli MD	
10:52 AM	Simplex vs. Zoster	Sadeer B Hannush MD	24
11:01 AM	Bacteria vs. Fungus	Prashant Garg MD	26
11:10 AM	Viral vs. *Acanthamoeba*	Jennifer R Rose-Nussbaumer MD	29
11:19 AM	Not Your Usual Keratitis	Vishal Jhanji MD FRCOphth	30

Section IV: **Case Presentations**

Moderators: Sonal S Tuli MD, Christina R Prescott MD PhD, and Christopher S Sales MD

Section V: **Ocular Surface Pearls**

Moderators: Christina R Prescott MD PhD, Christopher S Sales MD, and Sonal S Tuli MD

Section VI: **Anterior Segment**

Moderators: Christopher S Sales MD, Christina R Prescott MD PhD, and Sonal S Tuli MD

Section VII: **Hot Topics**

Moderators: Sonal S Tuli MD, Christina R Prescott MD PhD, and Christopher S Sales MD

4:28 PM	Introduction	Sonal S Tuli MD	
4:30 PM	Corneal Stem Cell Regeneration	Sophie X Deng MD PhD	49
4:39 PM	The Robot Will See You Now	Maria A Woodward MD MS	50
4:48 PM	MythBusters—Pushing the Limits	Somasheila I Murthy MD	51
4:57 PM	Corneal Tissue Engineering: Gel Keratoplasty, 3-D Bioprinting, and More	David Myung MD	52
5:06 PM	Synthetic Endothelial Replacement	Victor A Augustin MD	53
5:15 PM	Discussion		
5:30 PM	Closing Remarks	Sonal S Tuli MD Christina R Prescott MD PhD Christopher S Sales MD	
5:31 PM	ADJOURN		

DSEK: When DMEK Just Won't Do

Jod Mehta MBBS PhD

Endothelial keratoplasty (EK) has revolutionized corneal endothelial surgery. As the procedure has evolved with time, we have seen the transition from posterior lamellar keratoplasty (PLK) to Descemet-stripping (automated) EK (DS[A]EK) and now to Descemet membrane EK (DMEK). As the tissue has become thinner, the complexity of the donor manipulation has also increased.

This evolution has also seen changes in insertion techniques, from the initial folding technique to "repurposed devices" for glide insertion (eg, Sheets glide, IOL injectors) to newer devices specifically for graft insertion. These newer devices allowed surgeons to push the limits with their respective cases, since graft insertion became more reproducible and controlled. Hence in the early days of EK, DSEK was all for cases of mild to moderate corneal decompensation, while more advanced cases required PK. Over time, more advanced cases were being performed with DSEK, since graft insertion was more reproducible, and we have seen EK in the form of DS(A)EK become the dominant procedure for endothelial surgery.

As EK has evolved into DMEK, with the thinner tissue and an endo-out insertion technique, visualization is important—hence the use of vital dyes for staining. However, in contrast to the effect DS(A)EK had on PK, despite the numbers of DMEK increasing substantially in the United States and worldwide, the percentages of DMEK and DS(A)EK being performed are almost equivalent. Despite the advantages of DMEK with respect to visual recovery, lower rejection rates, and lower incidence of raised IOP, it still has a steeper learning curve with respect to graft insertion and higher rates of graft detachment (requiring rebubbling). It requires good visualization and good anterior chamber (AC) stability (ie, iris/lens diaphragm) in order to unscroll the graft, and it may not be suitable in cases of advanced stromal scarring.

The lecture will cover cases in which I currently prefer to perform DS(A)EK. This procedure now makes up only 3% of my EK cases since switching to an endothelial-in insertion technique for DMEK, allowing me to perform DMEK in cases that are otherwise challenging (eg, patients with deep AC, as following scleral fixation; patients with AC IOL; patients with advanced stromal edema, precluding good visualization; and patients with incomplete lens/iris diaphragm, as in aphakic cases, patients with fixed dilated pupil or atrophic/pseudopolycoria, and patients requiring extensive iris reconstruction).

These include the following:

1. Children with complex syndromic conditions in which posturing postop will be an issue; hence graft fixation will be required at primary surgery. In addition, it is often not ideal to have to take such children for a second GA to do a rebubbling procedure.
2. Patients who had moderate to advanced stromal disease: Often in these situations a secondary deep anterior lamellar keratoplasty (DALK) procedure may be required; hence, having performed a primary DS(A)EK, is more advantageous than a DMEK.
3. Patients with medical problems precluding them from posturing postoperatively (eg, spinal problems).

Reproducibility of insertion techniques has allowed us to push the barrier with respect to indications for EK surgery. However, in certain situations, DS(A)EK is still preferred over DMEK.

Descemet Membrane Endothelial Keratoplasty: Pushing Limits

Greg Moloney MD

Introduction

Descemet membrane endothelial keratoplasty (DMEK) has solidified its position as the gold standard operation for Fuchs endothelial dystrophy. The next horizon we are approaching is medical therapies for Fuchs dystrophy and techniques to exploit the latent healing potential of the corneal endothelium. I will review the journey we have been on with stimulants to endothelial healing and what appear to be the current barriers or limitations to these techniques.

Summary

- Review of DMEK, hemi-DMEK, Descemet membrane endothelial transfer (DMET), Descemetorrhexis without EK (DWEK)/Descemet stripping only (DSO)
- Review of failed cases in the above categories, which give an indication of the boundaries of nontransplant endothelial surgery
- Review of long-term outcomes of successful DWEK/DSO in 42 eyes from Sydney Eye Hospital cohort
- Review of what appear to be barriers to future minimally invasive techniques, including factors affecting endothelial migration and monolayer formation
- Briefly review cell suspension as a treatment option

Saving a Deep Anterior Lamellar Keratoplasty

Caterina Sarnicola MD, Enrica Sarnicola MD, and Vincenzo Sarnicola MD

Background

Deep anterior lamellar keratoplasty (DALK) is the mainstay surgery for corneal stromal diseases with a functioning endothelium. DALK offers substantial advantages compared to full-thickness penetrating keratoplasty (PK), primarily the avoidance of endothelial rejection and longer graft survival, while providing comparable visual outcomes. However, the slow adoption of DALK is probably related to a more difficult and time-consuming technique compared to PK. Descemet membrane (DM) intraoperative ruptures represent a common complication with DALK even in expert hands (4.5% and 45% of cases), leading to a PK conversion in 0% to 86% of cases.[1-9] The rate of DM rupture and PK conversion gradually decreases as surgeons become more experienced.

Only a few studies in the literature have reported on outcomes of intraoperative DM ruptures.[4,10-11] We have recently published our series, where the incidence of DM rupture was 8.25% with no PK conversions recorded over 1443 DALK surgeries.[12] Being able to repair the ruptures would increase the success of DALK and allow patients to benefit from all its advantages.

Classifications of DALK Surgical Techniques

Several DALK techniques have been described, broadly classified in the literature as "predescemetic DALK (pdDALK)" to indicate manual dissections techniques and "descemetic DALK (dDALK)" to refer to techniques that were thought to expose the DM, making the surgery faster and more reliable, like with big bubble (BB) and viscodissection. It has been recently demonstrated that BB type 1 does not separate DM from stroma but is in fact an intrastromal bubble, whereas only BB type 2 truly exposes the DM.[13] This newer knowledge has made the terms "dDALK" and "pdDALK" obsolete. A new classification has been proposed by our group:[14]

Deep anterior lamellar keratoplasty (DALK)

All the manual dissection techniques that leave a residual bed that does not measure more than 80 µ of thickness (ie, peeling off, layer by layer manual dissection, hydrodissection, etc.)

Sub-total anterior lamellar keratoplasty (STALK)

Techniques that were called "dDALK" (except for the type 2 big bubble), in which the DM seems to be intraoperatively exposed but a microscopic layer of stroma is in fact left in place, too (ie, big bubble type 1, viscodissection, air-viscobubble)

Total anterior lamellar keratoplasty (TALK)

Cases where the DM is truly exposed (big bubble type 2)

General Management of Descemet Membrane Ruptures

We have recently described in detail different approaches for managing a DM rupture, based on specific scenarios. First,

we must consider whether we are doing a STALK/TALK or a manual DALK because the recipient bed, after a rupture, will behave differently (like a Descemet membrane EK/predescemetic EK or a Descemet-stripping automated AEK graft). However, there are some general rules that can be valid in most cases.[14-18]

Once a recipient bed rupture is encountered, the stromal removal should be completed as deeply and smoothly as possible to minimize any stromal irregularities between the donor and recipient layers that could keep the DM rupture patent. When completing the stromectomy in the area of DM rupture, it is not uncommon for the rupture to enlarge, especially in STALK and TALK cases, making subsequent stromectomy elsewhere more difficult to perform. Therefore, when completing the stromectomy, the area of DM rupture should always intentionally dissected last. Once the stromectomy is completed, the donor graft, denuded of its endothelium, can be sutured to the recipient. An air bubble should be injected into the anterior chamber (AC), about 70% of the AC, to tamponade the rupture. At the end of surgery, the eye should be rotated in different positions to facilitate the drainage of interface fluid and to promote adherence between the recipient layer and donor graft.[18]

Postoperatively, the patient's head should be positioned so that the air bubble in the AC tamponades the DM rupture (ie, sitting position for superior ruptures, lying on the opposite site of a DM break for lateral ruptures, and supine position with chin hyperextension for inferior ruptures).

Pharmacological pupil dilation and close patient monitoring are needed to prevent/manage pupillary block.

Double AC management

In cases in which the air bubble (left in the AC at the end of surgery) shrank and is insufficient to tamponade the rupture, rebubbling should be performed, emphasizing the head position to the patient. In addition, regularity of the sutures has to be carefully assessed, and tight sutures should be replaced during rebubbling.

Significant donor–recipient disparity of curvature, in the presence of a DM rupture during manual DALK, may cause a persistent double chamber. In these cases, rebubbling may not work, requiring surgical correction (total or subtotal full-thickness recipient bed cut).[16,17]

Conclusion

DALK has become the gold standard technique for treating stromal diseases when the endothelium is functioning. Moreover, DALK's avoidance of endothelial rejection makes a very meaningful impact, not only on the prognosis of patients with keratoconus but also for high-risk corneal transplants (ie, disorders that need large grafts, presence of neovascularization, inflammation, active infections, etc.). With appropriate rescue techniques to repair the recipient bed rupture and to manage postoperative double AC, conversion to PK can be avoided in the majority of cases.

References

1. Smadja D, Colin J, Krueger RR, et al. Outcomes of deep anterior lamellar keratoplasty for keratoconus: learning curve and advantages of the big bubble technique. *Cornea* 2012; 31:859-863.

2. Sarnicola E, Sarnicola C, Sabatino F, et al. Cannula DALK versus needle DALK for keratoconus. *Cornea* 2016; 35:1508-1511.

3. Ogawa A, Yamaguchi T, Mitamura H, et al. Aetiology-specific comparison of long-term outcome of deep anterior lamellar keratoplasty for corneal diseases. *Br J Ophthalmol.* 2016; 100:1176-1182.

4. Huang OS, Htoon HM, Chan AM, et al. Incidence and outcomes of intraoperative Descemet membrane perforations during deep anterior lamellar keratoplasty. *Am J Ophthalmol.* 2019; 199:9-18.

5. Gadhvi KA, Romano V, Fernández-Vega Cueto L, et al. Deep anterior lamellar keratoplasty for keratoconus: multisurgeon results. *Am J Ophthalmol.* 2019; 201:54-62.

6. Fogla R. Deep anterior lamellar keratoplasty in the management of keratoconus. *Indian J Ophthalmol.* 2013; 61:465-468.

7. Al-Torbak AA, Al-Motowa S, Al-Assiri A, et al. Deep anterior lamellar keratoplasty for keratoconus. *Cornea* 2006; 25:408-412.

8. Kubaloglu A, Sari ES, Unal M, et al. Long-term results of deep anterior lamellar keratoplasty for the treatment of keratoconus. *Am J Ophthalmol.* 2011; 151:760-767.e1.

9. Leccisotti A. Descemet's membrane perforation during deep anterior lamellar keratoplasty: prognosis. *J Cataract Refract Surg.* 2007; 33: 825-829.

10. Senoo T, Chiba K, Terada O, et al. Visual acuity prognosis after anterior chamber air replacement to prevent pseudo-anterior chamber formation after deep lamellar keratoplasty. *Jpn J Ophthalmol.* 2007; 51:181-184.

11. Den S, Shimmura S, Tsubota K, et al. Impact of the Descemet membrane perforation on surgical outcomes after deep lamellar keratoplasty. *Am J Ophthalmol.* 2007; 143:750-754.

12. Sarnicola C, Sarnicola E, Cheung AY, Sarnicola V. Deep anterior lamellar keratoplasty: can all ruptures be fixed? *Cornea* 2023; 42(1):80-88.

13. 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(9):1778-1785.

14. Sarnicola E, Sarnicola C, Cheung AY, Holland EJ, Sarnicola V. Surgical corneal anatomy in deep anterior lamellar keratoplasty: suggestion of new acronyms. *Cornea* 2019; 38(4):515-522.

15. Sarnicola E, Sarnicola C, Sarnicola V. Deep anterior lamellar keratoplasty: surgical technique, indications, clinical results and complications. In: Guell JL, ed. *Cornea.* ESASO course series, vol. 6. Karger; 2015.

16. Sarnicola E, Sarnicola C, Cheung AY, Panico E, Panico C, Sarnicola V. Total or subtotal full thickness recipient bed cut to repair donor-recipient curvature disparity in cases of DM rupture with manual DALK. *Eur J Ophthalmol.* 2020:1120672120932833.

17. Sarnicola E, Sarnicola C, Cheung AY, Panico E, Panico C, Sarnicola V. Manual deep anterior lamellar keratoplasty after partial unintentional full-thickness trephination. *Eur J Ophthalmol.* 2020:1120672120932108.

18. Sarnicola V, Sarnicola E, Sarnicola C. Recovery techniques in DALK. In: Mannis MJ, Holland EJ, eds. *Cornea,* 4th ed., vol. 2. Elsevier; 2016.

Customized Patch Grafts . . . Fitting the Puzzle Together

Sunita Chaurasia MD

There are diverse methods of managing corneal perforations and corneal melts/thinning with impending perforations, such as glue application, multilayered amniotic membrane grafting, tenon grafting, Gunderson flaps, and corneal patch grafts. The decision-making about surgical intervention varies with the clinical scenario, size of the perforation/thinning, and availability of the biological tissues, such as donor cornea and amniotic membrane. Patch grafts using donor cornea are preferred for peripheral/midperipheral corneal perforations, with the aim of salvaging the globe integrity and restoring the corneal topography with a close match to near normal. In central corneal perforations, larger grafts are favored, as the aim is to achieve tectonic stability and visual restoration simultaneously.

When to Do Patch Grafts

Perforations larger than 3-4 mm in diameter, not amenable to other alternatives such as glue application, amniotic membrane grafting

Types of Patch Grafts

- Based on depth: lamellar/full thickness
- Based on geometric shapes: circular, crescentric, semicircular, annular

Highlighted Clinical Scenarios

- Infective keratitis with perforation
- Phaco tunnel infection
- Parasitic infections: *Microsporidia*
- Peripheral ulcerative keratitis with circumferential progression: Mooren ulcer
- Collagen vascular diseases: rheumatoid arthritis
- Corneal degenerations: Terrien marginal degeneration, pellucid marginal corneal degeneration
- Primary repair of cornea injury associated with tissue loss
- Developmental corneal conditions: limbal dermoid
- Miscellaneous/special situations: long-standing fistula repair in isolation/combined with other corneal surgery (DSEK)

Methods of Sizing and Shaping Patch Grafts

- Trephines of 2 variable sizes
- Free-hand scissors dissection
- Donor cornea mounted on artificial anterior chamber to achieve best fit match

Follow-up Management in Patch Grafts

- Topical steroids
- Treatment of primary clinical condition
- Suture management

Complications (Immediate and Late Postop) That Can Arise in Patch Grafts

- Graft-host mismatch
  - Lamellar grafts: Potential interface space
  - Full-thickness grafts: Suboptimal corneal contour
- Suture-related infection
- Graft opacification
- Graft melt
- Focal ectasia/gape
- Recurrence of primary condition
- High astigmatism

Complex Corneal Transplants

Soledad Cortina MD

Introduction

Keratoplasty is the most successful solid organ transplant in the body. In fact, certain indications, including noninflammatory conditions such as Fuchs dystrophy and keratoconus, can have >70% success rate at 10 years. The evolution of keratoplasty to layer selective transplantation has further decreased the risk of rejection (eg, Descemet membrane endothelial keratoplasty [DMEK] and deep anterior lamellar keratoplasty [DALK]). However, a number of patients with corneal disease requiring keratoplasty present much more complex situations, with higher risk of failure and a more guarded prognosis. In these cases, modification of surgical techniques and special considerations in management are required.

Immunological High-Risk Keratoplasty

Risk factors for immunologic rejection in keratoplasty include the following:

- Corneal stromal vascularization
- Herpes simplex (HSV) and herpes zoster virus (HZV) infections
- Prior graft rejection and graft failure
- Increased graft diameters and eccentric grafts
- Anterior synechiae
- Prior intraocular surgery
- History of anterior segment inflammation
- Ocular surface disease
- Young age, especially infants and children
- Glaucoma

Main preoperative considerations in these patients include measures to minimize ocular inflammation and rehabilitation of the ocular surface prior to considering surgical intervention.

Tissue matching has been shown to have some benefit in high-risk keratoplasty, and attempts to reduce corneal neovascularization may also be helpful in reducing the risk of rejection.[1]

Postoperatively, these patients require a more intensive immunosuppressive regimen, including not only frequent topical steroids but also topical tacrolimus or cyclosporine and often systemic immunosuppression with single or combination agents. Keratoprosthesis (KPro) has emerged as a viable alternative in many high-risk cases.

