Cornea 2018
What's Tried, True, and New

Program Directors
Carol L Karp MD, Jennifer Y Li MD, Sanjay V Patel MD FRCOphth

In conjunction with the Cornea Society

Cornea Society
Advancing the treatment of corneal disease

McCormick Place
Chicago, Illinois
Saturday, Oct. 27, 2018

Presented by:
The American Academy of Ophthalmology

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2018 Cornea Subspecialty Day Planning Group

On behalf of the American Academy of Ophthalmology and the Cornea Society, it is our pleasure to welcome you to Chicago and **Cornea 2018: What's Tried, True, and New**

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Cornea 2018 Contents

CME Credit

Academy's CME Mission Statement

The purpose of the American Academy of Ophthalmology's Continuing Medical Education (CME) program is to present ophthalmologists with the highest quality lifelong learning opportunities that promote improvement in physician practices, resulting in the best possible eye care for their patients.

2018 Cornea Subspecialty Day Learning Objectives

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

- List common causes of corneal infections and best practices for management
- Discuss the role of keratoplasty in the management of patients with corneal disease
- Review the role of imaging and in-office diagnostics in the treatment of corneal disorders
- Provide a rationale for treatment of dry eye and other ocular surface diseases and inflammatory disorders

2018 Cornea Subspecialty Day Target Audience

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

2018 Cornea Subspecialty Day CME Credit

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

The Academy designates this live activity for a maximum of 7 *AMA PRA Category 1 Credits*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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Before processing your requests for CME credit, the American Academy of Ophthalmology must verify your attendance at Subspecialty Day and/or AAO 2018. In order to be verified for CME or auditing purposes, you must either:

- Register in advance, receive materials in the mail, and turn in the *Subspecialty Day Syllabi* exchange voucher(s) onsite;
- Register in advance and pick up your badge onsite if materials did not arrive before you traveled to the meeting;
- Register onsite; or
- Scan the barcode on your badge as you enter an AAO 2018 course or session room.

CME Credit Reporting

South Building Level 2.5 and Academy Resource Center

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The Academy transcript cannot list individual course attendance. It will list only the overall credits claimed for educational activities at Subspecialty Day and/or AAO 2018.

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Proof of Attendance

The following types of attendance verification are available during AAO 2018 and Subspecialty Day for those who need it for reimbursement or hospital privileges, or for nonmembers who need it to report CME credit:

- CME credit reporting/proof-of-attendance letters
- Onsite registration receipt
- Instruction course and session verification

You must have obtained your proof of attendance at a CME Credit Reporting kiosk onsite, located in South, Level 2.5, and in the Academy Resource Center.

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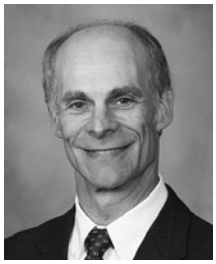

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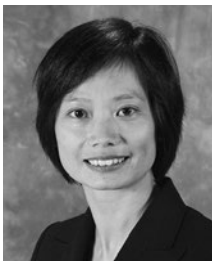

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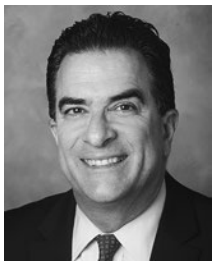

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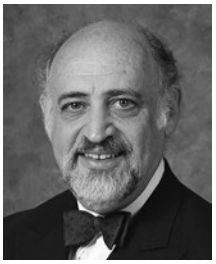

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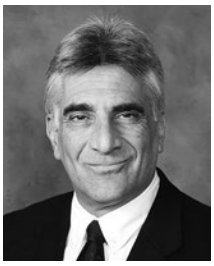

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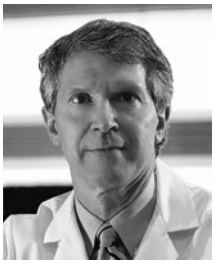

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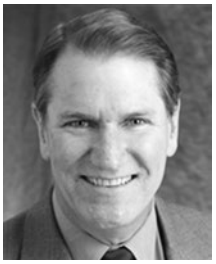

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Cornea Subspecialty Day 2018: What's Tried, True, and New

In conjunction with the Cornea Society

SATURDAY, OCT. 27

7:00 AM	CONTINENTAL BREAKFAST		
8:00 AM	Welcome and Introductions	Carol L Karp MD	

Section I: Anterior Segment Imaging—Tried and True and a New View

Moderator: Carol L Karp MD

8:02 AM	Introduction	Carol L Karp MD	
8:04 AM	Imaging for Keratoconus	Michael W Belin MD*	1
8:12 AM	Preoperative Options for Imaging for Cataract Surgery	Bonnie An Henderson MD*	2
8:20 AM	Intraoperative Imaging for Cataract Surgery	Zaina N Al-Mohtaseb MD*	3
8:28 AM	Imaging for LASIK and Its Complications	Sonia H Yoo MD*	4
8:36 AM	Imaging for Infectious Keratitis	Elmer Y Tu MD*	5
8:44 AM	Imaging in Corneal Surgery: Preop Planning and Intra EK	Sadeer B Hannush MD	7
8:52 AM	Case: How Imaging Saved Me	Roberto Pineda II MD*	8
9:00 AM	Panel Discussion		

Section II: Concerning Keratoplasty—Stripping Away the Layers of Mystery

Moderator: Jennifer Y Li MD

Virtual Moderator: Amy Lin MD*

9:10 AM	Introduction	Jennifer Y Li MD	
9:12 AM	Perfecting Penetrating Keratoplasty: Lessons Learned Over Time	Mark J Mannis MD	9
9:20 AM	Digging Deep: Improving Outcomes With Deep Anterior Lamellar Keratoplasty	Luciene B Sousa MD	11
9:28 AM	DSAEK—Still the Gold Standard?	Shahzad I Mian MD*	12
9:36 AM	DMEK—Addressing the Challenges of Transitioning to a New Procedure	Mark A Terry MD*	14
9:44 AM	Descemet Stripping Only (DSO)—Can We Do Without a Graft?	Kathryn A Colby MD PhD*	15
9:52 AM	Do Corneas Grow on Trees? Understanding the Evolving Role of Eye Banks	Marian Sue Macsai-Kaplan MD*	16
10:00 AM	Case: A Challenging Cornea to Cure	Francis W Price Jr MD*	17
10:08 AM	Panel Discussion		
10:18 AM	REFRESHMENT BREAK and AAO 2018 EXHIBITS		

Section III: Conjunctival Tumors—Is It a "Toomah"?

Moderator: Carol L Karp MD

10:48 AM	Introduction	Carol L Karp MD	
10:50 AM	Advocating for the Profession and Patients	Stephanie J Marioneaux MD	18

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

10:55 AM	There's Pigment on the Conjunctiva: When to Worry	Carol L Shields MD*	21
11:03 AM	Ocular Surface Squamous Neoplasia: What to Do With This Tumor?	Fairooz Puthiyapurayil Manjandavida MD	23
11:11 AM	It's a Salmon Patch: What to Do With Lymphoproliferative Lesions	Bita Esmaeli MD FACS	27
11:19 AM	It's Fleshy Tumor: What to Do With Pterygium—An Evidence-Based Approach	Guillermo Amescua MD	28
11:27 AM	What Is Going on With This Eye? Is It a Tumor?	Swathi Kaliki MD	29
11:35 AM	Conjunctival Lesions in Children	Jacob J Pe'er MD	30
11:43 AM	Case: Is It a "Toomah"?	Christopher John Murphy DVM PhD*	31
11:51 AM	Panel Discussion		
12:01 PM	LUNCH and AAO 2018 EXHIBITS		

Section IV: Hot Topics

Moderator: Sanjay V Patel MD FRCOphth

1:26 PM	Introduction	Sanjay V Patel MD FRCOphth	
1:28 PM	Pediatric Corneal Opacity: New Paradigms	Kanwal K Nischal MBBS*	32
1:36 PM	DREAM Study: Omega 3 Fatty Acids and Dry Eye Disease	Penny A Asbell MD FACS*	33
1:44 PM	What's Hot With Cicatrizing Disease?	James Chodosh MD MPH*	34
1:52 PM	Simple Limbal Epithelial Transplantation: Indications and Outcomes	Sayan Basu MBBS MS	35
2:00 PM	Fuchs Dystrophy: Future Horizons	Anthony J Aldave MD*	37
2:08 PM	Updates From the Cornea Preservation Time Study	Jonathan H Lass MD*	38
2:16 PM	Panel Discussion		

Section V: Ocular Surface Disease—Whetting Your Appetite on the Latest Advances

Moderator: Jennifer Y Li MD

2:26 PM	Introduction	Jennifer Y Li MD	
2:28 PM	Detecting Dry Eyes: The Utility of Diagnostic Tests Old and New	Christopher J Rapuano MD*	41
2:36 PM	Managing Meibum: Addressing Meibomian Gland Dysfunction in Dry Eye Disease	Roni M Shtein MD	42
2:44 PM	Blood, Sweat, and Tears: Topical Hematopoietic Therapies for Dry Eyes	Victor L Perez MD*	43
2:52 PM	Sniffing Out New Solutions: Devices and Technology in the Management of Dry Eyes	Stephen C Pflugfelder MD*	44
3:00 PM	Cutting to the Chase: Surgical Options for the Treatment of Ocular Surface Disease	Edward J Holland MD*	45
3:08 PM	A Painful Problem: The Diagnosis and Management of Neuropathic Corneal Pain	Anat Galor MD*	46
3:16 PM	Case: Not Your Standard Dry Eyes	Sophie X Deng MD PhD*	47
3:24 PM	Panel Discussion		
3:34 PM	REFRESHMENT BREAK and AAO 2018 EXHIBITS		

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

Section VI: Corneal Infections—Medical Therapy and Beyond

Moderator: Sanjay V Patel MD FRCOphth

4:04 PM	Introduction	Sanjay V Patel MD FRCOphth	
4:06 PM	Atypical Keratitis: What Not to Miss	Gerami D Seitzman MD	48
4:14 PM	Zoster: Give It a Shot	Keith Hugh Baratz MD	49
4:22 PM	Viral Endotheliitis: Recognizing and Defeating the Players	Todd P Margolis MD PhD*	52
4:30 PM	When Medical Therapy Fails, What Next?	Namrata Sharma MD MBBS	53
4:38 PM	Interface and Wound Infections: Special Considerations for Special Situations	Bennie H Jeng MD*	55
4:46 PM	Crosslinking and Keratitis: Treatment, or Risk Factor?	Vishal Jhanji MD	56
4:54 PM	Case Presentation	Charles McGhee PhD FRCOphth FRANZCO	57
5:02 PM	Panel Discussion		
5:12 PM	CLOSING REMARKS and ADJOURN	Jennifer Y Li MD Sanjay V Patel MD FRCOphth	

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Imaging for Keratoconus

Michael W Belin MD

I. Curvature is analogous to measuring spectacle lens power.
   A. It may be accurate, but it tells you nothing about the shape of the lens.
   B. That is, multiple spectacle lenses (different shapes) can have the same power.

II. Curvature and power will change with orientation.
   A. Lens tilt and/or measurement axis
   B. The same lens (shape) can have multiple powers.