Pediatric Keratoplasty

Several factors make keratoplasty a complex surgery in children. There is a significant degree of ocular comorbidity in congenital disease, including anterior segment anomalies, glaucoma, cataract, and retinal disease. The aggressive healing response and high risk of rejection in this patient population present two of the biggest challenges. In addition, examination can be difficult and often limited unless under anesthesia, and this, combined with the coordination of care and counsel of family members that caring for these patients demands, makes postoperative management very labor intensive. Finally, even if keratoplasty is successful, treatment of amblyopia is required for a successful outcome.

The type of intervention depends on the underlying conditions and may include all forms of corneal transplantation, including penetrating keratoplasty (PKP), DMEK, Descemet-stripping automated EK (DSAEK), DALK or KPro, favoring delaying or avoiding corneal transplantation whenever possible with lamellar surgery or interventions such as optical iridectomy and selective endothelial removal where appropriate. In our series of 46 pediatric grafts, we found a 56% rate of graft failure, with a mean time to failure of 16 months. Sixty-four percent of patients achieved ambulatory vision. Our study determined the following factors were associated with improved graft survival in children:

- Age at keratoplasty >2 years
- Indication of keratoconus vs. postoperative decompensation or congenital anomalies
- Keratoplasty performed alone vs. combined with other procedures

Despite its complexity, keratoplasty in children with corneal disease has an important role. Severe visual impairment has a profound effect on the development of a child, and keratoplasty has been shown to improve behavior, communication, and ambulation even if vision better than 20/200 is never achieved.[2] In fact, Snellen VA is not a fair measurement of pediatric keratoplasty success. Therefore, even if keratoplasty fails after a period of time, there is still a benefit that justifies the intervention.

Keratoplasty in the Neurotrophic Cornea

The reduction or absence of corneal sensation is a poor prognostic factor for PKP, as is the presence of active inflammation or epithelial breakdowns. A reasonable period of ocular surface stability and disease quiescence is required prior to keratoplasty. Corneal transplantation in patients with HSV and HZV requires some special considerations, including appropriate antiviral prophylaxis, control of underlying inflammation, and possible treatments for corneal neovascularization. The treating physician must be aware of the higher risk of rejection and possibility of recurrence of keratitis in these patients. Furthermore, keratouveitis and graft rejections can be difficult to differentiate, and epithelial recurrences can mimic nonhealing defects from other causes after surgery.

Therapeutic Keratoplasty

Unresponsive corneal infections, impending perforations, and perforations are the usual indications for therapeutic keratoplasty. The most common indication is bacterial infection, but the rate of fungal and *Acanthamoeba* keratitis requiring grafting is approximately 50%. Success rates for surgical therapies are best for bacterial corneal infections and worst for fungal infections. Long-term survival is poor, mostly due to

the requirement of large, eccentric grafts and the presence of inflammation. Outcomes are best when keratoplasty is not performed in the acute phase.[3] Tissue is scarce in many countries, and cryopreserved tissue followed by optical keratoplasty can be a good option.

Surgical techniques for therapeutic keratoplasty may need to be adapted according to the extent and location of the infection/perforation. Large corneal-scleral grafts may be needed in some cases. In patients with noninfectious ocular surface disease and perforations, avoiding further host tissue removal can be advantageous, and innovative techniques such as small DSAEK grafts combined with amniotic membrane pack can be considered.

Complex Endothelial Keratoplasty

Endothelial keratoplasty in eyes with abnormal anterior segment structures—in particular the absence of a stable lens-iris diaphragm, the presence of filtering devices, extensive anterior synechiae, poor visualization, and abnormal posterior surface—can be much more challenging and result in worse outcomes.[4] Both DMEK and DSAEK are doable in most cases, and selection of the technique is individualized to each patient, with consideration of the anatomy, visual potential, and surgeon's comfort.

Techniques such as air fill, topical glycerin, epithelial debridement, and use of intraoperative OCT can aid in cases of poor visualization. Consider IOL fixation when needed to re-establish lens-iris diaphragm and repositioning shunts to the sulcus or posterior segment to reduce contact with the graft. Modification of the insertion technique or use of SF_6, tube tamponade, or ligation may be required in some cases. In eyes with hypotony and poor attachment despite rebubbling, fixation sutures can be attempted. Anterior segment OCT can also help identify abnormalities in the posterior corneal surface that can affect graft attachment.[3]

Keratoplasty in Patients With Glaucoma

Uncontrolled IOP is a significant risk factor for endothelial failure, as is the presence of a glaucoma drainage device or the development of hypotony. Every attempt should be made to ensure optimal IOP control prior to surgery, and patients with glaucoma should be counseled of their higher risk of graft failure.[5]

References

1. Fink N, Stark WJ, Maguire MG, et al. Effectiveness of histocompatibility matching in high-risk corneal transplantation: a summary of results from the Collaborative Corneal Transplantation Studies. *Cesk Oftalmol.* 1994; 50(1):3-12.

2. Stulting RD, Summers KD, Cavanagh HD, et al. Penetrating keratoplasty in children. *Ophthalmology* 1984; 91:1222-1230.

3. Tan DTH, Janardhanan P, Zhou H, et al. Penetrating keratoplasty in Asian eyes: the Singapore Cornea Transplant Study. *Ophthalmology* 2008; 115(6):975-982.e.1.

4. Siddiqui A, Chamberlain WD. Descemet membrane endothelial keratoplasty in complex eyes. *Curr Opin Ophthalmol.* 2022; 33(4):324-331.

5. Saini C, Davies EC, Chodosh J, Shen LQ. Glaucoma in patients with endothelial keratoplasty. *Cornea* 2022; 41(12):1584-1599.

Management of Graft Complications

Ashiyana Nariani MD MPH

NOTES

Descemet Stripping Only: No Graft, No Problem!

Kathryn Colby MD PhD

Fuchs endothelial corneal dystrophy (FECD) affects up to 4% of patients in the United States and is the most common indication for corneal transplantation, accounting for approximately 35% of the transplants done in the U.S. each year. Despite having been described over 100 years ago, FECD remains an enigmatic disease. Multiple different mechanisms have been suggested to play a role in its underlying pathophysiology, including oxidative stress, mitochondrial dysfunction, unfolded protein response, and epithelial-mesenchymal transition. Numerous genetic mutations have been associated with FECD, although the vast majority of cases in White patients manifest a trinucleotide repeat expansion on chromosome 18.[1] While there is ongoing work to develop medical therapies for FECD, this remains a surgical disease. In 2023, Descemet membrane endothelial keratoplasty (DMEK) is the preferred corneal transplant technique for the majority of FECD cases. DMEK is a safe and effective surgical technique, with generally rapid visual recovery and low risks of immunologic rejection.

Over 10 years ago, multiple lines of evidence suggested that the endothelium in FECD might be capable of self-rejuvenation. These included isolated case reports of corneal clearance after inadvertent removal of Descemet membrane,[2] after detachment of endothelial grafts,[3,4] or after destruction of the corneal endothelium by cryotherapy.[5] The first series of deliberate stripping of Descemet membrane as a treatment for endothelial dysfunction showed inconsistent results.[6] Our Descemet stripping only (DSO) series was the first to demonstrate a reasonable rate of success.[7] This finding has since been replicated by numerous groups, leading to a recent editorial and a meta-analysis about DSO.[8-10] An expanding body of evidence suggests that topical Rho kinase inhibitors can facilitate corneal clearance after DSO.[8,11,12] This talk will review the current state of DSO, the indications/contraindications for this procedure, and future directions for nongraft therapies for treatment of FECD.

References

1. Sarnicola C, Farooq A, Colby KA. Fuchs endothelial corneal dystrophy: update on pathogenesis and future directions. *Eye Contact Lens.* 2019; 45(1):1-10.

2. Koenig SB. Long-term corneal clarity after spontaneous repair of an iatrogenic descemetorhexis in a patient with Fuchs dystrophy. *Cornea* 2013; 32:886-888.

3. Shah RD, Randleman JB, Grossniklaus HE. Spontaneous corneal clearing after Descemet's stripping without endothelial replacement. *Ophthalmology* 2012; 119:256-260.

4. Dirisamer M, Yeh RY, van Dijk K, et al. Recipient endothelium may relate to corneal clearance in Descemet membrane endothelial transfer. *Am J Ophthalmol.* 2012; 154:290-296.

5. Koizumi N, Okumura N, Ueno M, et al. Rho-associated kinase inhibitor eye drop treatment as a possible medical treatment for Fuchs corneal dystrophy. *Cornea* 2013; 32:1167-1170.

6. Bleyen I, Saelens IEY, van Dooren BTH, van Rij G. Spontaneous corneal clearing after Descemet's stripping. *Ophthalmology* 2013; 120:215.

7. Borkar DS, Veldman PV, Colby KA. Treatment of Fuchs endothelial dystrophy by Descemet stripping without endothelial keratoplasty. *Cornea* 2016; 35:1267-1273.

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. Colby K. Descemet stripping only for Fuchs endothelial corneal dystrophy: will it become the gold standard? *Cornea* 2022; 41(3):269-271.

10. Din N, Cohen E, Popovic M, et al. Surgical management of Fuchs endothelial corneal dystrophy: a treatment algorithm and individual patient meta-analysis of Descemet stripping only. *Cornea* 2022; 41(9):1188-1195.

11. 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.

12. Kinoshita S, Colby KA, Kruse FE. A close look at the clinical efficacy of rho-associated protein kinase inhibitor eye drops for Fuchs endothelial corneal dystrophy. *Cornea* 2021; 40(10):1225-1228.

Endothelial Cell Injection Therapy

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Unmet Need

Disorders of the corneal endothelial cells (CECs), such as Fuchs endothelial corneal dystrophy (FECD) or pseudophakic bullous keratopathy, alter the structure of the Descemet membrane and impair the function of CEC, leading to visual impairment and ultimately edema and scarring. Current treatment options such as Descemet-stripping automated endothelial keratoplasty (DSAEK), Descemet membrane endothelial keratoplasty (DMEK), and penetrating keratoplasty require the use of a donor tissue. However, for every 70 diseased eyes, there is only 1 donor cornea available. Thus, Kinoshita and coworkers developed a novel technique, which requires only 1 donor cornea for more than 100 recipient eyes.

Principle of Cell Injection Therapy

As shown in Figure 1, cell injection therapy utilizes cultured donor cells that are injected into the anterior chamber of a patient. While the surgery is simple, the critical step is the expansion, starting from juvenile endothelial cells, to achieve a balance between young proliferating cells and mature, fully differentiated cells (Figure 1A). Thus, several sets of biomarkers have been identified that help to monitor the level of differentiation. Among other factors, the presence of inhibitors of the Rho-associated kinase in the culture system seems to be indispensable for the success of the procedure.

Once cells are obtained from a specialized laboratory, surgery can be performed under topical anesthesia, first removing diseased cells from the Descemet membrane (Figure 1B), then injecting about 300-µL cell suspension containing about 1 million cultured human CECs (CHCECs) (Figure 1C) and asking the patient to lie with the face down for 3 hours, thus allowing the cells to accumulate in the corneal curvature (Figure 1D).

Prerequisite for Success and Safety

Development of ex vivo expansion of CHCECs first required ground-breaking work in the laboratory to ensure that nearly 100% of the cells used for transplantation acquire and maintain the mature effector cell type. Secondly, the mode of transportation of viable cells from a central laboratory to a given surgical location was established. Most importantly, preclinical trials had to ensure that grafted cells would not only survive in the anterior chamber but neither proliferate nor invade the trabecular meshwork nor dedifferentiate into an unwanted phenotype.

Clinical Experience

In the first clinical trial, 11 eyes of 11 Japanese patients with bullous keratopathy underwent intracameral injection of CHCECs in which less than 90% of cells were of the pure type. By 24 weeks after injection, 10 of 11 eyes had restoration of corneal transparency, with a CHCEC density of greater than 1000 cells/mm^2. At 3 years, 10 eyes had clear corneas with improved BCVA, and the mean endothelial count of 1257 cells/mm^2 at 5 years was close to that reported in eyes undergoing DMEK or DSAEK.

In the second trial, 7 eyes underwent intracameral injection of suspensions of cultures in which more than 90% of cells were mature. At 4 weeks follow-up, corneal epithelial edema
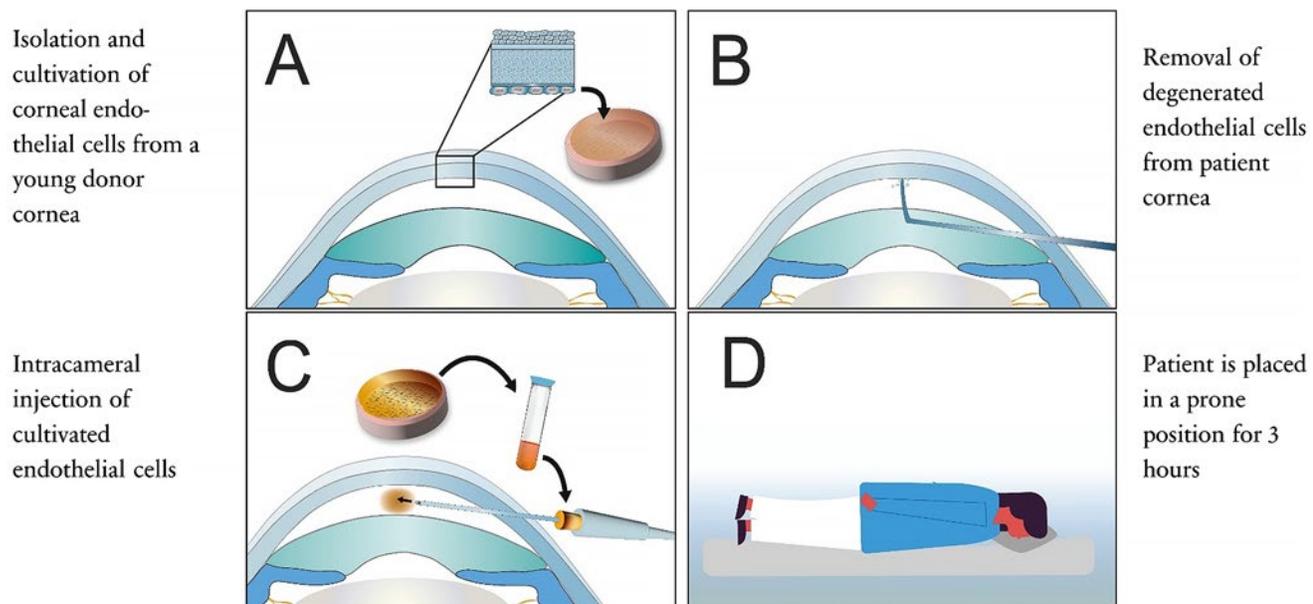

Figure 1. Principle of cultured human corneal endothelial cell injection therapy.

completely cleared in all 7 eyes, compared to only 4 of the 11 eyes by that time in the first trial. Additionally, endothelial cell density was more than 3000 cells/mm^2 at 24 weeks, with little decay over 3 years. Meanwhile, Kinoshita et al performed the CHCEC injection procedure in 65 eyes of 65 subjects across 3 clinical trials conducted in Japan, including a first-in-human trial (*n* = 38), an endothelial cell dose ranging trial (*n* = 15), and a confirmatory trial (*n* = 12).

An additional 89 procedures have been performed in Central America, showing similar safety and efficacy outcomes as seen in Japan.

Toward Routine Clinical Application

Aurion Biotech, a clinical-stage biotech company based in Seattle, Cambridge, and Tokyo, has received regulatory approval for cell injection therapy in Japan (in March 2023) and has also made cell injection available to patients enrolled in studies in Central America to prove that cells cultured in Kyoto could be used in the Americas. The company is planning clinical trials in the United States this year in order to obtain USFDA approval.

Limitations and Perspective

Several indications have been investigated, and one of the most promising seems to be pseudophakic bullous keratopathy. So far surgery has been utilizing intact Descemet membrane for cell attachment and migration; thus, removal of the Descemet (with guttae), which would be necessary in FECD, has not been undertaken. Thus, the relationship between injected cells and bare stroma needs to be clarified.

Without doubt, cell injection therapy is a milestone in corneal surgery. According to Kinoshita, it can be concluded that "this novel procedure offers the potential to completely transform the treatment paradigm for corneal endothelial disease, with an ample supply of fully differentiated, allogeneic corneal endothelial cells; a minimally invasive, elegant procedure; and potentially less onerous recovery for patients."

Selected Readings

1. Kinoshita S, Koizumi N, Ueno M. Injection of cultured cells with a ROCK inhibitor for bullous keratopathy. *N Engl J Med*. 2018; 378(11):995-1003.

2. Numa K, Imai K, Ueno M, et al. Five-year follow-up of first 11 patients undergoing injection of cultured corneal endothelial cells for corneal endothelial failure. *Ophthalmology* 2021; 128(4):504-514.

3. Ueno M, Toda M, Numa K, et al. Superiority of mature differentiated cultured human corneal endothelial cell injection therapy for corneal endothelial failure. *Am J Ophthalmol*. 2022; 237:267-277.

4. Hamuro J, Ueno M, Asada K, et al. Metabolic plasticity in cell state homeostasis and differentiation of cultured human corneal endothelial cells. *Invest Ophthalmol Vis Sci*. 2016; 57(10):4452-4463.

Lamellar Keratectomy
Alternative to Keratoplasty
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I. Introduction

Cornea opacities limiting vision have traditionally been treated using keratoplasty. Despite excellent outcomes, there are risks with keratoplasty, both short and long term. In certain cases, lamellar keratectomy may be utilized as an alternative, either with manual dissection or laser-assisted keratectomy.

II. Superficial Keratectomy

   A. Epithelial disease: anterior basement membrane dystrophy, Salzman nodules

   B. A little deeper: band keratopathy, superficial scarring

   C. Way deep: stromal diseases and dystrophies

III. Bowman Keratectomy With or Without Transplant

IV. Stromal Keratectomy

V. Alternatives and Concurrent Treatments to Visual Rehab

   A. Haze treatment

   B. Scleral lenses

VI. Conclusion

Selected Readings

1. Ashena Z, Niestrata M, Tavassoli S. Management of stromal cornea dystrophies; review of the literature with a focus on phototherapeutic keratectomy and keratoplasty. *Vision (Basel)* 2023; 7(1):22.

2. Fasolo A, Galzignato A, Pedrotti E, et al. Femtosecond laser-assisted implantation of cornea stroma lenticule for keratoconus. *Int Ophthalmol.* 2021; 41(5):1949-1957.

3. Dapena I, Parker JS, Melles GRJ. Potential benefits of modified corneal tissue grafts for keratoconus: Bowman layer "inlay" and "onlay" transplantation and allogenic tissue ring segments. *Curr Opin Ophthalmol.* 2020; 31(4):276-283.

Corneal Inlays and Onlays

Bowman Layer Transplantation for the Treatment of Advanced Keratoconus: From Inlay to Onlay Transplantation

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Please note that this study has been submitted to the American Journal of Ophthalmology *and is currently under review.*

Introduction

Keratoconus (KC) is a complex, multifactorial ecstatic cornea disease. Traditional invasive treatments for advanced KC with their accompanying intra- and postoperative risks have been well described over the last decades. In 2011, we introduced a less invasive approach for this challenging group of patients, the Bowman layer (BL) inlay transplantation—positioning a donor BL within a stromal pocket—as an alternative to penetrating keratoplasty and deep anterior lamellar keratoplasty in the treatment of advanced KC.[1-5] Given the surgical difficulty of dissecting thin keratoconic corneas with advanced disease, we more recently introduced BL onlay transplantation, in which the donor BL is positioned onto a cornea after removal of its surface epithelium.[6,7] The main drawback of BL inlay transplantation was intraoperative perforation into the anterior chamber, potentially producing a iatrogenic hydrops.[1] With the BL onlay transplantation, this complication is eliminated since the corneal integrity is not compromised, except for the epithelial debridement; no corneal incisions or dissections are required.[6]

When successful, BL inlay showed major advantages over conventional transplantation techniques like deep anterior lamellar keratoplasty and perforating keratoplasty, both of which carry a well-known complication profile, even more so in advanced KC, in which the recipient peripheral rim may show progressive thinning after transplantation.[1] Treatment of end-stage KC may be further complicated by its variety in clinical presentation—for example, the preoperative keratometric readings, ocular surface reactivity, extent of the cone, etc. These challenges also have to be faced when a BL onlay transplantation is anticipated, since steeper cones should require more downward "redressing" and atopic patients may have a higher risk of epithelial defects or incomplete re-epithelialization.

The aim of the current study was therefore to describe which clinical approach(es) were chosen to manage 21 cases with advanced KC (see Table 1) and compare a less advanced KC (Group 1: preoperative maximum keratometry [Kmax] < 69 D) and a more advanced KC (Group 2: preoperative Kmax ≥ 69 D). In each individual case, the main objective of performing BL onlay transplantation was to obtain corneal stabilization in order to allow continued contact lens wear and/or to preserve the contact lens visual acuity.

Table 1. Baseline Characteristics of the Total Study Group and the 2 Subgroups (Groups 1 and 2) Based on Preoperative Kmax Values

	Total Group (*n* = 21)	Group 1 (Kmax < 69 D; *n* = 7)	Group 2 (Kmax ≥ 69 D; *n* = 14)
Patients/eyes (*n*)	21/20[a]	7/7	14/14
Patient age (± SD) (years)	33.9 ± 10	33.4 ± 8	34.1 ± 11
Female/male (*n*)	6 (30%)/14 (70%)	3 (43%)/4 (57%)	3 (21%)/11 (79%)
KC grading (*n*)[b]			
Stage III	5 (24%)	4 (57%)	1 (7%)
Stage III-IV	8 (38%)	2 (29%)	6 (43%)
Stage IV	8 (38%)	1 (14%)	7 (50%)
Patient risk factors for KC (*n*)			
Atopy	6 (29%)	1 (14%)	5 (36%)
Allergy	18 (86%)	6 (86%)	12 (86%)
Asthma	6 (29%)	1 (14%)	5 (36%)
Persistent eye rubbing		4 (57%)	8 (57%)
Persistent scar formation	5 (24%)	2 (29%)	3 (21%)

Abbreviations: KC, keratoconus; Kmax, maximum keratometry; SD, standard deviation.

[a]One patient's eyes were in different groups.

[b]Based on Pentacam topographic KC classification.

Methods

Twenty-one eyes of 20 patients underwent BL onlay grafting. After removing the epithelium, a single or double BL-graft was "stretched" onto the corneal surface, allowed to dry-in, and a soft bandage lens was placed until the graft was re-epithelialized (video). Best spectacle- and/or best contact lens-corrected VA (BSCVA/BCLVA), corneal tomography, and postoperative complication rates were analyzed for the total group and 2 subgroups (Group 1: preoperative Kmax < 69 D, *n* = 7; Group 2: preoperative Kmax ≥ 69 D, *n* = 14). Follow-up ranged from 6 to 36 months (mean: 21 ± 11 months).

Results

All 21 surgeries were uneventful. The total study group showed well-integrated BL grafts (see Figures 1 and 2). Pre- and postoperative outcomes of the procedures are summarized in Table 2. For the entire group, Kmax changed from 76 ± 12 D preoperatively to 72 ± 9 D at 6-36 months postoperatively (*P* = .015). Kmax decreased by 6 D in Group 2 (*P* = .002) but did not change in Group 1 (see Figure 3). Average BSCVA remained stable for Group1 and improved from 0.8 ± 0.4 preoperatively to 0.4 ± 0.2 logMAR postoperatively in Group 2 (*P* = .032, see Figure 4). BCLVA remained stable (*P* > .05). Within the first postoperative weeks, 2 eyes required a BL graft repositioning after inadvertent bandage lens removal, and 4 eyes underwent BL retransplantation for incomplete re-epithelialization. One eye underwent BL regrafting 12 months postoperatively after traumatic corneal erosion. All eyes showed a completely re-epithelialized graft at the last available follow-up.
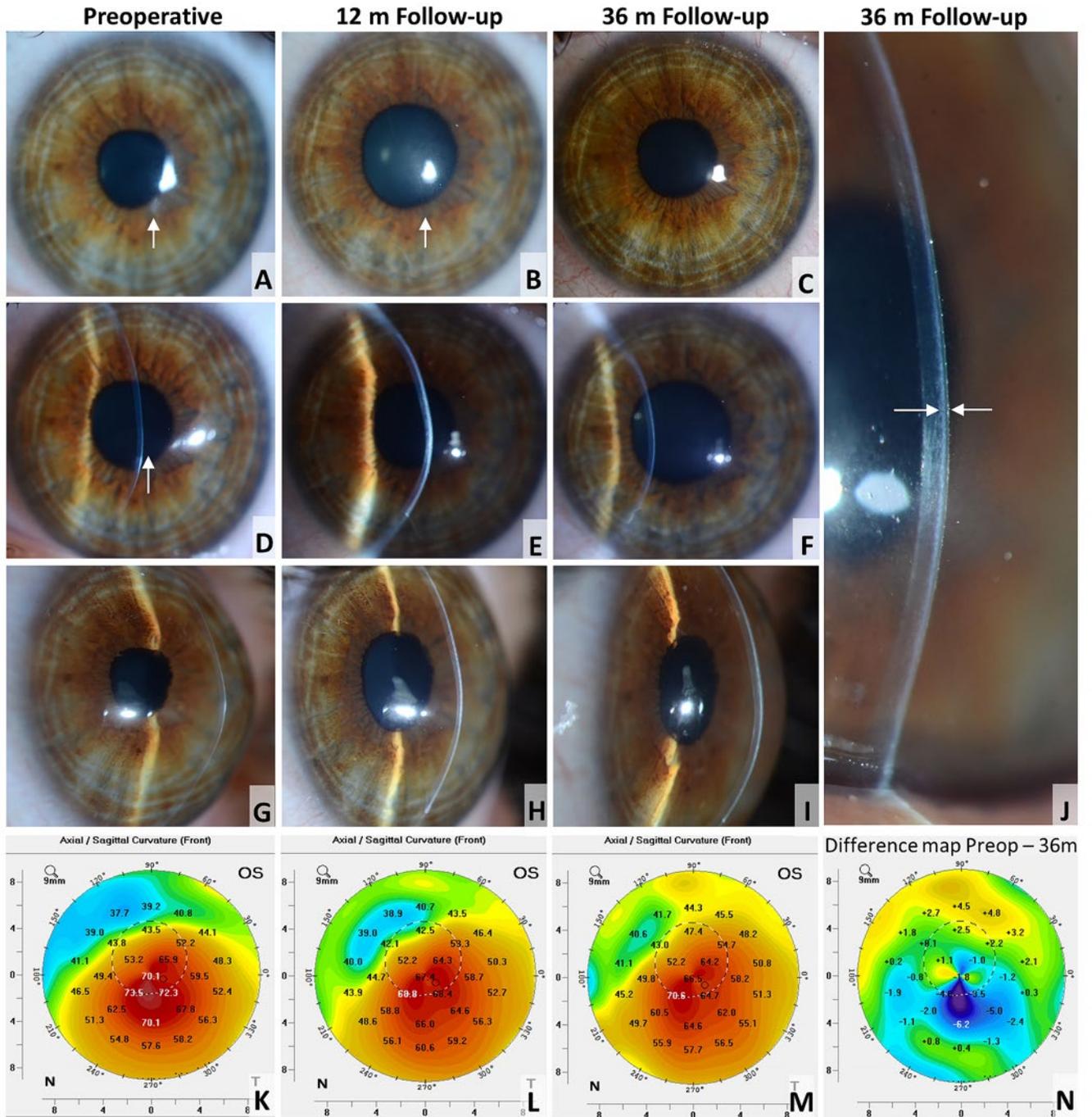
Figure 1. Slit-lamp images and topographic maps before and after Bowman layer (BL) onlay transplantation. Slit-lamp images (A-I) show an eye (Group 2) before (A, D, G) surgery and at 12 months (B, E, H) and 36 months (C, F, I) postoperatively. The enlarged slit-lamp image in (J) shows the integrated BL graft (white arrows) 36 months after BL onlay transplantation. Topographic maps (K-M) show the flattening of the anterior corneal topography from preoperative (K) to postoperatively (L, M), with (N) demonstrating the difference map between preoperative and 36 months postoperatively.
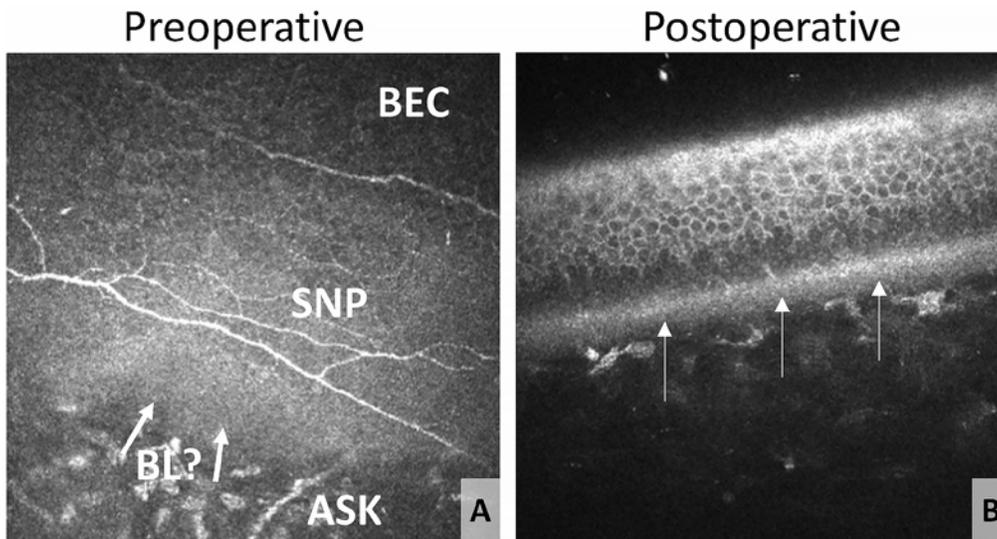
Figure 2. Confocal microscopy images focusing on the anterior central cornea before and after Bowman layer (BL) onlay transplantation. In the preoperative confocal image (A), basal epithelial cells (BEC), sub-basal nerve plexus (SNP), and anterior stromal keratocytes (ASK) are clearly visible prior to BL onlay transplantation, while the BL (white arrows) seems to be absent in this area. In the confocal microscopy image after BL onlay transplantation, the hyperreflective line (white arrows) located between the basal epithelial cells and the anterior stromal keratocytes most likely corresponds to the integrated BL graft.

Table 2. Clinical Outcomes After Bowman Onlay for the Total Study Group and Groups 1 and 2

	Total Group (*n* = 21)	Group 1 (Kmax < 69 D; *n* = 7)	Group 2 (Kmax ≥ 69 D; *n* = 14)	*P*-value (Group 1 vs. Group 2)
BSCVA, mean ± SD logMAR				
Preoperative	0.7 ± 0.4 (*n* = 21)	0.6 ± 0.4 (*n* = 7)	0.8 ± 0.4 (*n* = 14)	0.393
1m	0.7 ± 0.4 (*n* = 21)	0.7 ± 0.4 (*n* = 7)	0.7 ± 0.4 (*n* = 14)	0.798
6m	0.6 ± 0.4 (*n* = 19)	0.7 ± 0.4 (*n* = 6)	0.5 ± 0.3 (*n* = 13)	0.397
Last available FU	0.5 ± 0.3 (*n* = 21)	0.6 ± 0.4 (*n* = 7)	0.4 ± 0.2 (*n* = 14)[a]	0.468
BCLVA, mean ± SD logMAR				
Preoperative	0.3 ± 0.2 (*n* = 18)	0.4 ± 0.3 (*n* = 6)	0.3 ± 0.2 (*n* = 12)	0.597
1m	0.2 (*n* = 2)	0.2 (*n* = 1)	0.3 (*n* = 1)	-
6m	0.3 ± 0.4 (*n* = 15)	0.5 ± 0.5 (*n* = 2)	0.3 ± 0.4 (*n* = 13)	0.483
Last available FU	0.2 ± 0.2 (*n* = 20)	0.2 ± 0.3 (*n* = 7)	0.2 ± 0.2 (*n* = 13)	0.608
Kmax, mean ± SD				
Preoperative	75.8 ± 12 (*n* = 21)	61.8 ± 5 (*n* = 7)	82.8 ± 7 (*n* = 14)	0.001
1m	71.4 ± 11 (*n* = 21)[a]	59.6 ± 6 (*n* = 7)	77.4 ± 8 (*n* = 14)[a]	0.001
6m	73.3 ± 11 (*n* = 19)	61.1 ± 5 (*n* = 6)	78.9 ± 7 (*n* = 13)[a]	0.001
Last available FU	72.2 ± 9 (*n* = 21)[a]	62.6 ± 5 (*n* = 7)	77.1 ± 7 (*n* = 14)[a]	0.001
Kmean, mean ± SD				
Preoperative	62.3 ± 9 (*n* = 21)	52.4 ± 7 (*n* = 7)	67.3 ± 6 (*n* = 14)	0.001
1m	60.3 ± 8 (*n* = 21)[a]	52.3 ± 7 (*n* = 7)	64.3 ± 6 (*n* = 14)[a]	0.001
6m	60.5 ± 9 (*n* = 19)	51.0 ± 7 (*n* = 6)	65.0 ± 7 (*n* = 13)	0.001
Last available FU	60.6 ± 8 (*n* = 21)	52.8 ± 7 (*n* = 7)	64.6 ± 5 (*n* = 14)[a]	0.001
TPT, mean ± SD				
Preoperative	336 ± 80 (*n* = 21)	359 ± 58 (*n* = 7)	324 ± 88 (*n* = 14)	0.353
1m	351 ± 83 (*n* = 21)	376 ± 61 (*n* = 7)	339 ± 91 (*n* = 14)	0.334
6m	348 ± 83 (*n* = 19)	395 ± 54 (*n* = 6)	327 ± 87 (*n* = 13)	0.098
Last available FU	360 ± 56 (*n* = 21)	372 ± 64 (*n* = 7)	354 ± 53 (*n* = 14)	0.508
CCT, mean ± SD				
Preoperative	392 ± 87 (*n* = 21)	393 ± 39 (*n* = 7)	391 ± 104 (*n* = 14)	0.966
1m	407 ± 74 (*n* = 20)	412 ± 47 (*n* = 7)	403 ± 87 (*n* = 13)	0.800
6m	417 ± 82 (*n* = 19)	416 ± 50 (*n* = 6)	417 ± 95 (*n* = 13)	0.990
Last available FU	420 ± 42 (*n* = 21)[a]	413 ± 74 (*n* = 7)	423 ± 65 (*n* = 14)	0.737

Abbreviations: *n* = number of eyes; Kmax, maximum keratometry; BSCVA, best spectacle-corrected VA; m, month; FU, follow-up; BCLVA, best contact lens-corrected VA; Kmean, mean keratometry; TPT, thinnest point of the cornea; CCT, central corneal thickness.

[a]Statistically significant change compared to preoperative. *P*-values in bold indicate a significance difference.
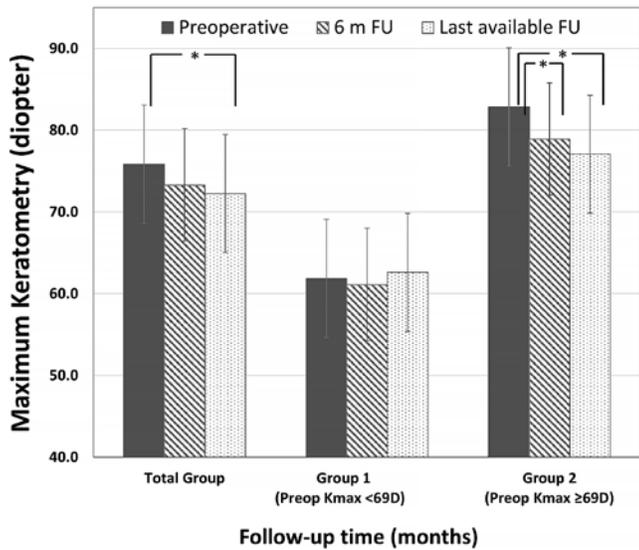
Figure 3. Bar graphs showing the maximum keratometry for the total study group and the 2 subgroups. Mean maximum keratometry (Kmax, in diopters) is displayed for the total study group and the less advanced (Group 1) and the more advanced keratoconus group (Group 2) before surgery and for the 6 months and the last available follow-up (FU). Vertical lines present standard deviations. Asterisk denotes statistically significant differences between preoperative and postoperative mean Kmax values.