III. Angle Kappa
   A. Angle between the pupillary and visual axis
   B. Displacement of up to 5 degrees is physiologic and considered normal.
   C. A "normal" angle kappa is enough to produce an "abnormal" curvature map.

IV. This is why I don't look at curvature, inferior steepening, or I/S values.

V. Locating the Cone
   A. Curvature falsely locates the cone—regardless of machine / technology.
   B. The more peripheral the cone, the more erroneous the information.
   C. Almost all "pellucid marginal degeneration" (PMD) is just inferior keratoconus.

VI. When the apex is decentered, the curvature map misplaces cone location.

VII. Peripheral Marginal Degeneration
   A. Curvature patterns such as "crab claw" are measurement (curvature) anomalies and do not represent peripheral shape changes.
   B. Almost all "topographic" PMD is just inferior keratoconus.

VIII. Forme Fruste Keratoconus
   A. Forme fruste keratoconus (FFKC) was first proposed by Amsler in 1961.
      1. Defined as a cornea that has no abnormal findings by either slit-lamp examinations or Placido-based corneal topography, with the fellow eye of clinical keratoconus
      2. Predates any type of modern imaging
   B. Modern (tomographic) imaging eliminates the need for ambiguous terms that are overly confusing and have little clinical significance.

IX. How do we image keratoconus?
   A. We need a device that:
      1. Images both corneal surfaces: anterior and posterior, with accurate posterior data
      2. Images out to the periphery; generates a full pachymetric map

X. What is "subclinical" keratoconus ?
   A. It is *true* keratoconus. It is not "suspect."
   B. The corneas are abnormal …
      1. Abnormal posterior elevation
      2. Abnormal pachymetric progression
   C. … but with normal anterior curvature.
      1. Patients retain good vision.
      2. "Subclinical keratoconus"

XI. Why is posterior data mandatory?
   A. Changes on the posterior corneal surface will typically be the earliest sign of ectatic disease (ability to diagnose disease prior to visual loss).
   B. Least effected by outside forces (eg, RGP contact lenses)
   C. Changes on the posterior surface will always exceed those on the anterior surface.
   D. Why is this the case?

XII. The only way to get thinning and anterior steepening is for the posterior surface to move *more*.

XIII. How do we image keratoconus?
   A. Modern imaging requires tomographic devices that accurately measure all corneal surfaces with near limbus-to-limbus coverage.
   B. Supplemental imaging with Placido-based systems is not necessary, and often will convey misleading (inaccurate) information.

Preoperative Options for Imaging for Cataract Surgery

Bonnie An Henderson MD

I. Background
   A. Current practice: Preoperative imaging for cataract surgery (biometry, Ks)
   B. What is needed and why
   C. Diagnoses that can be missed

II. Topography
   A. Available technology
   B. How to interpret
   C. Pros/cons

III. Tomography and/or Hybrids
   A. Available technology
   B. How to interpret
   C. Pros/cons

IV. Digital Mapping / Guidance Systems
   A. Preoperative modules: iris registration, conjunctival vessels
   B. Integration into multi-instrument systems
   C. Uses: toric IOL placements, corneal incisional astigmatism correction

Selected Readings

1. Donaldson K, Fernández-Vega-Cueto L, Davidson R, et al; ASCRS Refractive–Cataract Surgery Subcommittee. Perioperative assessment for refractive cataract surgery. *J Cataract Refract Surg.* 2018; 44(5):642-653.
2. Fram NR, Masket S, Wang L. Comparison of intraoperative aberrometry, OCT-based IOL formula, Haigis-L, and Masket formulae for IOL power calculation after laser vision correction. *Ophthalmology* 2015; 122(6):1096-1101.
3. Gupta PC, Caty JT. Astigmatism evaluation prior to cataract surgery. *Curr Opin Ophthalmol.* 2018; 29(1):9-13.
4. Ruiz-Belda C, Rodrigo F, Piñero DP. Validation of keratometric measurements obtained with an intraoperative image-guided system: intra-session repeatability and interchangeability with an optical biometer. *Clin Exp Optom.* 2018; 101(2):200-205.
5. Lin HY, Chen HY, Fam HB, Chuang YJ, Yeoh R, Lin PJ. Comparison of corneal power obtained from VERION image-guided surgery system and four other devices. *Clin Ophthalmol.* 2017; 11:1291-1299.
6. Schultz M, Oberheide U, Kermani O. Comparability of an image-guided system with other instruments in measuring corneal keratometry and astigmatism. *J Cataract Refract Surg.* 2016; 42(6):904-912.
7. Huerva V, Ascaso FJ, Soldevila J, Lavilla L. Comparison of anterior segment measurements with optical low-coherence reflectometry and rotating dual Scheimpflug analysis. *J Cataract Refract Surg.* 2014; 40(7):1170-1176.
8. Piñero DP. Technologies for anatomical and geometric characterization of the corneal structure and anterior segment: a review. *Semin Ophthalmol.* 2015; 30(3):161-170.
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Intraoperative Imaging for Cataract Surgery

Zaina N Al-Mohtaseb MD

I. Introduction: Description of Automated Image-Guided Techniques

A. Used for capsulorrhexis centration; wound and astigmatic keratotomy placement; IOL centration, especially multifocal IOLs; and toric alignment

B. Preoperative mapping of the astigmatic axis, location of wounds, etc. relative to visible anatomic landmarks in photographs of the iris and/or conjunctiva

C. Intraoperative alignment of the toric IOL relative to these previously identified anatomic markers

II. Examples of Image-Guided Technology

A. Zeiss Callisto

1. Callisto is one component of the Zeiss cataract suite (IOLMaster, Callisto Eye, and Opmi Lumera)

2. Computer-assisted cataract surgery system that bypasses preoperative and intraoperative manual marking, allowing for marker-less toric IOL alignment

3. Uses photographs taken of vessels around the cornea that are matched and tracked intraoperatively, allowing for overlays of axis lines

4. Utilized in capsulorrhexis centration, arcuate and main incision placement, and multifocal IOL centration

5. In a study comparing manually marked vs. the Callisto Eye and Z Align, deviation from the target axis of implantation was significantly less in the latter.[1]

B. Alcon Verion

1. Consists of Verion Reference Unit and Verion Digital Marker, which capture a reference image documenting scleral vessels, limbus, and iris features for use in intraoperative incisions, capsulotomies, and IOL alignment

2. Real-time intraoperative imaging / display of astigmatic axis and anatomic landmarks for toric IOL alignment

3. Compensates for eye movement, zoom, instruments, and subconjunctival hemorrhage

4. Can be used with LenSx laser and most surgical microscopes

5. Randomized controlled trial studying the Alcon Verion showed statistically significant better refractive outcomes compared to manual marking for toric IOLs.[2]

C. Truevision / Cassini

1. Integration with Cassini diagnostic device which, with the TrueVision software, provides real-time calculations, optimizing IOL positioning and limbal relaxing incision / AK guidance

2. Uses preoperative anterior segment photographs to map images and project the steep axis throughout surgery

3. Similar to other systems, provides real-time overlay of information during surgery

4. TrueVision is compatible with preoperative diagnostic devices, Cassini / Pentacam / OA-2000, and LenStar.

5. No statistical difference found between TrueVision 3-D and manual ink marking[3]

D. Optiwave Refractive Analysis (ORA) system

1. Intraoperative wavefront aberrometer that allows for intraoperative refraction of phakic and pseudophakic eye

2. Uses superluminescent light-emitting diode and Talbot-Moiré interferometer to take 40 measurements in less than 1 minute

3. Considers parameters such as posterior corneal astigmatism and higher-order aberrations, allowing the surgeon to confirm or revise the IOL power chosen according to preoperative biometry

4. Allows for optimal IOL selection and adjustments after IOL implantation

5. Ninety-six percent of eyes using ORA achieved a target refraction within 0.50 D, compared with 56% of eyes using the traditional method of IOL alignment[4]

References

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Imaging for LASIK and Its Complications

Sonia H Yoo MD

Imaging techniques for assessing the normal structure and function of the cornea are crucial for determining if a patient can undergo refractive surgery. LASIK screening must be performed to determine corneal shape and patterns of astigmatism on topography before refractive surgery can be performed safely. Topography can also be used postoperatively to evaluate etiology for unsatisfactory visual outcomes, such as decentered or incomplete ablations.

Corneal tomography, another imaging technique for refractive screening, is different from topography in that it uses slit-imaging technology. This allows us to measure not only the anterior corneal surface but the posterior surface and to define the spatial relationship between the two (thickness map), and subsequently to characterize corneal architecture in three dimensions.

Finally, anterior segment OCT (AS-OCT) produces high-resolution imaging of the cornea, iris, and anterior. It is analogous to ultrasound, but it utilizes light waves instead of sound to produce extremely high-resolution images of very small ocular structures. AS-OCT uses 2 scanning beams of light, which are reflected off an ocular structure and then detected and compared to a reference beam to create a cross-sectional image. It is useful in determining corneal thickness, flap thickness, and residual bed thickness for LASIK enhancement surgery.

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Imaging for Infectious Keratitis

Elmer Y Tu MD

I. Diagnostic Imaging Tools
   A. Slit lamp biomicroscopy
   B. Confocal microscopy
   C. Optical coherence tomography
II. Slit Lamp Biomicroscopy in Infectious Keratitis
   A. Bacterial keratitis: clinical presentation
      1. Generally discrete "colony" lesion
      2. Similar to an Agar culture plate
      3. ± Hypopyon
   B. Fungal keratitis: clinical signs
      1. Minimal necrosis
      2. Minimal inflammation
      3. Growth pattern: branching filaments
         a. Punctate "on-end" opacities
         b. Additive to corneal contour
      4. Satellite lesions
      5. Feathery, irregular margin
      6. Hyphae or pseudohyphae (yeast)
      7. Invasion with minimal necrosis
      8. Translucent, raised, frosted-glass appearance
      9. Endothelial plaque
      10. Elevated IOP
   C. Fungal keratitis: clinical course
      1. Penetration of fungal elements into the anterior chamber
      2. Sudden onset or worsening of hypopyon
      3. *Any* pigmentation strongly suggests a fungal etiology; lack of pigment does not rule out a pigmented fungi.
   D. Filamentous septated fungi
      1. Nonpigmented
         a. *Fusarium*
         b. *Aspergillus*
      2. Pigmented
         a. *Curvularia*
         b. *Cladosporium*
         c. *Acremonium*
         d. *Exserohilum*
   E. *Acanthamoeba* keratitis
      1. Mainly infiltrative pattern of proliferation
      2. Smooth, firm bed
      3. Clinical appearance
         a. Epithelial cysts
         b. Radial neuritis
         c. Ring infiltrates: 18%
         d. Corneal ulceration: 19%
   F. Reliability of clinical presentation: Dahlgren et al. *AJO*, 2007
      1. 15 ophthalmologists asked to predict culture result
         a. 92% correctly predicted culture positivity
         b. 37% correctly predicted culture negativity
         c. Microbial kingdom: 73%
            i. Bacterial: 79%
               (a) Pseudomonas: 65% positive predictive value (PPV)
               (b) Other bacteria: 48% PPV
            ii. Fungal: 45% PPV
            iii. *Acanthamoeba*: 89% PPV; 7/9 cases ring infiltrate*
      2. Hampered clinical prediction
         a. Prior antibiotic use
         b. Corticosteroid use
   G. Indications for smear and culture
      1. Large corneal infiltrate that is large and extends to the middle to deep stroma
      2. Infiltrates that are chronic in nature or unresponsive to broad-spectrum antibiotic therapy
      3. Atypical clinical features suggestive of fungal, amoebic, or mycobacterial keratitis.
      4. Unusual history (eg, vegetable matter, contact lenses while in a hot tub)
      5. Before initiating antimicrobial therapy, cultures are indicated in sight-threatening or severe keratitis of suspected microbial origin.
      6. The hypopyon that occurs in eyes with bacterial keratitis is usually sterile, and aqueous or vitreous taps should not be performed unless there is a high suspicion of microbial endophthalmitis, such as following an intraocular surgery, perforating trauma, or sepsis.