BL onlay grafting was designed as an alternative to BL inlay transplantation to avoid the technical challenges of the mid-stromal dissection of the latter technique and to avoid the risk of perforation during the dissection in these very steep and thin corneas. While BL onlay grafting sidesteps the risk of perforation that is inherent both to the BL inlay and deep anterior lamellar keratoplasty procedures[8] and avoids any suture-related complications observed after the deep anterior lamellar keratoplasty procedure, postoperatively some other complications were noted. The greatest challenge after BL onlay transplantation turned out to be proper corneal re-epithelialization. Particularly, in the first BL onlay cases, decentering of the graft and incomplete epithelialization were observed. In most cases this was triggered by either unintentional or premature removal of the bandage lens. Furthermore, for this same group, some peripheral graft notches (see Figure 5) were observed, despite a full integration of the BL onlay graft. This phenomenon seems most likely to be caused by the difference in thickness of the BL grafts in combination with a mechanical force of a non-customized bandage lens on the graft edges, which could lead to a variable re-epithelialization and wound healing response. Longer-term follow-up will be needed to corroborate the observed stabilization effect on the corneal curvature. It should also be kept in mind that the presented cases constitute the learning curve of this new technique, and some of the observed postoperative complications may be preventable in the future with more experience and the use of customized bandage lenses.
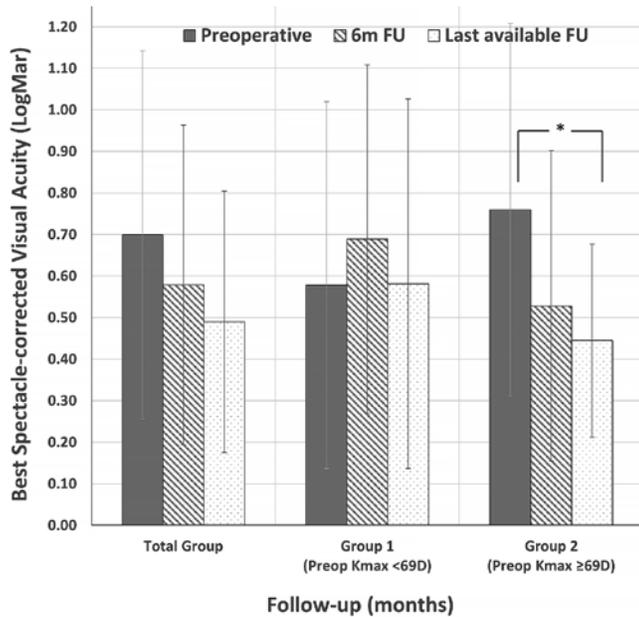

Figure 4. Bar graphs showing the best spectacle-corrected visual acuity (BSCVA) for the total study group and the 2 subgroups. Mean BSCVA (in logMAR) is displayed for the total group and the less advanced (Group 1) and more advanced keratoconus (Group 2) groups before surgery and for the 6 months and last available follow-up (FU). Vertical lines represent standard deviations. Asterisk denotes a statistically significant difference between BSCVA before surgery and at the last available follow-up for Group 2.

Figure 5. Slit-lamp images and topographic maps before and after Bowman layer (BL) onlay transplantation. The preoperative slit-lamp images (A, C) of an eye (Group 2) show an opacification (orange arrows) that shows some clearance 36 months after BL onlay transplantation (B, D; orange arrows). For the same eye, the BL onlay graft presented postoperatively with an inferior peripheral notch (E, F), which is highlighted with white dot lines. The graft notch appeared at around 1 month postoperatively and was still visible at the 7-month follow-up (E) without any further progression until the 36-month follow-up (F). Topographic maps (G, H) show a flattening in anterior curvature from pre- to postoperatively, with the difference map (I) displaying the flattening effect between preoperative and 36 months postoperatively.

Conclusions

BL onlay grafting is a completely extraocular, minimally invasive surgical technique providing stabilization and up to 6 D of corneal flattening in eyes with advanced progressive KC, allowing for continued (scleral) contact lens wear and therefore preserving the BCLVA. BL onlay transplantation has the potential to flatten and stabilize far advanced keratoconic corneas without the risk of severe intraoperative complications since the technique is completely extraocular and has a minimal risk of allograft rejection due to the acellular character of an isolated BL membrane. Especially for patients with very steep and thin corneas who still have a subjectively acceptable visual performance, this new technique may be a promising alternative for this challenging group of patients compared to more invasive treatment options.

References

1. Van der Star L, van Dijk K, Vasiliauskaite I, et al. Long-term outcomes of Bowman layer inlay transplantation for the treatment of progressive keratoconus. *Cornea* 2022; 41(9):1150-1157.

2. van Dijk K, Parker J, Tong CM, et al. Midstromal isolated Bowman layer graft for reduction of advanced keratoconus: a technique to postpone penetrating or deep anterior lamellar keratoplasty. *JAMA Ophthalmol.* 2014; 132:495-501.

3. van Dijk K, Parker JS, Baydoun L, et al. Bowman layer transplantation: 5-year results. *Graefes Arch Clin Exp Ophthalmol.* 2018; 256:1151-1158.

4. Dapena I, Parker J, Melles GRJ. Potential benefits of modified corneal tissue grafts for keratoconus: Bowman layer 'inlay' and 'onlay' transplantation, and allogenic tissue ring segments. *Curr Opin Ophthalmol.* 2020; 31:276-283.

5. Luceri S, Parker J, Dapena I, et al. Corneal densitometry and higher order aberrations after Bowman layer transplantation: 1-year results. *Cornea* 2016; 35(7):959-966.

6. Dapena I, van der Star L, Groeneveld-van Beek E, et al. Bowman layer onlay grafting: proof-of-concept of a new technique to flatten corneal curvature and reduce progression in keratoconus. *Cornea* 2021; 41(12)1561-1566.

7. Groeneveld-van Beek EA, Parker J, Lie JT, et al. Donor tissue preparation for Bowman layer transplantation. *Cornea* 2016; 35:1499-1502.

8. Gadhvi KA, Romano V, Fernández-Vega Cueto L, et al. Femtosecond laser-assisted deep anterior lamellar keratoplasty for keratoconus: multi-surgeon results. *Am J Ophthalmol.* 2020; 220:191-202.

Video Synopsis

Bowman Layer Onlay Transplantation: Surgical Technique

The BL onlay grafting was performed under retrobulbar anesthesia and was combined with a manual anterior stromal superficial keratectomy by using surgical sponges and a hockey stick knife to remove the recipient epithelium. The stromal bed was then thoroughly irrigated with BSS to remove any epithelial remnants. Once the corneal surface was completely denuded, a single (*n* = 2) or a "double" BL graft (*n* = 19), stained with 0.06% trypan blue (VisionBlue; DORC International), was carefully positioned onto the apex of recipient cornea with the epithelial side of the graft facing upward. To further shape the cornea and ensure adherence of the BL graft onto the anterior stromal surface without folds, the graft was carefully unfolded by tapping with thin forceps and/or with syringes and a 30-gauge cannula, first on one side until completely unfolded and subsequently on the other side. Once the BL graft was completely flattened on the corneal stroma, it was carefully stretched at the periphery and "ironed" across the entire graft surface by using a second thin forceps and/or a bent 30-gauge cannula to squeeze out any interface fluid. The edges of the graft were further dried with sterile eye spears all along the periphery. The BL transplant was then allowed to dry-in and left to attach to the recipient's cornea, without using any sutures, for 45 minutes. At the end of the surgery a bandage lens was placed to cover the BL graft.

What's New in Artificial Corneas

Esen Karamursel Akpek MD

Approximately 12.7 million individuals suffer from loss of corneal clarity worldwide.[1] Corneal blindness is particularly sad as it is a preventable cause of blindness affecting younger individuals from lower socioeconomic backgrounds.[2] Replacement of the opaque cornea has the potential to restore vision. Although donor corneal transplantation is known to be one of the most successful tissue/organ transplantations and leads to excellent outcomes in many individuals, two major challenges have yet to be addressed.

Availability of donor corneas is extremely limited outside of developed countries, where corneal blindness is disproportionately more prevalent. This is largely due to perishability of the tissues and requirements of the eye banking system that make the surgery costly.[3] Currently, approximately half of all the world's corneal transplantations are performed in the United States alone.[4]

Penetrating keratoplasty has been the mainstay of donor corneal transplantation for decades. At the turn of the 21st century, widespread adoption of endothelial keratoplasty to address corneal edema due to Fuchs dystrophy or postsurgical bullous keratopathy, and later introduction of corneal crosslinking for early treatment of keratoconus, led to significant changes in the modern keratoplasty landscape.[5,6] While almost all (98.8%) corneal transplants in the United States were penetrating keratoplasties in 2000, this percentage decreased to one-third (33.1%, approximately 15,000 cases) in 2021.[7] Prior graft failure is now the leading preoperative indication for penetrating keratoplasty in North America and Europe.[7] The outcomes of penetrating keratoplasty have historically been excellent, with graft survival rates between 99% and 93% at 5 to 25 years, respectively. However, today's results might not be as favorable due to a greater proportion of penetrating keratoplasty surgeries being high-risk cases or repeat grafts.[8] Unfortunately, with each subsequent transplant, the likelihood of vision restoration decreases.

Prosthokeratoplasty, also known as artificial corneal transplantation, is considered in cases where donor corneal transplantation does not have a reasonable expectation of success. The Boston type I keratoprosthesis (Massachusetts Eye and Ear Infirmary, Boston, MA) is the most commonly implanted prosthetic corneal device globally. Despite the superior outcomes of this device in comparison to repeat penetrating keratoplasty in patients with complex corneal problems, there has been a downward trend in the number of devices implanted yearly, largely due to worsening outcomes over longer-term follow-up, even with frequent postoperative care. These postoperative complications are unfortunately due to design flaws that cannot be completely overcome. Due to the rigidity and compact nature of its materials (polymethyl methacrylate and titanium), the Boston type I keratoprosthesis does not integrate into the recipient corneal stroma, which poses a risk for intraocular invasion of micro-organisms through the perioptic space. In addition, the perpetual micro-oscillation of the device within the corneal stroma with every blink triggers inflammation, leading to sterile keratolysis, retroprosthetic membrane, iris synechiae,

and glaucoma. Glaucoma is the most common cause of permanent and profound loss of vision after Boston keratoprosthesis. Moreover, a donor cornea as a carrier is a requisite, which limits its usage in the developing world, where corneal blindness is most prevalent. Even in the United States, keratoprosthesis is infrequently offered to patients who have previously failed a donor graft. Approximately 200 Boston type 1 keratoprosthesis surgeries are performed yearly in the United States, whereas the number of repeat donor corneal transplantations is approximately 3500, emphasizing that the biomedical research needed to develop newer artificial corneal devices is relevant.

Although yet to be invented, an ideal artificial cornea could potentially solve both the access and donor failure issues. The features of an ideal artificial cornea have been detailed previously.[5] In summary, the device should be fully synthetic and should (1) bond with the recipient cornea, (2) bend with the recipient cornea, and (3) blend with the recipient cornea.

This presentation will focus on the artificial corneal devices currently under clinical investigation, with particular emphasis on the 3 most important aspects: (1) biointegration/bioadhesion features of the material, (2) anatomical structure of the device, and (3) surgical technique for implantation.

References

1. Flaxman SR, Bourne RRA, Resnikoff S, et al. Global causes of blindness and distance vision impairment 1990-2020: a systematic review and meta-analysis. *Lancet Glob Health.* 2017; 5:e1221-e1234.

2. Oliva MS, Schottman T, Gulati M. Turning the tide of corneal blindness. *Indian J Ophthalmol.* 2012; 60:423-427.

3. Gain P, Jullienne R, He Z, et al. Global survey of corneal transplantation and eye banking. *JAMA Ophthalmol.* 2016; 134:167-173.

4. Mathews PM, Lindsley K, Aldave AJ, Akpek EK. Etiology of global corneal blindness and current practices of corneal transplantation: a focused review. *Cornea* 2018; 37:1198-1203.

5. Bigan G, Puyraveau M, Saleh M, et al. Corneal transplantation trends in France from 2004 to 2015: a 12-year review. *Eur J Ophthalmol.* 2018; 28(5):535-540.

6. Flockerzi E, Maier P, Böhringer D, et al. Trends in corneal transplantation from 2001 to 2016 in Germany: a report of the DOG-section cornea and its keratoplasty registry. *Am J Ophthalmol.* 2018; 188:91-98.

7. Eye Bank Association of America. 2021 Eye Banking Statistical Report. Published online April 2022.

8. Claesson M, Armitage WJ. Clinical outcome of repeat penetrating keratoplasty. *Cornea* 2013; 32(7):1026-1030.

9. Hicks CR, Fitton JH, Chirila TV, Crawford GJ, Constable IJ. Keratoprostheses: advancing toward a true artificial cornea. *Surv Ophthalmol.* 1997; 42:175-189.

United for Sight: A Vision for Effective Advocacy

2023 Cornea Subspecialty Day

Lee A Snyder MD

Action Requested: *Donate to strengthen ophthalmology's legislative voice and protect patients and your profession*

Please respond to your Academy colleagues and join the community that advocates for ophthalmology: OPHTHPAC, the Surgical Scope Fund, and your State Eye PAC. Ensure you and your patients are heard by our nation's lawmakers by giving to each of these funds.

Where and How to Contribute

During AAO 2023 in San Francisco, please contribute to OPHTHPAC® and Surgical Scope Fund at one of our two convention center booths or online. You may also donate via phone to both funds by sending two texts:

- Text **MDEYE** to **41444** for OPHTHPAC
- Text **GIVESSF** to same number (**41444**) for the Surgical Scope Fund

We also encourage you to support our congressional champions by making a personal investment via OPHTHPAC Direct, a unique and award-winning program that lets *you decide* who receives your political support.

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.

Why Should You Contribute?

Member support of the Academy's advocacy funds—OPHTHPAC and the Surgical Scope Fund—powers our advocacy efforts at the federal and state levels. When you give to OPHTHPAC, you give ophthalmology a voice on Capitol Hill on critical issues like Medicare payment, optometry's scope expansion efforts in the VA, and prior authorization and step therapy burdens. When you give to the Surgical Scope Fund, you're funding our efforts to fight dangerous optometric surgery initiatives at the state level, whenever and wherever they arise. And finally, when you give to your state Eye PAC, you help elect officials in your state who will support the interests of you and your patients. Giving to *each* of these three funds is essential to helping protect sight and empower lives.

Protecting quality patient eye care and high surgical standards is a "must" for everybody. 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 thrive and patients receive optimal care.

OPHTHPAC for Federal Advocacy

OPHTHPAC is the Academy's award-winning, non-partisan political action committee representing ophthalmology on Capitol Hill. OPHTHPAC works to build invaluable relationships with our federal lawmakers to garner their support on issues such as:

- **Improving** the Medicare payment system, so ophthalmologists are fairly compensated for their services, and working to prevent impending payment cuts of 3.36% scheduled to take effect in 2024
- **Securing** payment equity for postoperative visits, which will increase global surgical payments
- **Stopping** optometry from obtaining surgical laser privileges in the veterans' health-care system
- **Increasing** patient access to treatment and care by reducing prior authorization and step therapy burdens

Academy member support of OPHTHPAC makes all this possible. Your support provides OPHTHPAC with the resources needed to engage and educate Congress on our issues, helping advance ophthalmology's federal priorities. Your support also ensures that we have a voice in helping shape the policies and regulations governing the care we provide. Academy member support of OPHTHPAC is the driving factor behind our advocacy push, and we ask that you get engaged to help strengthen our efforts and make sure that the ophthalmology specialty has a seat at the table for the critical decisions being made that affect our ability to care for our patients.

At the Academy's annual Mid-Year Forum, the Academy and the Cornea Society ensure a strong presence of cornea specialists to support ophthalmology's priorities. As part of this year's meeting, the Cornea Society supported participation of fellowship trainees via the Academy's Advocacy Ambassador Program. During Congressional Advocacy Day, they visited Members of Congress and their key health care staff to discuss ophthalmology priorities. The Cornea Society remains a crucial partner with the Academy in its ongoing federal and state advocacy initiatives.

Surgical Scope Fund (SSF) for State Advocacy

The Surgical Scope Fund works in partnership with state ophthalmic societies to protect patient safety from dangerous optometric surgery proposals through advocacy. The Fund's mission is to ensure surgery by surgeons, and since its inception, it has helped 43 state/territorial ophthalmology societies reject optometric scope-of-practice expansions into surgery.

Support for the Surgical Scope Fund from ophthalmic interest societies like the Cornea Society makes our advocacy efforts possible. These efforts include research, lobbyists, political organization, polling, advertising, social media, digital commu-

Surgical Scope Fund	OPHTHPAC®	State EyePAC
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 state House, Senate and governor
	Support for candidates for U.S. Congress	
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: Personal contributions are limited to $5,000. Corporate contributions are confidential.	Contribution limits vary based on state regulations.
Individual, practice, corporate, and organization		
Contributions are 100% confidential.	Personal contributions of $199 or less and all corporate contributions are confidential. Personal contributions of $200 and above are public record.	Contributions are on the public record depending upon state statutes.

nications, and grassroots mobilization. However, the number of states facing aggressive optometric surgery legislation each year has grown exponentially. And with organized optometry's vast wealth of resources, these advocacy initiatives are becoming more intense— and more expensive. That's why ophthalmologists must join together and donate to the Surgical Scope Fund to fight for patient safety.