H. Culture methods
   1. Superficial lesions
      a. Corneal scraping
      b. Calcium alginate swab
   2. Deep lesions
      a. Corneal biopsy

I. Tactile feedback from corneal scraping
   1. Bacterial ulcers
      a. Superficial necrosis
      b. Soft pliable bed
   2. Fungal keratitis
      a. Stiff fungal hyphae
      b. "Rough" corneal bed (may also be felt with some atypical mycobacterial ulcers)
   4. *Acanthamoeba* keratitis
      a. Mainly infiltrative pattern of proliferation
      b. Smooth, firm bed

III. OCT: Anterior Segment OCT (AS-OCT)
   A. Long wavelength source (1310 nm)
      1. Zeiss Visante, Tomey Casia, Heidelberg SL-OCT, etc.
      2. Deeper penetration, stronger light source
      3. Reduced axial resolution
      4. Improved anterior segment imaging over corneal resolution
   B. Shorter wavelength source (adapted retinal devices)
      1. Optovue RT-Vue, Optovue iVue, Zeiss Cirrus, Heidelberg Spectralis, etc.
      2. Shallower penetration, weaker light source
      3. Increased axial resolution
      4. Improved corneal detail
   C. Applications in corneal infectious disease
   D. Currently, limited diagnostic capability
   E. Special uses
      1. CMV endotheliitis
      2. Retrocorneal plaque assessment
      3. Depth and location definition in smaller lesions

IV. Confocal Microscopy
   A. Applications
      1. Alternative to corneal biopsy
         a. High magnification
         b. En face image
            i. Cellular shape, structures
            ii. Context of adjacent tissues / cells
            iii. Abnormal structures
      2. Real-time imaging
         a. Blood flow
         b. Dynamic imaging
   B. Limitations
      1. Patient cooperation: Movement
      2. Dense opacities: Cannot penetrate or overcome scatter
      3. Imperfect depth measurements
      4. Limited intraocular penetration
   C. Confocal microscopy: What can you discern?
      1. 1-micron step motor (Z axis)
      2. Lateral resolution, ~1-2 microns
      3. Most atypical organisms are large: Cell walls allow differentially greater reflectivity vs. surrounding structures.
      4. Bacterial keratitis
         a. Bacteria are too small to image.
         b. Corneal morphology can be imaged.
         c. Crystalline keratopathy
      5. Fungal keratitis: clinical characteristics
         a. Yeast
         b. Filamentous molds
         c. Microscopic: Tissue and culture morphology are significantly different.
      6. *Acanthamoeba* keratitis
         a. Confocal microscopy findings
         b. Multiple studies confirming utility in atypical keratitis

Imaging in Corneal Surgery: Preop Planning and Intra EK

Sadeer B Hannush MD

NOTES

Case: How Imaging Saved Me!

Roberto Pineda MD, Reena Gupta MD, and Emma Davies MD

A case presentation demonstrating how anterior segment imaging can be useful in directing management following a case of corneal trauma after femtosecond LASIK surgery.

Perfecting Penetrating Keratoplasty: Lessons Learned Over Time

What the Contemporary Lamellar Surgeon Needs to Know About an "Outdated" Procedure

Mark J Mannis MD

I. The Age of Selective Keratoplasty
   A. Endothelial keratoplasty
      1. Descemet-stripping automated endothelial keratoplasty (DSAEK)
      2. Descemet membrane EK (DMEK)
      3. Pre-Descemet EK (PDEK)
   B. Deep anterior lamellar keratoplasty (DALK)
   C. Cell-based therapy: endothelial cell seeding
   D. Ocular surface reconstruction in its many forms

II. Eye Bank Association of America Statistics (2017)

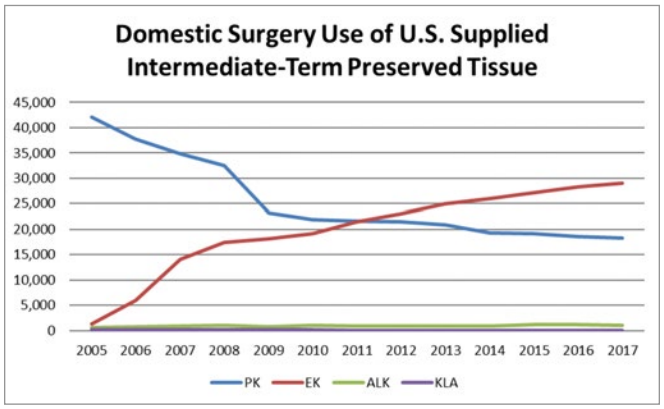

Figure 1.