The Academy's Secretariat for State Affairs thanks the Cornea Society for its past support of the Surgical Scope Fund and looks forward to its 2023 contribution. The Cornea Society's support for the Surgical Scope Fund is essential to fighting for patient safety and quality eye care!

State Eye PAC

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.

Support Your Colleagues Who Are Working on Your Behalf

Two Academy committees made up of your ophthalmology colleagues are working hard on your behalf. 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 used to protect Surgery by Surgeons during scope battles at the state level.

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Simplex vs. Zoster

Sadeer B Hannush MD

I. Herpes Simplex Virus (HSV) Keratitis

   A. Primary ocular infection

      1. Clinical presentation

         a. Unilateral blepharon-conjunctivitis

         b. Possible epithelial keratitis

         c. Rarely stromal keratitis or uveitis

         d. Differential diagnosis (DDX): adenoviral conjunctivitis

      2. Laboratory evaluation

         a. Serological testing helpful when negative

         b. Vesicle scrapings may be tested by cytology for presence of HSV antigen.

         c. Conjunctival scrapings or impression cytology may be analyzed by culture, antigen detection, or polymerase chain reaction.

      3. Management

         a. Self-limiting

         b. May consider topical or oral antiviral

   B. Recurrent ocular infection

      1. Blepharoconjunctivitis

         a. Self-limiting

         b. Role of topical or oral antivirals

      2. Epithelial keratitis

         a. Punctate keratitis

         b. Dendritic keratitis

         c. Geographic ulcer

         d. DDX for dendriform epithelial lesions: varicella zoster virus (VZV), *Acanthamoeba*, adenovirus, Epstein-Barr (EBV), epithelial regeneration line, neurotrophic, topical meds, deposits (iron, amiodarone, Fabry disease)

         e. Management

            i. topical: trifluridine, ganciclovir, acyclovir

           ii. oral: acyclovir, valacyclovir, famciclovir

      3. Stromal keratitis

         a. Interstitial

            i. non-necrotizing

           ii. necrotizing

           iii. DDX: VZV, *Acanthamoeba*, syphilis, EBV, mumps, Lyme, sarcoidosis, Cogan syndrome

         b. Disciform: primarily an endotheliitis

         c. Management

            i. topical steroids

           ii. topical antivirals

           iii. role of oral antivirals

      4. Iridocyclitis/trabeculitis

         a. Granulomatous or nongranulomatous

         b. Increased IOP

         c. Iris atrophy

      5. Long-term sequelae

         a. Recurrent disease: infectious or inflammatory

         b. Neurotrophic

         c. Corneal scarring

         d. Uncontrollable IOP

      6. Medical/surgical treatment

         a. Role of oral antiviral

         b. Role of punctal occlusion

         c. Role of tarsorrhaphy

         d. Role of amnion

         e. Role of tissue adhesive

         f. Role of penetrating and deep anterior lamellar keratoplasty

   C. Herpes Eye Disease Studies (HEDS)

      1. HEDS I

         a. Do topical corticosteroids treat stromal keratitis? Yes, with faster resolution.

         b. Is addition of oral acyclovir to treatment with topical trifluridine and corticosteroids helpful in healing stromal keratitis? No.

         c. Is adding oral acyclovir to topical corticosteroids and trifluridine helpful in treating HSV iridocyclitis? Possibly . . . but not statistically significant.

2. HEDS II

   a. Does oral acyclovir prevent patients with epithelial keratitis from developing stromal keratitis and iritis? No, but oral acyclovir reduced by 50% the probability of return of a more severe form of stromal keratitis.

   b. Does oral acyclovir prophylaxis minimize HSV recurrences? Yes.

   c. What triggers HSV recurrences? Some triggers suspected, but none identified.

D. Conclusions

  1. HSV keratitis may have various manifestations.

  2. Treatment should be directed to:

   a. Inhibition of viral replication

   b. Control of inflammation

   c. Managing long-term sequelae

II. Herpes Zoster

A. Definition

Herpes zoster ophthalmicus (HZO)is caused by the VZV, which has reactivated from its dormant state in the dorsal ganglion cells of the central nervous system. From there it may travel along neurons to the sensory axons of the skin to form vesicular lesions.

B. Signs

  1. Erythematous skin lesions with macules, papules, vesicles, pustules, and crusting lesions in the distribution of the trigeminal nerve

  2. Hutchinson's sign is defined as a skin lesion at the tip of the nose. This is a strong predictor of ocular inflammation and corneal denervation in HZO.

  3. An immunocompromised patient is more likely to have a prolonged illness, more likely to recur, and more likely to develop myelitis and vasculopathy. Environmental factors (stress, sunlight, systemic infection, and contact lens wear) can act as triggers.

C. Medical therapy

  1. Acyclovir, famciclovir, or valacyclovir

  2. Topical steroids for stromal keratitis and uveitis

  3. In scleritis, retinitis, and optic neuritis, consider systemic steroids.

  4. Pain may be managed by nonsteroidals, gabapentin, and occasionally narcotics.

  5. Neuropathic pain responds to amitriptyline, which can decrease the incidence of postherpetic neuralgia (PHN).

D. Herpes zoster virus vaccine: Shingrix

  1. Non-live recombinant vaccine made from a glycoprotein subunit and a combination of immune boosting adjuvants

  2. FDA approved for healthy adults > 50 years of age

  3. FDA approved for immunocompromised adults > 19 years of age

  4. Preferred vaccine for preventing shingles and related complications

  5. No waiting period with history of shingles as long as nonactive

  6. Recommended for adults who previously received Zostavax

  7. Two intramuscular injections separated by 2-6 months

  8. Immune response > 5 years

E. Zoster Eye Disease Study (ZEDS)

  1. 2017-2023

  2. Multicenter, randomized, placebo-controlled clinical trial to determine whether prolonged use of valacyclovir reduces complications of HZO

III. Herpes Simplex and Zoster: What's New?

A. Repurposed antiviral compounds

B. Off-label use of other medications

C. Gene therapy

D. Botanicals: algae, fungus, oils may be synergistic with antivirals

E. Newer herpes vaccines

  1. Animal studies looking at immunogenicity generated by mRNA vaccines (those encoding VZVgE antigen and others)

  2. BionTech/Pfizer working on new mRNA vaccine for herpes zoster

  3. Moderna working on mRNA vaccines for HSV, VZV, and checkpoint cancer

Bacteria vs. Fungus

Prashant Garg MD

I. Introduction

Corneal opacity resulting from corneal infections is an important cause of unilateral vision loss in low- and mid-income countries. In 1996 Gonzales et al reported the annualized incidence of corneal ulceration in Madurai District, Tamil Nādu, South India, to be 11.3 per 10,000 population, which is 10 times the incidence reported in the United States. Applying this incidence rate to all of India gives an estimated 840,000 new cases of corneal ulcer occurring annually in India alone.

The epidemiology of the condition varies among nations. Contact lens use is a predominant risk factor for corneal ulcer in developed nations, while trauma is the most important risk factor in developing nations. In both scenarios the process starts with corneal epithelial changes. A simple epithelial irregularity gets secondarily infected to result in corneal ulcer.

It is now established that simple measures, such as use of chloramphenicol, reduce the risk not only of bacterial but also of fungal infections. Even for established infections, timely diagnosis of the causative micro-organisms and institution of appropriate medical management results in reduction of morbidity and vision loss.

During this talk the presenter will present:

- How good clinical examination helps establish etiological diagnosis

- Different laboratory tools available for identifying causative micro-organisms and their pros and cons

- How to start treatment in a case of bacterial and fungal keratitis

II. Etiological Diagnosis

What features help differentiate bacterial from fungal etiology? (See Table 1)

III. Laboratory Tools

What laboratory tools are available for identifying causative micro-organisms, and what are their pros and cons?

A. Is laboratory diagnosis essential?

Before we discuss different laboratory tools, let us understand the need for laboratory diagnosis. There is enough evidence suggesting that clinical features of microbial keratitis may vary considerably, and no one sign can be considered absolutely pathognomonic of a particular etiologic agent. Therefore, ophthalmologists are advised to perform laboratory workup to identify causative micro-organisms.

B. Classical laboratory workup

The classical laboratory workup comprises corneal scraping performed with Kimura spatula or number 15 surgical blade and subjecting the scraped material to microscopic examination using various stains. At the same time, the material is also inoculated on various solid and liquid culture media. The microscopic examination coupled with the growth on culture media subjected to a variety of biochemical reactions helps identify the causative micro-organism. The growth is also subjected to antimicrobial susceptibility tests to determine drug susceptibility or resistance in vitro.

Pros and cons of the classical microbiology workup are mentioned in Table 2.

Sensitivity and specificity of various staining techniques in identifying bacteria, fungi, and *Acanthamoeba* are shown in Table 3.

Table 1. Clinical Differentiation of Bacterial and Fungal Etiology

Characteristics	Bacterial Keratitis	Fungal Keratitis
Duration of symptoms	Short (days)	Longer (week)
Onset of symptoms	Acute	Slow
Symptoms	Severe	Mild to moderate
Clinical signs	Dense yellow to white infiltrate with tissue necrosis	• Cotton wool infiltrate with hyphate edges • Pigmented infiltrate • Satellite lesions
Progression	Rapid	Slow

C. What are other recent advances in the bedside diagnosis of corneal ulcer?

1. In vivo confocal microscopy: The technique allows direct visualization of causative organisms. The pros and cons of the technology are enumerated in Table 4.

2. Molecular methods: These tests are based on amplifying and rendering detectable minute quantities of microbial DNA in pathological specimens. Pros and cons of the technology are enumerated in Table 5.

3. Machine learning: Image processing and machine learning are being evaluated to differentiate bacterial and fungal keratitis. This modality is in its infancy, but its evaluation is gaining momentum. Convolutional neural network with ensemble learning showed excellent performance in discriminating fungal from bacterial keratitis compared with single architecture models.

Table 2. Pros and Cons of the Classical Microbiology Workup

Pros	Cons
Visualization of organisms on microscopy and immediate primary information for starting appropriate treatment	Need for a well-equipped laboratory
Definitive micro-organism identification by characterization of culture growth	Need for support from trained microbiologist
Antibiotic susceptibility	Additional cost
Helps identify rare or uncommon organisms	Sensitivity and specificity of microscopy and poor rate of positive yield on culture

Table 3. Sensitivity and Specificity of Various Staining Techniques for Identifying Bacteria, Fungi, and *Acanthamoeba*

Smears	Bacteria		Fungi		*Acanthamoeba*	
	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
Gram 3442	56.6	97.8	89.8	93.7	73.3	99.8
Giemsa 2774	ND	ND	85.2	96.1	72.2	99.8
KOH + CFW 2555	ND	ND	90.6	94.3	84.0	99.8

Abbreviations: ND, not done; KOH + CFW, potassium hydroxide + calcofluor white.

Table 4. Pros and Cons of Confocal Microscopy

Pros	Cons
Rapid in-clinic test, prompt treatment initiation	Bacteria are too small to be visualized.
Helps assess depth of infection	Patient cooperation and patience are essential.
Can be repeated during treatment for monitoring response	User dependent, both for acquiring and interpreting images
High sensitivity and specificity	High cost and low availability

Table 5. Pros and Cons of Molecular Methods

Pros	Cons
Relatively rapid test (2-8 hours)	High cost and low availability
Requires small amount of sample and DNA	Relatively low specificity and high false positivity
High sensitivity	Primer selection is critical; miss diagnosis if selection is incorrect
Detects both viable and nonviable organisms	Do not distinguish active from inactive infection
Helps identify new, rare, or uncommon organisms	Less robust understanding on diagnostic thresholds

IV. Treatment

How should one start treatment in cases of bacterial and fungal keratitis?

A. Empirical treatment

1. Indication: Only for small ulcers where clinical picture is not suggestive of fungal or parasitic etiology and patient can come for follow-up

2. Preferred drugs: One of the commercially available broad-spectrum antibiotics (eg, fluoroquinolone) administered in therapeutic doses

B. Treatment guided by laboratory test

1. Indications

   a. All severe cases

   b. Cases not responding to empirical therapy

   c. Clinically suspected fungal or parasitic keratitis cases

2. Preferred drugs: Based on the results of laboratory tests

   a. Antibacterial therapy

      i. combination of antibiotics covering both gram-positive and gram-negative bacteria (preferably fortified) to be modified once culture results are available

      ii. alternatively, commercially available fourth-generation fluoroquinolone

   b. Antifungal therapy

      i. natamycin 5%

      ii. alternatively, amphotericin b or voriconazole

   c. Antiparasitic therapy

      i. polyhexamethyl biguanide (PHMB) 0.02%-0.06%

      ii. chlorhexidine 0.02%

      iii. brolene

Selected Readings

1. Ung L, Bispo PJM, Shanbhag SS, Gilmore MS, Chodosh J. The persistent dilemma of microbial keratitis: global burden, diagnosis, and antimicrobial resistance. *Surv Ophthalmol*. 2019; 64:255-271.

2. Whitcher JP, Srinivasan M. Corneal ulceration in the developing world—a silent epidemic. *Br J Ophthalmol*. 1997; 81:622-623.

3. Whitcher JP, Srinivasan M, Upadhyay MP. Prevention of corneal ulceration in the developing world. *Int Ophthalmol Clin*. 2002; 42:71-77.

4. Hossain P. Microbial keratitis—the true costs of a silent pandemic? *Eye (Lond)*. 2021; 35(8):2071-2072.

5. Upadhyay MP, Karmacharya PC, Koirala S, et al. The Bhaktapur Eye Study: ocular trauma and antibiotic prophylaxis for the prevention of corneal ulceration in Nepal. *Br J Ophthalmol*. 2001; 85:388-392.

6. Rathi VM, Thokala P, MacNeil S, Khanna RC, Monk PN, Garg P. Early treatment of corneal abrasions and ulcers—estimating clinical and economic outcomes. *Lancet Reg Health Southeast Asia*. 2022; 4:100038.

7. Vaddavalli PK, Garg P, Sharma S, Sangwan VS, Rao GN, Thomas R. Role of confocal microscopy in the diagnosis of fungal and *Acanthamoeba* keratitis. *Ophthalmology* 2011; 118(1):29-35.

8. Chidambaram JD, Prajna NV, Larke NL, et al. Prospective study of the diagnostic accuracy of the in vivo laser scanning confocal microscope for severe microbial keratitis. *Ophthalmology* 2016; 123(11):2285-2293.

9. Shivshetty N, Swift T, Pinnock A, et al. Evaluation of ligand modified poly (N-isopropyl acrylamide) hydrogel for etiological diagnosis of corneal infection. *Exp Eye Res*. 2022; 214:108881.

10. Ting DSJ, Gopal BP, Deshmukh R, Seitzman GD, Said DG, Dua HS. Diagnostic armamentarium of infectious keratitis: a comprehensive review. *Ocul Surf*. 2022; 23:27-39.

11. Deng L, Lyu J, Huang H, Deng Y, Yuan J, Tang X. The SUSTech-SYSU dataset for automatically segmenting and classifying corneal ulcers. *Sci Data*. 2020; 7(1):23.

12. Qasmieh IA, Alquran H, Zyout A, Al-Issa Y, Mustafa WA, Alsalatie M. Automated detection of corneal ulcer using combination image processing and deep learning. *Diagnostics (Basel)* 2022; 12(12):3204.

13. Kuo MT, Hsu BW, Yin YK, et al. A deep learning approach in diagnosing fungal keratitis based on corneal photographs. *Sci Rep*. 2020; 10(1):14424.

14. Ghosh AK, Thammasudjarit R, Jongkhajornpong P, Attia J, Thakkinstian A. Deep learning for discrimination between fungal keratitis and bacterial keratitis: DeepKeratitis. *Cornea* 2022; 41(5):616-622.

Viral vs. *Acanthamoeba*

Jennifer Rose-Nussbaumer MD

Introduction

When treating infectious keratitis (IK), it is important to talk with the patient about their risk factors and to do a careful examination and testing to get the diagnosis right.

Viral Keratitis

Herpes simplex virus (HSV) keratitis is the most common cause of IK in the United States. It comes in 3 forms: epithelial, stromal, and endotheliitis. The epithelial form is characterized by a dendrite with terminal bulbs, geographic ulcers, and ghost dendrite underneath; the ulcer stains with fluorescein, but edges stain with rose bengal. Stromal keratitis, a hypersensitivity reaction, is characterized by stromal edema and thinning, white blood cells, keratic precipitates, iritis, neovascularization, and limbitis. Endotheliitis, also known as disciform keratitis, is characterized by corneal edema and keratic precipitates.

The Herpetic Eye Disease study found (1) acyclovir or trifluridine with steroids for stromal keratitis, (2) topical steroids are good for stromal but not epithelial disease, and (3) prophylactic oral acyclovir prevents recurrent stromal keratitis and uveitis.

Varicella zoster virus (VZV) keratitis is a reactivation of varicella zoster virus in dorsal root ganglion, V1 distribution of the trigeminal nerve. Vaccination in recent years has resulted in changing demographics. VZV keratitis is characterized by a vesicular rash, Hutchinson sign, microdendritic "pseudo-dendrites," neurotrophic ulcers, iritis, and elevated eye pressure. More unusual manifestations such as optic neuritis, retinitis, and CN palsy are also possible. The Zoster Eye Disease Study is exploring long-term oral antiviral suppression for zoster keratitis.

Danger!

What are the danger signs that this could be something other than viral keratitis? *Acanthamoeba* keratitis can also present with a corneal dendrite. Mistaking it for viral keratitis results in treatment delays and inappropriate use of topical steroids. History of contact lens wear, hot tub or other water exposure, recent trauma, pain out of proportion with exam should always alert you to the possibility of *Acanthamoeba*.