III. When Penetrating Keratoplasty (PK) Remains Indicated
   A. Pan-layered corneal opacity
   B. Therapeutic keratoplasty
      1. Infection
      2. Trauma
      3. In regions with advanced disease

IV. Important Preoperative Factors in Performing PK
   A. Patient selection
   B. Patient preparation (setting appropriate expectations for the short and long terms)
   C. Optimization of the ocular surface
   D. Choice of planned anesthesia
   E. Know your eye bank

V. Important Intraoperative Factors in Performing PK
   A. Establish a team approach
   B. Patient positioning
   C. Speculum choice
   D. Meticulous surgical technique (suture with the refraction in mind)
   E. Preparation for the worst complication

VI. Follow-up
   A. Close monitoring
   B. Patient education
   C. Simplification of medical management
   D. Patient preparation: next steps and time course
   E. Know when enough is enough

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Digging Deep: Improving Outcomes With Deep Anterior Lamellar Keratoplasty

Luciene B Sousa MD

Current concepts of the anatomy of the cornea and deep anterior lamellar keratoplasty will be presented, differentiating the different types of bubbles that can be formed during the procedure. Several techniques will be presented to reach the Descemet membrane, such as big bubble, pachybubble, and the use of different femtosecond lasers and intraoperative OCT use to achieve better surgical results. Complications and results from those procedures will be compared and discussed.

DSAEK—Still the Gold Standard?

Shahzad I Mian MD

I. Goals
   A. Maximize
      1. Corneal clarity
      2. Endothelial cell counts
      3. Structural integrity
   B. Minimize
      1. Refractive error
      2. Astigmatism
      3. Surface incisions
      4. Sutures

II. Endothelial Keratoplasty (EK)
   A. Descemetorrhexis, 2004:

      Melles GR, et al. A technique to excise the Descemet membrane from a recipient cornea. *Cornea* 2004; 23(3):286.

   B. Descemet-stripping EK (DSEK), 2005:

      Price FW Jr, Price MO. Descemet's stripping with endothelial keratoplasty in 50 eyes: a refractive neutral corneal transplant. *J Refract Surg*. 2005; 21(4):339.

   C. Descemet-stripping automated EK (DSAEK), 2006:

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III. U.S. Eye Banking Statistics

IV. DSAEK Indications
   A. Endothelial dysfunction that has become visually disabling in the absence of severe stromal opacity or scarring
      1. Fuchs endothelial dystrophy
      2. Bullous keratopathies
         a. Glaucoma drainage device
         b. Aphakia
         c. Anirdia
         d. Anterior chamber IOL
   B. Iridocorneal-endothelial (ICE) syndrome
   C. Late failure of penetrating keratoplasty (PKP), if refractive outcome was acceptable prior to endothelial failure
   D. Failed DSEK

V. DSAEK: Visual Acuity

VI. DSEK: Refractive Error

VII. DSAEK Advantages
   A. Tectonic stability: small incision
   B. Reduced sutures
   C. Stability in refractive error: reduced astigmatism
   D. Decreased rejection
   E. Faster recovery of vision

VIII. DSAEK Challenges
   A. Limited best corrected vision: lamellar interface abnormalities
   B. Refractive error
      1. Hyperopic shift
      2. Astigmatism
   C. Endothelial injury: graft failure
      1. Primary
      2. Long-term survival

IX. DMEK Advantages Over DSEK
   A. No additional stroma transplanted
   B. Faster and more complete visual recovery
   C. Minimizes surgically induced astigmatism
   D. No additional equipment to prepare tissue
   E. Lower rejection rate

X. Indications
   A. Fuchs corneal dystrophy
   B. Pseudophakic bullous keratopathy: visually disabling in the *absence* of stromal opacity or scarring
   C. Descemet detachment after cataract surgery: graft failure
      1. Following DSAEK
      2. Late failure of PKP

XI. Eye Bank Association of America: EK
   A. 2017
   B. Total: 48,763
      1. PKP: 18,346
      2. EK: 28,993
      3. DMEK
         a. 7628 (15-fold increase since 2012)
         b. 26.3% of all EK

XII. DMEK Limitations
   A. Learning curve
   B. Donor graft preparation: thin graft and removal of endothelium–Descemet membrane (EDM) without tears
   C. Donor EDM insertion: proper orientation in anterior chamber
   D. Lack of standardized unfolding technique
   E. Shortage of teaching facilities

XIII. Contraindications
   A. Large iris defect
   B. Aniridia
   C. Aphakia
   D. Glaucoma drainage device
   E. Trabeculectomy
   F. Anterior chamber IOL
   G. High hyperopia
   H. Failed PKP
   I. Severe corneal edema

XIV. Conclusions
   A. DSAEK is the current gold standard for EK.
   B. DMEK is emerging as a viable EK procedure, but it has limited indications.
   C. DSAEK is more versatile, providing optimal outcomes in complex anterior segment cases.

DMEK—Addressing the Challenges of Transitioning to a New Procedure

Mark A Terry MD

I. Introduction

A. The last 2 decades have seen the transition from penetrating keratoplasty to deep lamellar endothelial keratoplasty (DLEK) to Descemet-stripping automated EK (DSAEK) to Descemet membrane EK (DMEK).

B. Published evidence shows that DMEK allows faster recovery and better quality of vision than DSAEK or ultrathin DSAEK.

C. All transplant surgeons must make the transition to DMEK, even as they maintain their DSAEK skills.

II. Understanding the Laws of DMEK

A. Totally different skill set than DSAEK

B. DMEK scroll *always* spontaneously rolls up with the endothelium on the *outside* of scroll, so touching the tissue directly kills the endothelium.

C. Always create "fluid waves" to manipulate and unscroll the tissue.

D. Keeping the chamber very shallow (but *not* flat) is *critical* to unscrolling.

E. Every tissue has different scroll tightness, so the "dance" to unscroll it will be slightly different for every case; patience is a virtue.

F. Donors older than 60 years old tend to be thicker and easier to unscroll.

G. When you think the tissue is right-side up, it can be upside down, so double check every time before finally injecting air/gas to place tissue up into position.

III. Critical Components of DMEK Surgery

A. Control anterior chamber depth at all times.

B. Avoid direct manipulation of the tissue.

C. Learn variations in scroll configurations and associated tapping steps in unscrolling.

D. Use an "S" or "F" stamp to verify graft orientation.

IV. Variations in Tissue Injection

A. Endo-out tapping method: Preloaded tissue video (Mark Terry)

B. Endo-in pull-through method: Preloaded tissue video (Donald Tan)

C. Endo-in pull-through method: Preloaded tissue video (Massimo Busin)

V. Eye Bank Revolution Has Kept Pace With EK Evolution

A. Precut tissue made DSAEK easier.

B. Prestripped tissue and now preloaded tissue remove risk from operating room, lower costs, and increase the ease of doing DMEK surgery.

VI. Final Recommendations for Transitioning to DMEK

A. Learning the procedure

1. Attend multiple AAO and ASCRS didactic and wet lab courses.

2. View dozens of YouTube videos on DMEK.

3. Understand the variations in DMEK techniques and the unique challenges of each.

4. *Most importantly*: Be the first assistant at the microscope with an experienced DMEK surgeon to learn the nuances of this surgery before doing your first case.

B. Doing your first cases

1. Start with DMEK in a Fuchs dystrophy eye that is already pseudophakic.

2. Avoid eyes with prior vitrectomy, anterior chamber IOL, large iris defects, tubes, trabs, etc.

3. Request tissue that is 60 years old or older.

4. Start with preloaded tissue.

5. If SF_6 (20%) is easily accessible, use it. If not, air is fine.

6. Rebubble at slit lamp to minimally disrupt your clinic.

C. *Have fun!*

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Descemet Stripping Only (DSO)—Can We Do Without a Graft?

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 29% of the 48,000 transplants done in 2017. 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. Exactly how this repeat expansion causes disease in FECD is unproven. Interference with cellular homeostasis via nuclear RNA foci ("RNA toxicity") or by cytoplasmic translation products from the expanded repeats ("RAN peptides") have been suggested as possible mechanisms.[1]

The surgical management of FECD has undergone a revolution in the past 20 years—selective endothelial replacement surpassed penetrating keratoplasty as the procedure of choice a number of years ago. Modern-day endothelial keratoplasty, including Descemet membrane endothelial keratoplasty (DMEK) and Descemet-stripping endothelial keratoplasty (DSEK), are safe and effective surgeries, with generally rapid visual recovery and low risks of immunologic rejection.

About 6 years ago, however, several 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 the Descemet membrane as a treatment for endothelial dysfunction showed inconsistent results.[6] Subsequently, we and others have shown that corneal clearance in FECD can be achieved after deliberate central Descemet stripping only (DSO), without graft placement.[7-9] Recent work suggests that ripasudil, a topical Rho kinase inhibitor, can facilitate corneal clearance after DSO.[8]

This presentation will review the current state of DSO, the indications / contraindications for this procedure, and future directions for nongraft therapies for the treatment of FECD.

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Do Corneas Grow on Trees? Understanding the Evolving Role of Eye Banks

Marian Sue Macsai-Kaplan MD

NOTES

Case: A Challenging Cornea to Cure

Francis W Price Jr MD

There are various corneas that are challenging to cure. The ones we most commonly see are cloudy and thick, making it difficult to place a thin Descemet membrane endothelial keratoplasty (DMEK) graft with the correct orientation. "S" stamps, double-scroll insertion, and asymmetrical edge marks can all be difficult to see through a cloudy cornea.

We find intraoperative OCT to be very helpful in these cases. The weakness of intraoperative OCT is the difficulty of seeing through the anterior chamber if there are many blood cells.

Another difficult cornea to treat is one with progressive melting that begins at or near the limbus and progressively extends over the rest of the cornea.

What is the differential? Mooren ulcer, autoimmune disease, infectious, exposure, dry eye disease? The cause may influence the treatment.

How do you treat it? Penetrating keratoplasty, deep anterior lamellar keratoplasty (DALK), conjunctival flap, glue, amniotic membrane?

These are the questions. What have we missed?

2018 Advocating for the Profession and Patients

Cornea Subspecialty Day

Stephanie J Marioneaux MD

Ophthalmology's goal to protect sight and empower lives requires active participation and commitment to advocacy from every ophthalmologist. Contributions to the following three critical funds are a part of that commitment:

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

Please join the dedicated community of ophthalmologists who are contributing to protect quality patient eye care for everyone. The OPHTHPAC Committee is identifying Congressional Advocates in each state to maintain close relationships with federal legislators in order to advance ophthalmology and patient causes. At Mid-Year Forum 2018, we honored nine of those legislators with the Academy's Visionary Award. This served to recognize them for addressing issues important to us and to our patients. The Academy's Secretariat for State Affairs is collaborating closely with state ophthalmology society leaders to protect Surgery by Surgeons at the state level.

Our mission of "protecting sight and empowering lives" requires robust funding of both the Surgical Scope Fund and the OPHTHPAC Fund. Each of us has a responsibility to ensure that these funds are strong.

OPHTHPAC® Fund

OPHTHPAC is a crucial part of the Academy's strategy to protect and advance ophthalmology's interests in key areas, including physician payments from Medicare and protecting ophthalmology from federal scope-of-practice threats. Established in 1985, OPHTHPAC is one of the oldest, largest, and most successful political action committees in the physician community. We are very successful in representing your profession to the U.S. Congress.

Advocating for our issues in Congress is a continuous battle, and OPHTHPAC is always under financial pressure to support our incumbent friends as well as to make new friends among candidates. These relationships allow us to have a seat at the table with legislators who are willing to work on issues important to us and our patients.