Acanthamoeba

Diagnosis of *Acanthamoeba* keratitis is achieved with corneal scraping, Giemsa stain, non-nutrient agar with *E. coli* overlay. In vivo confocal microscopy can give an "optical biopsy," and directed polymerase chain reaction and metagenomic deep sequencing are other options.

Treatment of *Acanthamoeba* keratitis includes epithelial debridement that debulks the organism load and increases drug penetration. Topical antiseptics, such as topical biguanides including chlorhexidine/polyhexamethylene biguanide 0.02%-0.06%, are usually first line as they are effective against trophozoites and cysts. One can consider adding a topical diamidine such as brolene 0.1% if the case is not improving. Therapy typically lasts 6 months or longer. Other possible treatments include oral alkylphosphocholines (miltefosine) and surgical intervention such as rose bengal photodynamic therapy, lamellar keratectomy, deep anterior lamellar keratoplasty, or Gunderson flap.

Not Your Usual Keratitis
Think EBV, CMV, *Microsporidia*

Vishal Jhanji MD FRCOphth

Infectious corneal ulceration remains the leading cause of corneal blindness worldwide. Advancements in diagnostics, the availability of new antimicrobials, and the ability to share data among experts all aim to achieve better treatment outcomes.

Atypical microbial keratitis is caused by micro-organisms not commonly encountered in clinical practice. These cases pose challenges in the identification of causative organisms with standard diagnostic techniques. There is a delay in the initiation of appropriate therapies, consequently resulting in worse clinical outcomes and visual prognosis.

This case-based presentation will highlight the current management and available evidence to diagnose and treat some of the commonly encountered atypical forms of microbial keratitis. The focus will be on cytomegalovirus endotheliitis, Epstein keratitis, and microsporidial keratitis.

Cytomegalovirus Endotheliitis

The diagnosis of cytomegalovirus endotheliitis requires a high degree of clinical suspicion and identification of signs on slit-lamp examination. These include sectoral corneal edema and coin-shaped or linear keratic precipitates in addition to ocular hypertension. Diagnostic anterior chamber tap should be considered early in the course of the disease in cases with persistent anterior chamber inflammation not responding to corticosteroids or antiviral treatment. Access to a microbiology or virology laboratory is very useful in determining the diagnosis. Treatment consists of oral valganciclovir and topical ganciclovir.

Epstein Keratitis

Three main forms of Epstein-Barr virus–associated keratitis have been described. The first type consists of subepithelial infiltrates resembling Thygeson superficial punctate keratitis. The second form is bilateral, interstitial nummular ring-shaped keratitis that has been described in young patients in the context of systemic mononucleosis. The third form is a multifocal, nonsuppurative keratitis involving the full thickness of the peripheral cornea with corneal neovascularization. The role of antivirals in the treatment of Epstein keratitis is not fully defined. Oral acyclovir treatment could be used just as it is used for herpetic eye disease.

Microsporidial Keratitis

Microsporidia are waterborne opportunistic pathogens commonly spread through contaminated water. It is largely endemic to southeast and south Asian countries. Microsporidia can cause epithelial keratoconjunctivitis, deep stromal keratitis, scleritis, and endophthalmitis. Microsporidial keratoconjunctivitis is said to be associated with immunosuppression, whereas deep stromal keratitis is largely seen among immunocompetent. The disease often mimics viral, fungal, and bacterial keratitis. There has been no consensus on the management of microsporidial keratitis. Fluoroquinolones, biguanides, diamidines, antifungals, and corticosteroids have been used to manage infection. Deeper infection often necessitates surgical intervention.

Novel Methods to Deliver Antimicrobials
Novel Corneal Medication Delivery

Allan Steigleman MD

I. Alternative Methods of Ocular Drug Delivery

Ocular drug delivery is a challenge, with topical medication disadvantages including low efficiency and poor compliance. Improved methods are sought after.

A. Contact lenses

B. Nanoparticles

C. Polymer inserts

D. Intrastromal injections

E. Surface devices

F. Punctal devices

II. Current Progress

Clinical trials are under way for several delivery methods. Viable commercial products are available for some alternative methods, but others have had limited success to date.

III. The Future

Future collaborative efforts in unconventional partnerships may be fruitful.

Selected Readings

1. Vandervoort J, Ludwig A. Ocular drug delivery: nanomedicine applications. *Nanomedicine* 2007; 2:11-21.

2. Patel NK, Jain NK. Ocular drug delivery: challenges and opportunities. *J Control Release*. 2014; 188:3-18.

3. Mukherjee P, Mitra AK. Nanoparticles for ocular drug delivery: a review. *Int J Pharm*. 2017; 530:17-32.

4. Meza-Rios A, Navarro-Partida J, Armendariz-Borunda J, et al. Therapies based on nanoparticles for eye drug delivery. *Ophthalmol Ther*. 2020; 9:1-14.

5. Graf TP, Qiu SY, Varshney D, et al. A scalable platform for fabricating biodegradable microparticles with pulsatile drug release. *Adv Mater*. 2023; 35(22):e2300228.

6. Gadziński P, Froelich A, Wojtyłko M, Białek A, Krysztofiak J, Osmałek T. Microneedle-based ocular drug delivery systems—recent advances and challenges. *Beilstein J Nanotechnol*. 2022; 13:1167-1184.

7. Gause S, Hsu KH, Shafor C, Dixon P, Powell KC, Chauhan A. Mechanistic modeling of ophthalmic drug delivery to the anterior chamber by eye drops and contact lenses. *Adv Colloid Interface Sci*. 2016; 233:139-154.

Noninfectious Keratitis

Hajirah N Saeed MD

NOTES

Case Presentations: Mystery Keratitis

Jennifer M Enright MD, Anvesh Annadanam MD, Tania E Padilla Conde MD, Minh T Nguyen MD, Leyla Saricay Yavuz MD and Rachel A Dandar MD

NOTES

Amniotic Membrane for Ocular Surface Reconstruction

Darren G Gregory MD

The use of amniotic membrane (AM) in ocular surface surgery has increased significantly in scope and volume over the last 2 decades, and there is extensive literature on the subject. This talk provides a practical guide for the use of AM, with examples highlighting specific points and techniques.

Both clinically and in vitro, AM has been shown to have significant anti-inflammatory, anti-scarring, and anti-angiogenic activity.[1,2] These effects help adjacent normal tissue, if available, to repopulate injured areas before inflammation and scar tissue take over the healing process. AM is commercially available in North America in 2 forms, cryopreserved and freeze-dried/dehydrated. The dehydrated form offers the convenience of not requiring refrigeration for storage. Unfortunately, there is limited literature describing its clinical use. One recent article, however, has shown it to be equivalent to cryopreserved AM for the treatment of persistent corneal epithelial defects.[3] Due to the current paucity of literature on the dehydrated version compared to the extensive literature on the cryopreserved form, this talk focuses mainly on clinical uses of cryopreserved AM.

Cryopreserved AM comes as a sheet in a variety of sizes, with the stromal surface attached to a piece of carrier paper. The AM is easy to free up from the paper using nontoothed forceps. Once fully freed up, it can be slid onto the ocular surface. The stromal surface, which was adherent to the carrier paper, is generally placed against the surface of the area being treated. The stromal surface can always be identified by using a cellulose sponge, which will stick to the stroma but not the epithelial surface. Cryopreserved AM is also available as a sheet of AM stretched across the lumen of a 16-mm ring that can be placed on the eye like a contact lens. This form of AM serves a protective role similar to that of a therapeutic contact lens, while also providing added anti-inflammatory and healing benefits in eyes with a disordered ocular surface. The AM portion covers only the cornea and perilimbal conjunctiva, however, and does not protect the fornices or tarsal conjunctiva. Inflammation or epithelial defects in those areas would need to be treated with a separate sheet of AM.

Depending on the therapeutic goals of the treatment and the ultimate fate of the membrane, the use of AM in ocular surface surgery can be divided into 2 broad categories: use as a temporary patch or as a permanent graft. As a temporary patch, AM is used to cover and protect injured areas of conjunctival or corneal epithelium. Its presence is temporary and helps promote the migration and healing of epithelium underneath the AM. The membrane is sloughed off or removed once the epithelium underneath has healed. As a permanent graft, the goal is to get epithelium to grow over the top of the AM rather than underneath it. The AM remains beneath the healed epithelium as part of the subepithelial substrate.

The membrane can be fixated over the affected areas with sutures or fibrin glue. Fibrin glue is generally quicker and causes less discomfort than sutures, but it does not fixate the membrane very effectively in areas where there is intact epithelium. Placing a large-diameter soft contact lens over top of the AM

sheet and performing a temporary partial tarsorrhaphy can decrease the chances of the membrane dislodging and may also slow the degradation of the AM. When AM is used as a permanent graft, it is important that it remain in place long enough for epithelialization to occur over the top of the AM sheet.

Temporary Patch Uses

- Persistent corneal epithelial defect without ulceration
- Acute Stevens-Johnson syndrome
- Acute graft versus host disease
- Acute chemical burns
- After superficial keratectomy
- High-risk corneal transplantation

Permanent Graft Uses

- Persistent corneal epithelial defects with ulceration
- Scar or tumor excision
- Band keratopathy
- Bullous keratopathy
- Symblepharon excision and fornix reconstruction
- Pterygium excision
- Leaking filtration blebs

As a permanent graft, AM helps facilitate epithelial healing with decreased scarring in areas where epithelium and subepithelial tissues have been damaged or removed. In the excision of noncancerous conjunctival lesions, such as a pterygium or scar tissue, it is generally preferable to use the patient's own conjunctival tissue for grafting. This may not always be feasible, though, if the area to be covered is large or if prior surgeries or disease have caused a relative lack of normal conjunctival tissue that may be harvested for grafting purposes.

For nonhealing corneal epithelial defects with ulceration, multiple layers of AM "pancakes" may be stacked in the defect to fill the hole.[4] The pancakes may be secured using sutures or fibrin glue. The area must then be covered with a larger sheet of AM and/or a contact lens to keep the pancakes from dislodging.

Conclusions

Knowledge of AM's uses and limitations is crucial for surgeons who treat disease of the ocular surface. Whether used as a temporary patch or as a permanent graft, AM has proven to be an extremely helpful tool in ocular surface surgery. The ability to fixate AM with fibrin glue has increased surgical efficiency and patient comfort. AM's ability to suppress inflammation has been shown to effectively prevent the potentially disastrous damage that can occur in acute Steven-Johnson syndrome.[5] AM has limitations, however. It does not provide epithelium, so a source of healthy epithelium from grafts or adjacent normal epithelium is needed for optimal healing.[6] Other disordered aspects of the ocular surface, such as dryness and exposure, must also be addressed to optimize outcomes.

References

1. Dua HS, Gomes JAP, King AJ, Maharajan VS. The amniotic membrane in ophthalmology. *Surv Ophthalmol*. 2004; 49:51-77.

2. Tseng SC, Espana EM, Kawakita T, et al. How does amniotic membrane work? *Ocul Surf*. 2004; 2:177-187.

3. Sell S, De La Presa M, Thakur S, et al. Comparison of persistent epithelial defect treatment with sutureless cryopreserved and dehydrated amniotic membrane. *Am J Ophthalmol*. 2023; 251:32-42.

4. Solomon A, Meller D, Prabhasawat P, et al. Amniotic membrane grafts for nontraumatic corneal perforations, descemetoceles, and deep ulcers. *Ophthalmology* 2002; 109:694-703.

5. Gregory DG. Treatment of acute Stevens-Johnson syndrome and toxic epidermal necrolysis using amniotic membrane: a review of 10 consecutive cases. *Ophthalmology* 2011; 118:908-914.

6. Kheirkhah A, Blanco G, Casas V, et al. Surgical strategies for fornix reconstruction based on symblepharon severity. *Am J Ophthalmol*. 2008; 146:266-275.

Simple Limbal Epithelial Transplantation

Swapna S Shanbhag MBBS

I. Introduction

The limbus contains limbal epithelial stem cells that are responsible for corneal epithelial regeneration. When the limbus is damaged by either trauma or inflammation, this leads to a state known as limbal stem cell deficiency (LSCD). When LSCD is unilateral, a small section of limbus can be harvested from the contralateral healthy eye and transplanted to the diseased eye. This technique of limbal stem cell transplantation (LSCT) is known as simple limbal epithelial transplantation (SLET). This innovative surgical technique has been gaining popularity over the last decade. It is different from previously described techniques, such as conjunctival limbal autograft (CLAU) and cultivated limbal epithelial transplantation (CLET) since it does not require harvesting a larger section of the limbus, does not require harvesting conjunctival tissue, and also does not require a stem cell laboratory for expansion of the epithelial cells, thus making this procedure more accessible.

SLET can be autologous (harvesting limbus from the contralateral healthy eye) in patients with unilateral LSCD, or it can be allogeneic (harvesting limbus from a living-related donor or from a cadaveric donor cornea). Allogeneic SLET requires long-term topical and systemic immunosuppression.

SLET is ideally done in the chronic phase after LSCD is established, but allogeneic SLET is also performed in acute ocular burns for early epithelization in order to salvage the globe and prevent sight-threatening complications.

II. Indications

Like all forms of LSCT, SLET should be performed only in a wet eye.

A. Autologous SLET: ocular burns, iatrogenic LSCD after ocular surface squamous neoplasia (OSSN) excision, iatrogenic LSCD after multiple surgical interventions, recurrent pterygia

B. Allogeneic: ocular allergy, Stevens-Johnson syndrome (SJS), ocular mucous membrane pemphigoid (MMP)

III. Preoperative Considerations

A. Ensure that the eye is wet.

B. Ensure all adnexal pathologies are corrected (entropion, trichiasis, lagophthalmos).

C. Perform anterior segment OCT to ensure that the underlying corneal stroma is relatively clear.

IV. Surgical Technique and Modifications

A. Only LSCD in the recipient eye: Perform SLET alone.

B. LSCD with symblepharon: Perform SLET with conjunctival autograft harvested from the contralateral eye with limbal biopsy.

C. LSCD with underlying full-thickness corneal scar: First perform SLET, followed by lamellar/ penetrating keratoplasty as a sequential procedure.

V. Clinical Outcomes of Autologous SLET

A. Anatomical success rate (completely epithelialized avascular cornea): 78% at 1.5 years

B. Functional success rate (2-line improvement in BCVA): 69% at 1.2 years

C. Long-term anatomical success rate: 79% at median follow-up of 5 years

D. Long-term functional success rate: 70% at median follow-up of 5 years

E. The postoperative management, complications, management of complications, and outcomes of allogeneic SLET will also be discussed.

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. 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.

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. 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.

5. Vazirani J, Ali MH, Sharma N, et al. Autologous simple limbal epithelial transplantation for unilateral limbal stem cell deficiency: multicentre results. *Br J Ophthalmol.* 2016; 100:1416-1420.

6. Prabhasawat P, Chirapapaisan C, Ngowyutagon P, et al. Efficacy and outcome of simple limbal epithelial transplantation for limbal stem cell deficiency verified by epithelial phenotypes integrated with clinical evaluation. *Ocul Surf.* 2021; 22:27-37.

Pterygium: New Techniques for an Old Problem

Bennie H Jeng MD

A pterygium is a "wing-like" mass of fibrovascular tissue extending from the conjunctiva to the cornea. Histopathologically, pterygia demonstrate elastotic degeneration of collagen of the substantia propria and normal, acanthotic, hyperkeratotic, or even dysplastic epithelium. Studies have shown that the prevalence of pterygia increases as one approaches the equator, and ultraviolet exposure is a known risk factor. Rarely (0.3%-0.6%), ocular surface squamous neoplasia is found in specimens sent as pterygia.

The management of pterygia primarily involves surgical excision and prevention of recurrence. Surgical excision techniques range from bare sclera excision to primary closure or conjunctival transposition to excision with conjunctival autografts. All of these can be done with some combination of adjunctive antimitotic therapies, such as mitomycin C (MMC), and amniotic membrane grafting. Fixation of free conjunctival grafts can be achieved with sutures or with fibrin glue, or even with autologous blood.

Recurrence rates after excision of pterygia vary by technique, with conjunctival autografts seeming to have the lowest rates. Most recurrences occur within the first year. In cases of recurrence, weekly injections of 5-fluorouracil, a pyrimidine analog that interferes with DNA and RNA synthesis and antiproliferative fibroblastic properties, has been demonstrated to result in regression of fibrovascular thickness and vascularity. If recurrent pterygia need to be excised, extensive tenon excision with conjunctival autograft ± MMC is recommended.

Pigmented Tumors . . . Melanoma and Mimics

Carol L Shields MD

Pigmented Tumors of Conjunctiva

  I. Complexion-Associated Melanosis

    A. Cobblestone with microfolds

    B. Bilateral symmetric

    C. Bulbar and fornix but rarely tarsal conjunctiva

    D. Transformation into melanoma: Nearly 0%

  II. Primary Acquired Melanosis

    A. Peppery flat freckle

    B. Unilateral asymmetric

    C. Transformation into melanoma: About 10%

  III. Nevus

    A. Pigmented: 85%; cystic: 65%

    B. Typically unilateral and horizontal limbus

    C. Transformation into melanoma: <1%

  IV Melanoma

    A. Most often occurs in Fitzpatrick skin tone I or II

    B. The first surgery is the most important surgery to avoid tumor spreading. It's best to send patient to an ocular oncologist without a biopsy prior to first surgery to protect patient from tumor seeding.

C. Biomarkers

    1. Biomarkers include a panel of tests run specifically on conjunctival melanoma looking for mutations, molecular rearrangements, protein abnormalities, and other features that characterize the malignancy. There is medication to use against some biomarkers. A good example of this is BRAF mutation, in which vemurafenib and dabrafenib have been found effective.

    2. Analysis of >100 cases of conjunctival melanoma showed mutations BRAF, NRAS, ATRX, and NF1.

Selected Readings

1. Shields JA, Shields CL, Mashayekhi A, et al. Primary acquired melanosis of the conjunctiva: risks for progression to melanoma in 311 eyes. The 2006 Lorenz E Zimmerman Lecture. *Ophthalmology* 2008; 115(3):511-519.

2. Shields CL, Fasiudden A, Mashayekhi A, Shields JA. Conjunctival nevi: clinical features and natural course in 410 consecutive patients. *Arch Ophthalmol.* 2004; 122:167-175.

3. Shields CL, Yaghy A, Dalvin LA, et al. Conjunctival melanoma: features and outcomes based on the Fitzpatrick skin type in 540 patients at a single ocular oncology center. *Ophthalmic Plast Reconstr Surg.* 2020; 36:490-496.

4. Lally SE, Milman T, Orloff M, et al. Mutational landscape and outcomes of conjunctival melanoma in 101 patients. *Ophthalmology* 2022; 129:679-693.
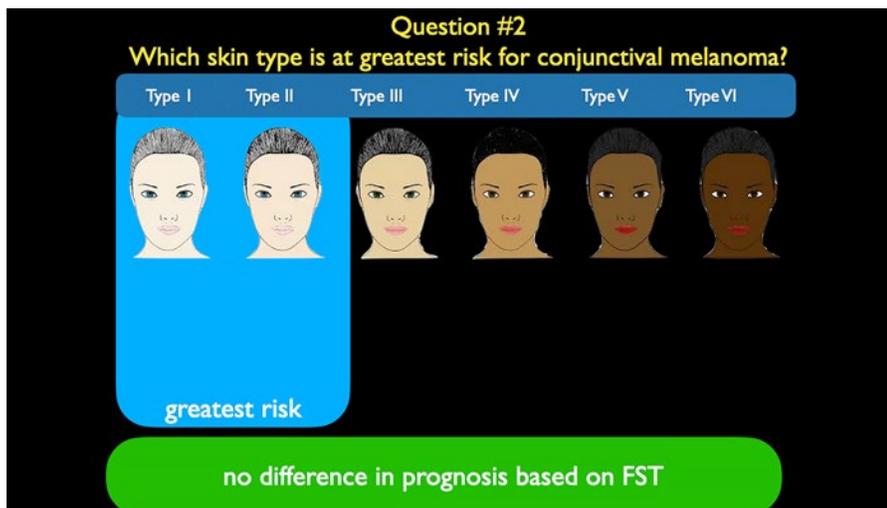
Figure 1

Ocular Surface Stem Cell Transplantation

Albert Y Cheung MD

I.   Introduction

   A.   Corneal epithelial stem cell location

   B.   Limbal stem cell deficiency (LSCD)

      1.   Etiologies

      2.   Sequelae

      3.   Medical treatments

II.   Surgical Management

   A.   Do not perform routine keratoplasty for limbal stem cell ± conjunctival deficiency.

   B.   Let patients know there are options for ocular surface reconstruction.

   C.   Why OSST is necessary

III.   Ocular Surface Stem Cell Transplantation (OSST)

   A.   Brief review of available surgical options, including donor and type of transplanted tissue (see Table 1)

      1.   Conjunctival limbal autograft (CLAU)

      2.   Living-related conjunctival limbal allograft (lr-CLAL)

      3.   Keratolimbal allograft (KLAL)

      4.   Cultivated limbal epithelial transplantation (CLET)

      5.   Simple limbal epithelial transplantation (SLET; see presentation earlier in session

      6.   Cultivated oral mucosal epithelial transplantation (COMET)

      7.   Combined procedure

         a.   CLAU + KLAL

         b.   lr-CLAL + KLAL

         c.   CLAU + lr-CLAL

   B.   Staged approach to surgery

      1.   Optimization of glaucoma, eyelid issues, ocular surface inflammation

      2.   OSST or keratoprosthesis (if not OSST candidate)

      3.   Keratoplasty

      4.   Keratoprosthesis

   C.   Surgical video example of KLAL

   D.   Surgical video example of CLAU/lr-CLAL if time permits

IV.   Allograft OSST Management

   A.   Preoperative workup: Cincinnati protocol for donor screening and selection

   B.   Perioperative: Systemic immunosuppression protocol

   C.   Postoperative management

      1.   Laboratory monitoring

      2.   Prophylactic antimicrobials

      3.   Postoperative adverse event monitoring

         a.   Rejection

         b.   Glaucoma

         c.   Persistent epithelial defects

         d.   Infectious keratitis

V.   Conclusions

Table 1

Procedure	Donor	Transplanted Tissue
Conjunctival limbal autograft (CLAU)	Fellow eye	Limbus + conjunctiva
Living-related conjunctival-limbal allograft (lr-CLAL)	Living relative eye	Limbus + conjunctiva
Keratolimbal allograft (KLAL)	Cadaver eye	Limbus + cornea
Cultivated limbal epithelial transplantation (CLET)	Fellow or cadaver eye	Limbus (ex vivo cultivated)
Simple limbal epithelial transplantation (SLET)	Fellow or cadaver eye	Limbus (in vivo expansion)
Cultivated oral mucosal epithelial transplantation (COMET)	Autologous oral mucosa	Oral epithelium
Combined procedure (CLAU + KLAL, lr-CLAL + KLAL, CLAU + lr-CLAL)	Multiple sources	Limbus/cornea + conjunctiva

Selected Readings

1. Echevarria TJ, Di Girolamo N. Tissue-regenerating, vision-restoring corneal epithelial stem cells. *Stem Cell Rev Rep.* 2011; 7;256-268.

2. Notara M, Alatza A, Gilfillan J, et al. In sickness and in health: corneal epithelial stem cell biology, pathology and therapy. *Exp Eye Res.* 2010; 90(2):188-195.

3. Deng SX, Borderie V, Chan CC, et al; International Limbal Stem Cell Deficiency Working Group. Global consensus on definition, classification, diagnosis, and staging of limbal stem cell deficiency. *Cornea* 2019; 38(3):364-375.

4. 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.

5. Holland EJ. Epithelial transplantation for the management of severe ocular surface disease. *Trans Am Ophthalmol Soc.* 1996; 94:677-743.

6. Movahedan A, Cheung AY, Eslani M, et al. Long-term outcomes of ocular surface stem cell allograft transplantation. *Am J Ophthalmol.* 2017; 184:97-107.

7. Holland EJ, Mogilishetty G, Skeens HM, et al. Systemic immunosuppression in ocular surface stem cell transplantation: results of a 10-year experience. *Cornea* 2012; 31:655-661.

Secondary Dry Eye

Anat Galor MD

Introduction

Dry eye disease (DED) is a multifactorial disease that manifests in patients with a variety of symptoms and signs, such as ocular pain, visual issues, rapid tear evaporation, and/or decreased tear production. A global health problem, it is the leading cause of optometry and ophthalmology clinic visits. The mainstay therapy for DED is artificial tears (ATs), which mimic tears and improve tear stability and properties. However, given the heterogeneity of DED, it is not surprising that ATs are not effective in all patients. When AT fails to relieve symptoms and/or signs of DED, it is critical to identify the underlying contributors to disease and escalate therapy appropriately. Possible underlying contributors include systemic diseases, meibomian gland dysfunction, anatomical abnormalities, and neuropathic dysfunction.

Background Observations

All of us who treat individuals with dry eye symptoms need to have a wide differential on potential contributors to symptoms.

Case

I will present a case of secondary dry eye in the setting of migraine and discuss contributors to symptoms and potential treatments.

Alternative IOL Options

Priyanka Sood MD

NOTES

Iris Reconstruction/Artificial Iris

Gregory S H Ogawa MD

I. Iris Suturing

A. Needles *and* sutures for iris repair

B. Surgical knots for iris repair

1. All based on the square knot

2. One or more wraps for each throw

3. Friction required for knots to hold

a. Internal suture friction

b. External tissue friction

c. External tissue pressure causing secondary internal friction

d. Combination of internal and external friction

4. Three types of intraocular knots

a. Tied and tightened externally (Siepser)

b. Tied externally; tightened with 1 intraocular instrument (Ogawa)

c. Tied and tightened with 2 intraocular instruments (Ahmed 2 coaxial forceps)

C. Main suture repair techniques

1. Simple interrupted

2. Iris gathering with multiple iris bites, yet 1 knot; large areas of pupil sphincter attenuation

3. Mattress suture: iridodialysis repair

4. Cerclage: complete, diffuse sphincter damage

D. Deciphering "single-pass 4-throw pupilloplasty": actually an interrupted, 4-wrap, single-throw Siepser knot to change to pupil shape

II. Iris Prosthesis

A. CustomFlex is the only one available in the United States and in much of the rest of the world.

1. Silicone material; custom painted to match other iris

2. Dimensions

a. 12.8 mm overall diameter

b. 0.40-mm thick centrally

c. 0.25-mm thick peripherally

d. 3.35-mm pupil size (~4-mm pupil when measured outside the eye)

3. Available without fibers for tighter fold, and in-bag placement; available with fibers for suturing strength

B. Placement locations

1. In the capsular bag with IOL

2. In the sulcus, sutured to sclera

3. In the sulcus, passive placement

4. Sutured to a scleral-fixated IOL, placed in eye concomitantly

Social Determinants in Ocular Trauma

Fasika Woreta MD

Social determinants of health (SDoH) are conditions in which people are born, grow, work, and age that account for over 80% of a population's health outcomes. SDoH are important contributors to health disparities in every subspecialty of ophthalmology, including cornea, anterior segment, and ocular trauma. Ocular trauma is a significant cause of vision impairment worldwide that is largely preventable. Disparities in ocular trauma by gender, race/ethnicity, geographic location, and socioeconomic status have been documented. A recent study using data from the IRIS® (Intelligence Research in Sight) Registry demonstrated that Black and Hispanic patients were more likely to undergo open globe injury repair than White patients, and Black patients were more likely to have worse visual acuity at final presentation. Understanding and addressing SDoH in the prevention and treatment of ocular trauma is paramount in the effort to reduce disparities in ocular trauma.

Selected Readings

1. Elam AR, Tseng VL, Rodriguez TM, Mike E, Warren AK, Coleman AL; American Academy of Ophthalmology Taskforce on Disparities in Eye Care. Disparities in vision health and eye care. *Ophthalmology* 2022; 129:e89-e113.

2. Kyriakaki EO, Symvoulakis EK, Chlouverakis G, Detorakis ET. Causes, occupational risk and socio-economic determinants of eye injuries: a literature review. *Med Pharm Rep.* 2021; 94:131-144.

3. Kyriakak EDO, Detorakis ET, Bertsias AK, et al. Clinical and social features of patients with eye injuries admitted to a tertiary hospital: a five-year retrospective study from Crete, Greece. *Healthcare (Basel)* 2023; 11:885.

4. Low L, Hodson J, Morris D, Desai P, MacEwen C. Socioeconomic deprivation and serious ocular trauma in Scotland: a national prospective study. *Br J Ophthalmol.* 2017; 101:1395-1398.

5. Tomaiuolo M, Woreta FA, Li A, et al; IRIS® Registry Analytic Center Consortium. Open-globe injury repairs in the American Academy of Ophthalmology IRIS® Registry 2014-2018: incidence, risk factors, and visual outcomes. *Ophthalmology* 2023; 130(8):812-821.

War on the Eye: Ocular Trauma in Conflict Settings

Marcus Colyer MD

I. Introduction

II. Disclosures/Disclaimer

III. Background

Ocular injuries are a frequent morbidity associated with combat-related trauma; the ocular surface represents only 0.27% of the body surface area but sustains a disproportionate degree of injury following trauma due to the manner in which the eye is exposed.

IV. Historical Perspectives

Munitions have greatly changed over the past 200 years, evolving from large munitions that caused nonsurvivable injuries to much higher-energy but smaller-sized munitions, as well as improved lifesaving measures, which have resulted in an increased rate of ocular injuries as a percentage of combat-associated ocular trauma.

V. Level of Care

Evacuation patterns and echelon-based capabilities dictate the level of care that can be offered in combat settings. Often there is a rationing of care that must take place. Civilian casualties often cannot receive the same level or speed of care delivery due to volatile evacuation routes and access.

VI. Management

Patterns of combat-associated trauma are multifactorial, with complex polytrauma being the rule rather than the exception. This leads to challenging management problems with high degree of collaboration.

VII. Unique Injury Factors/Features Uncovered With Combat Ocular Trauma

VIII. Role of Eye Protection and Preventative Measures in Reducing Morbidity

IX. Summary

Imaging of Cornea and Anterior Segment

Jayne S Weiss MD

I. Corneal Topography and Tomography

  A. Purpose: corneal curvature measurement

  B. Types: Placido disc, slit scanning Orbscan (B and L), Scheimpflug Pentacam (Oculus)

  C. Scale: absolute scale, relative scale

  D. Map types: curvature map, axial (sagittal): measures curvature at a certain point axial to center; meridional (tangential): measures curvature at certain point meridional to center. More sensitive measurement, elevation map

  E. Uses: refractive surgery, surgical planning in cataract surgery for IOL measurements, contact lens fitting, diagnosis of corneal keratoconus and other ectasias, postsurgical astigmatism, effect of corneal and ocular surface disorders

II. OCT

  A. Purpose

    1. Visualization of structures of anterior segment, conjunctiva, and cornea

    2. 2-7 microns of resolution

  B. Spectral domain OCT: Axial resolution is 2-3 times and scan speed is 60-110 times that of time domain OCT.

  C. Anterior segment and cornea OCT

    1. Examples are devices from Zeiss, Heidelberg, Topcon, Optovue, Nidek, etc.

    2. Uses: visualization of Descemet membrane endothelial keratoplasty, Descemet-stripping automated endothelial keratoplasty, corneal opacities, corneal epithelial thickness, angle structures

  D. Cornea and anterior surface

    1. Anterion, Spectralis (Heidelberg Engineering), Optovue Avanti or RTVue, Cirrus (Zeiss)

    2. Uses: Also visualize conjunctival and corneal lesions

  E. OCT limitations

    1. Image shadowing occurs with highly pigmented or thick lesions

    2. Limited by corneal opacities and poor ocular surface

  F. High-resolution OCT can provide detailed information about sclera architecture and thickness.

III. Ultrasound Biomicroscopy (UBM)

  A. Purpose

    1. Excellent tissue resolution

    2. Can provide corneal images despite opacification from edema or scarring

    3. Can visualize ciliary body

  B. High-frequency high-resolution ultrasound

    1. Traditional ultrasonography of the eye: 10-MHz transducer and 150-µm resolution

    2. With UBM 100-MHz transducer allows resolution of less than 20 µm.

    3. Helpful for evaluating for scleral invasion and posterior segment imaging

IV. Confocal Microscopy

  A. Purpose

    1. Can image cornea at microscopic level

    2. Small field of view allowing in vivo imaging

    3. Can see corneal cellular structures

    4. With resolution between 1.5 and 4 microns, identifies layers of the cornea including epithelium, Bowman layer, stroma, Descemet membrane and endothelium

  B. Mechanism

    1. Uses pinhole light source and pinhole detector

    2. The resultant small field of view provides optimal optical properties.

  C. Uses: Identification of corneal organisms like *Acanthamoeba*, bacteria, fungi; identification of neural tangles seen in neuropathic pain, neoplasias

V. Specular Microscopy

  A. Purpose

    1. Imaging the corneal endothelium in vivo

    2. Computer assisted morphometry can provide the size, shape, number, and density of corneal endothelial cells.

  B. Types

    1. Contact

    2. Noncontact

    3. Wide field

C. Uses: Diagnosis of endothelial diseases such as Fuchs, posterior polymorphous endothelial dystrophy, congenital hereditary endothelial dystrophy, irido corneal endothelial syndrome, and other diseases, endotheliopathies such as postoperative, contact-lens associated, post-uveitis, pseudoexfoliation, donor cornea examination, preoperative endothelial examination before anterior segment surgery

Selected Readings

1. Han SB, Liu YC, Mohamed-Noriega K, Mehta JS. Advances in imaging technology of anterior segment of the eye. *Hindawi J Ophthalmol.* 2021; 2021:9539765.

2. Helms RW, Minhaz AT, Wilson DL, Orge FH. Clinical 3D imaging of the anterior segment with ultrasound biomicroscopy. *Trans Vis Sci Tech.* 2021; 10(3):11.

3. Greenwald MF, Scruggs BA, Vislisel JM, Greiner MA. Corneal imagine: an introduction. TheRounds.org. http://eyerounds.org/tutorials/corneal-imaging/index.htm. Posted Oct. 19, 2016.

4. Prakash G, Feldman BH, Bunya VY, et al. Corneal topography. EyeWiki. https://eyewiki.aao.org/corneal_topography. Reviewed March 12, 2023.

5. Patel AS, Aref AA, Moore DB, Akkara JD, DelMonte DW. Anterior segment optical coherence tomography. EyeWiki. https://eyewiki.aao.org/anterior_segment_optical_coherence_tomography. Reviewed Febr. 10, 2023.

6. Nath S. Corneal topography and imagine. Medscape. https://emedicine.medscape.com/article/1196836. Updated Jan. 4, 2023.

"I Can't Believe They Did That!" and Other Bad Ideas

Iris Color Changing Implants, Eye Whitening, etc.

Roberto Pineda II MD

I. Iris Color Change

    A. Cosmetic iris implants

        1. NewIris

        2. Bright Ocular

        3. Complications

        4. Case examples

    B. Photoablative cosmetic iridoplasty

        1. STROMA

        2. Lumineyes

    C. Keratopigmentation

II. Eye Whitening Procedure

    A. Technique

    B. Outcomes

    C. Complications

III. Eye-Related Jewelry

    A. Subconjunctival jewelry

    B. Eyelid piercing

IV. Conjunctival Color Change/Tattooing

V. Just Bad Ideas!

    A. Eyeballing

    B. Oculolinctus

Selected Readings

1. Queiruga-Piñeiro J, Parra-Rodriguez T, Rodriguez-Una I. Long-term complications of cosmetic iris implants. *BMC Ophthalmol.* 2022; 22(1):459. Erratum in: *BMC Ophthalmol.* 2023; 23(1):8.

2. D'Oria F, Abu-Mustafa SK, Alio JL. Cosmetic change of the apparent color of the eye: a review on surgical alternatives, outcomes and complications. *Ophthalmol Ther.* 2022; 11(2):465-477.

3. Tran AQ, Hoeppner C, Venkateswaran N, Choi DS, Lee WW. Complications of cosmetic eye whitening. *Cutis* 2017; 100(3):E24-E26.

4. Moshirfar M, McCaughey MV, Fenzl CR, Santiago-Caban L, Kramer GD, Mamalis N. Delayed manifestation of bilateral scleral thinning after I-BRITE(®) procedure and review of literature for cosmetic eye-whitening procedures. *Clin Ophthalmol.* 2015; 9:445-451. Erratum in: *Clin Ophthalmol.* 2016; 10:187.

5. Rodríguez-Avila JO, Ríos Y Valles-Valles D, Hernández-Ayuso I, Rodríguez-Reyes AA, Morales Cantón V, Cernichiaro-Espinosa LA. Conjunctival tattoo with inadvertent ocular globe penetration and vitreous involvement: clinico-pathological correlation and scanning electron microscopy x-ray microanalysis. *Eur J Ophthalmol.* 2020; 30(5):NP18-NP22.

6. Bersani FS, Corazza O, Albano G, et al. The "eyeballing" technique: an emerging and alerting trend of alcohol misuse. *Eur Rev Med Pharmacol Sci.* 2015; 19(12):2311-2317.

7. Ascaso FJ. *Eyeball licking* o el placer de chupar los ojos ["Eyeball licking" or the pleasure of licking the eyes]. *Arch Soc Esp Oftalmol.* 2014; 89(5):212.

Corneal Stem Cell Regeneration

Sophie Deng MD PhD

Stem cell therapy has revolutionized the approach to treatment of corneal diseases, particularly in the context of limbal stem cell deficiency (LSCD). The first successful limbal stem cell transplantation for LSCD was reported in the 1980s, and since then, significant progress has been made in understanding the regeneration of corneal epithelium and stroma. Recent advancements in identifying and cultivating LSCs, as well as the development of standardized clinical diagnostic parameters, have enabled better assessment of LSC treatment outcomes and opened doors for innovative in vivo strategies to repopulate LSCs and restore vision in patients. These advancements hold great promise for enhancing the efficacy of current LSCD therapies.

Additionally, ongoing research focuses on regenerating a transparent corneal stroma, as the shortage of corneal tissue for transplantation remains a challenge. One intriguing avenue being explored is the therapeutic potential of extracellular vesicles (EVs). EVs have shown promising results in facilitating the regeneration of corneal stroma after injury. This presentation will provide an overview of the current progress and efforts in utilizing stem cells for the treatment of various corneal diseases, highlighting the significant advancements and potential future directions in this field.

The Robot Will See You Now

AI and Corneal Infections

Maria (Mia) A Woodward MD MS

The field of artificial intelligence (AI) has witnessed rapid advancements in recent years, offering valuable tools for supporting the diagnosis, management, and treatment of ophthalmic diseases. Recent peer-reviewed publications indicate that the majority of AI approaches have centered around the development of deep learning algorithms, leveraging various imaging techniques. In ophthalmology, the development of image-based AI in the field of ophthalmology primarily concentrated on diseases affecting the posterior segment of the eye. These diseases included macular degeneration, diabetic retinopathy, and glaucoma, mainly due to their high prevalence in the population and the routine use of ophthalmic imaging in clinical practice.

The management of microbial keratitis presents numerous complexities. These challenges arise from delayed patient presentation, difficulties in accurately identifying the causative organism, the absence of a comprehensive staging system tied to outcomes, and the lack of quantified methods to assess the progression of healing or nonhealing in microbial keratitis cases. Consequently, adapting the appropriate management approach becomes a demanding task. Furthermore, clinicians who handle microbial keratitis often have limited expertise in dealing with this specific condition.

Algorithms have been designed to identify and differentiate different classes of microbial keratitis and to quantify relevant features associated with this condition (see Selected Readings). It is worth noting that there is considerable variability in the reporting of methodology, patient population, and outcome metrics across studies. Additionally, few algorithms have been validated with external datasets or testing in real-world settings (ie, effectiveness trials).

In conclusion, AI holds immense promise in its ability to detect, diagnose, grade, and measure various diseases in the field of ophthalmology. However, it is crucial to establish standardized reporting practices to enhance transparency, validity, and comparability of algorithms used in this domain.

Selected Readings

1. Kang L, Ballouz D, Woodward MA. Artificial intelligence and corneal diseases. *Curr Opin Ophthalmol*. 2022; 33:407-417.

2. Loo J, Kriegel MF, Tuohy MM, et al. Open-source automatic segmentation of ocular structures and biomarkers of microbial keratitis on slit-lamp photography images using deep learning. *IEEE J Biomed Health Inform*. 2020; 25:88-99.

3. Kuo M-T, Hsu BW-Y, Yin Y-K, et al. A deep learning approach in diagnosing fungal keratitis based on corneal photographs. *Sci Rep*. 2020; 10:14424.

4. Lv J, Zhang K, Chen Q, et al. Deep learning-based automated diagnosis of fungal keratitis with in vivo confocal microscopy images. *Ann Transl Med*. 2020; 8:706.

5. Loo J, Woodward MA, Prajna V, et al. Open-source automatic biomarker measurement on slit-lamp photography to estimate visual acuity in microbial keratitis. *Transl Vis Sci Technol*. 2021; 10:2.

6. Xu F, Jiang L, He W, et al. The clinical value of explainable deep learning for diagnosing fungal keratitis using in vivo confocal microscopy images. *Front Med*. 2021; 8:797616.

7. Koyama A, Miyazaki D, Nakagawa Y, et al. Determination of probability of causative pathogen in infectious keratitis using deep learning algorithm of slitlamp images. *Sci Rep*. 2021; 11:22642.

8. Ghosh AK, Thammasudjarit R, Jongkhajornpong P, et al. Deep learning for discrimination between fungal keratitis and bacterial keratitis: DeepKeratitis. *Cornea* 2021; 41:616-622.

9. Hung N, Shih AK-Y, Lin C, et al. Using slit-lamp images for deep learning based identification of bacterial and fungal keratitis: model development and validation with different convolutional neural networks. *Diagnostics* 2021; 11:1246.

10. Redd TK, Prajna NV, Srinivasan M, et al. Image-based differentiation of bacterial and fungal keratitis using deep convolutional neural networks. *Ophthalmol Sci*. 2022; 2:100119.

11. Woodward MA, Niziol LN, Ballouz D, et al. Prediction of visual acuity in patients with microbial keratitis. *Cornea* 2023; 42:217-223.

MythBusters—Pushing the Limits

Somasheila Murthy MD, Anubha Rathi MD, and Sunita Chaurasia MD

Background for the Study

The human cornea is an avascular structure but develops new vessels following insult, such as injury or infection and various other pathologies, and the vessels can persist even after the inciting stimulus has been apparently removed.[1,2] The definite treatment for scarred corneas is penetrating keratoplasty, whereas for pure stromal and endothelial diseases lamellar keratoplasty is preferred. Corneal neovascularization is perhaps the most important factor that puts the corneal graft at risk of endothelial rejection, especially in full-thickness keratoplasty. While the rates of endothelial rejection have been reported to be far lower in endothelial keratoplasty, the incidence would increase in the presence of a vascularized bed. In deep anterior lamellar keratoplasty, the presence of host vessels and lymphatics contributes to stromal rejection and loss of stromal clarity due to lipid deposition, necessitating a repeat surgery. Keratoplasties, when performed for therapeutic indications such as active corneal infection, end up with failure, and these failed grafts again are highly prone to endothelial rejection due to the presence of vascularization, among other causes.[3]

Strategies for Tackling Corneal Neovascularization

The multiple strategies that have evolved to address this include the use of topical corticosteroids and other immunosuppressants, topical anti-VEGF agents, argon laser cautery, and fine needle diathermy (FND).[4-6] Only some of these techniques, such as FND, are able to regress mature corneal vessels variably. Overall, despite various methods, in a majority of cases the vessels return. Thus novel approaches are required to address this problem.

The Role of Corneal Collagen Crosslinking (CXL)

CXL appears to be a promising option in this scenario. Since 2003 it has been widely applied, safely and effectively, to treat corneal ectatic disorders, particularly progressive keratoconus, and it received U.S. Food and Drug Administration approval in 2016 for this indication.[7] CXL has also been seen to be safe and effective in corneal ulcers and prevention of corneal melting.[8] The procedure involves release of reactive singlet oxygen and oxygen radicals, causing apoptosis of keratocytes in the cornea. Along similar lines, it has been hypothesized that CXL using riboflavin and ultraviolet A (UVA) radiation may also affect the endothelial cells of abnormal vessels and lymphatics in the cornea. A study in a murine model revealed that CXL with local application of riboflavin and UVA can regress pre-existing corneal blood vessels and lymphatics.[9]

One retrospective case series of 5 patients who underwent CXL in vascularized corneas has recently been published with favorable preliminary results.[10] This pilot series reported promising results and opened future possibilities but is limited by numbers and heterogeneity of timing and technique and documentation of regression, warranting a more elaborate prospective study. In this talk we share our preliminary results of this technique.

References

1. Dana MR. Angiogenesis and lymphangiogenesis: implications for corneal immunity. *Semin Ophthalmol.* 2006; 21:19-22.

2. Cursiefen C, Chen L, Dana MR, et al. Corneal lymphangiogenesis: evidence, mechanisms, and implications for corneal transplant immunology. *Cornea* 2003; 22:273-281.

3. Patel SP, Dana R. Corneal lymphangiogenesis: implications in immunity. *Semin Ophthalmol.* 2009; 24:135-138.

4. Cursiefen C, Cao J, Chen L, et al. Inhibition of hemangiogenesis and lymphangiogenesis after normal-risk corneal transplantation by neutralizing VEGF promotes graft survival. *Invest Ophthalmol Vis Sci.* 2004; 45:2666-2673.

5. Le VNH, Schneider AC, Scholz R, et al. Fine needle-diathermy regresses pathological corneal (lymph)angiogenesis and promotes high-risk corneal transplant survival. *Sci Rep.* 2018; 8:5707.

6. Bock F, Maruyama K, Regenfuss B, et al. Novel anti(lymph)angiogenic treatment strategies for corneal and ocular surface diseases. *Prog Retin Eye Res.* 2013; 34:89-124.

7. Belin MW, Lim L, Rajpal RK, Hafezi F, Gomes JAP, Cochener B. Corneal cross-linking: current USA status: report from the Cornea Society. *Cornea* 2018; 37(10):1218-1225.

8. Titiyal JS, Karunakaran A, Kaur M, Rathi A, Agarwal T, Sharma N. Collagen cross-linked therapeutic grafts in fungal keratitis. *Ophthalmology* 2018; 125(9):1471-1473.

9. Hou Y, Le VNH, Toth G, et al. UV light crosslinking regresses mature corneal blood and lymphatic vessels and promotes subsequent high-risk corneal transplant survival. *Am J Transpl.* 2018; 18:2873-2884.

10. Shaub F, Hou Y, Zhang W, et al. Corneal cross linking to regress pathologic corneal neovascularization before high risk keratoplasty. *Cornea* 2021; 40:147-155.

Corneal Tissue Engineering: Gel Keratoplasty, 3-D Bioprinting, and More

David Myung MD

I. Global Clinical Need for Bioengineered Corneal Tissue

II. Approaches to Engineering Corneal Donor Tissue Equivalents That Are Under Development

   A. Bench-top hydrogel crosslinking and molding

   B. In situ-forming hydrogels and sutureless stromal defect filling

   C. 3-D bioprinting

   D. Multilayered corneal constructs

   E. Other approaches

      1. Electrospinning

      2. Engineered xenograft tissue

      3. Stromal lenticules

      4. Organoid culture

Synthetic Endothelial Replacement

Victor A Augustin MD, Hyeck-Soo Son MD, and Gerd U. Auffarth MD

The past 2 decades have shown a growing global trend toward posterior lamellar procedures to treat corneal endothelial diseases. Thanks to optimized surgical techniques and excellent postoperative results after endothelial keratoplasty procedures such as Descemet membrane endothelial keratoplasty (DMEK), this method has now become the procedure of choice for patients with corneal endothelial dysfunction such as Fuchs endothelial corneal dystrophy (FECD) or pseudophakic bullous keratopathy.[1]

Yet the surgical success after DMEK can be undermined by several factors. Primary or secondary graft failure, graft medium–associated infections, refractive changes, immunologic graft rejections, and inadequate postoperative supine positioning or secondary interventions such as rebubbling procedures may all lead to suboptimal outcomes.[2-5] Consequently, alternative treatment strategies have been developed to bypass or decrease the rate of such complications, including techniques such as "Descemet stripping only" or intracameral injection of cultured corneal endothelial cells combined with rho-kinase inhibitors.[6,7]

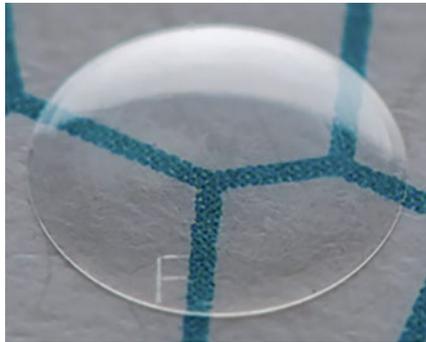The artificial endothelial layer, the EndoArt (EyeYon Medical; Ness Ziona, Israel), also presents such an alternative.

Recently awarded with the Breakthrough Therapy designation by the U.S. Food and Drug Administration (FDA), the 50-μm thin, 6.0-mm diameter, dome-shaped implant is composed of flexible, hydrophilic acrylic material that can replace the diseased endothelium and serve as an artificial fluid barrier between the posterior stroma and aqueous humor (see Figure 1). Preliminary outcomes after implantation as compassionate use in 2 patients have shown promising results, with rapid corneal deturgescence at as early as 1 day postoperatively (see Figure 2A).[8] The implant has also been shown to stay adherent to the posterior corneal surface for up to 3 years postoperatively (see Figure 2B).

Thus, the implantation of the artificial endothelial layer may serve as a viable and effective alternative for patients suffering from chronic corneal edema, particularly in cases of difficult anterior chamber situations with high risk of graft failure.[8]

References

1. 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.

2. Dunker S, Winkens B, van den Biggelaar F, Nuijts R, Kruit PJ, Dickman M; Dutch Cornea Consortium. Rebubbling and graft failure in Descemet membrane endothelial keratoplasty: a prospective Dutch registry study. *Br J Ophthalmol*. 2023; 107(1):17-23.

3. Augustin VA, Weller JM, Kruse FE, Tourtas T. Fungal interface keratitis after Descemet membrane endothelial keratoplasty. *Cornea* 2018; 37(11):1366-1369.

4. Schaub F, Bachmann BO, Cursiefen C, Hos D. Midterm followup of immune reactions after Descemet membrane endothelial keratoplasty (DMEK). *Graefes Arch Clin Exp Ophthalmol*. 2019; 257(8):1811-1812.

Figure 1. The EndoArt is a dome-shaped, 50-μm thin synthetic endothelial corneal implant with a 6.0-mm diameter.
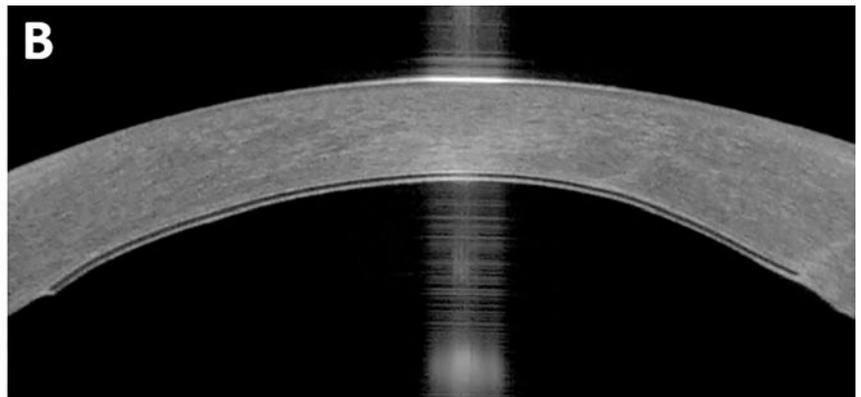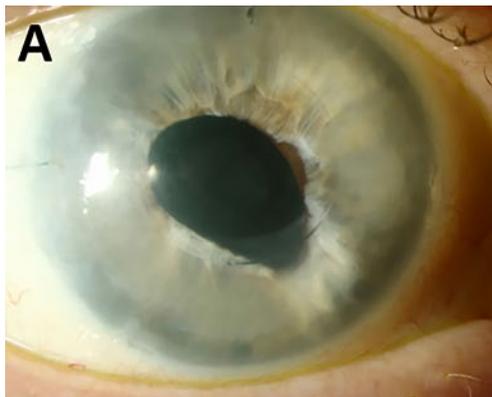

Figure 2. (A) This slit-lamp image demonstrates rapid central corneal deturgescence at 1 day postoperatively. (B) The anterior segment OCT shows stable adherence of the implant at 3 years postoperatively.

5. Augustin VA, Son HS, Yildirim TM, et al. Refractive outcomes after Descemet membrane endothelial keratoplasty: a meta-analysis. *J Cataract Refract Surg.* Epub ahead of print 2023 May 4. doi:10.1097/j.jcrs.0000000000001212.

6. 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(11):995-1003.

7. Moloney G, Garcerant Congote D, Hirnschall N, et al. Descemet stripping only supplemented with topical ripasudil for Fuchs endothelial dystrophy: 12-month outcomes of the Sydney Eye Hospital Study. *Cornea* 2021; 40(3):320-326.

8. Auffarth GU, Son HS, Koch M, et al. Implantation of an artificial endothelial layer for treatment of chronic corneal edema. *Cornea* 2021; 40(12):1633-1638.

Financial Disclosure

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