The relationships OPHTHPAC builds with members of Congress is contingent on the financial support we receive from Academy members. Academy member support of OPHTHPAC allows us to advance ophthalmology's federal issues. We need to increase the number of our colleagues who contribute to OPHTHPAC and to the other funds. Right now, major transformations are taking place in health care. To ensure that our federal fight and our PAC remain strong, we need the support of every ophthalmologist to better our profession and ensure quality eye care for our patients.

Among the significant impacts made by OPHTHPAC are the following:

- Secured relief from the burdens and penalties associated with the existing Medicare quality improvement programs for 2018
- Halted applications of MIPS penalties to Part B drug payments to physicians
- Convinced CMS to revisit drastic cuts to retina and glaucoma surgical codes
- Halted the flawed Part B Drug Demonstration
- Derailed an onerous global surgery payment data collection plan
- Continued efforts in collaboration with subspecialty societies to preserve access to compounded and repackaged drugs such as Avastin

Contributions to OPHTHPAC can be made here at AAO 2018, or online at www.aao.org/ophthpac by clicking "Join." You can also learn more by texting "OPHTH" to 51555.

Leaders of the Cornea Society are part of the American Academy of Ophthalmology's Ophthalmic Advocacy Leadership Group (OALG), which meets annually in January in Washington, D.C., to provide critical input and to discuss and collaborate on the Academy's advocacy agenda. At the January 2018 OALG meeting, panel discussions took place on the outlook for Medicare reimbursement and implementation of the Merit-based Incentive Payment System (MIPS), as well as specialty research related to the IRIS™ Registry. In addition, meeting participants discussed the changing paradigm for optometric scope battles, held a roundtable to discuss challenges for surgical subspecialties, and considered how telemedicine could impact ophthalmology.

At Mid-Year Forum 2018, the Academy and the Cornea Society ensured a strong presence of cornea specialists to support ophthalmology's priorities. Ophthalmologists visited members of Congress and their key health staff to discuss ophthalmology priorities as part of Congressional Advocacy Day. The Cornea Society remains a crucial partner with the Academy in its ongoing federal and state advocacy initiatives.

Surgical Scope Fund

Thanks to contributions to the 2018 Surgical Scope Fund (SSF) from ophthalmologists across the country, the Academy's Surgery by Surgeons initiative has had a successful year preserving patient surgical safety and surgical standards in state legislatures across the country. The SSF is key to the Academy's Surgery by Surgeons campaign. *If you have not yet made a 2018 SSF contribution*, visit our contribution booth at AAO 2018 or contribute online at www.aao.org/ssf. If you already have made that 2018 contribution, please consider making a crucially needed supplemental contribution.

The SSF provides grants to state ophthalmology societies in support of their efforts to derail optometric surgery proposals that pose a threat to patient safety. Since its inception, the Surgery by Surgeons campaign and the SSF, in partnership with

state ophthalmology societies, has helped 34 state/territorial ophthalmology societies reject optometric scope-of-practice expansion into surgery.

To date in 2018, thanks to financial resources from the SSF, the Surgery by Surgeons campaign has netted patient safety and surgery standard preservation victories in the following battleground states:

- Florida
- Iowa
- Maryland
- Mississippi
- Nebraska
- North Carolina
- South Carolina
- Vermont
- Virginia

The 2018 battle is far from over, though. For example, California, Illinois, Massachusetts, and Pennsylvania are currently under assault. Furthermore, as of submission of this update in June 2018, the optometric surgery push had sprouted in six additional states.

Dollars from the SSF are critical in the state surgery campaigns. In each of these legislative battles, the benefits from SSF distributions are abundantly clear. The best lobbyists and public relations consultants are contracted as necessary. Additionally, media campaigns (including TV, radio, and social media) are launched to educate the voting public when needed. This helps to secure success in protecting patient safety by thwarting optometry's attempts at expanding its scope of practice to include surgery privileges.

Each of these endeavors is very expensive, and no one state has the resources to wage one of these battles on its own. Ophthalmologists must join together and donate to the SSF to fight for patient safety when a state faces a scope battle over optometric surgery.

The Secretariat for State Affairs encourages subspecialty societies to join state ophthalmology societies in contributing to the SSF. These ophthalmologic organizations complete the necessary SSF support structure for the creation and implementation of successful Surgery by Surgeons campaigns.

State Eye PAC

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

ACTION REQUESTED: *Advocate for Your Profession & Your Patients*

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

Please respond to your Academy colleagues and be part of the community that contributes to OPHTHPAC, the Surgical Scope Fund, and your State Eye PAC. Please be part of the community advocating for your patients now.

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Surgical Scope Fund	OPHTHPAC® Fund	State EyePAC
To derail optometric surgical scope-of-practice initiatives that threaten patient safety and quality surgical care	Ophthalmology's interests at the federal level Support for candidates for U.S. Congress	Support for candidates for state House, Senate, and governor
Political grassroots activities, lobbyists, PR and media campaigns	Campaign contributions, legislative education	Campaign contributions, legislative education
No funds may be used for campaign contributions or PACs.		
Contributions: Unlimited	Contributions: Limited to $5,000	Contribution limits vary based on state regulations.
Individual, practice, and organization		
Contributions are 100% confidential.	Contributions above $200 are on the public record.	Contributions are on the public record depending upon state statutes.

There Is Pigment on the Conjunctiva: When to Worry

Conjunctival Pigmented Lesions

Carol L Shields MD

I. Complexion-Associated Melanosis (CAM)
   A. Terminology: Also termed "racial melanosis"
   B. Clinical features
      1. Flat with microfolds and cobblestones
      2. Bilateral, limbus
      3. Dark complexion
      4. Symmetric, somewhat
   C. Management
      1. Observation
      2. Resection
      3. Cryotherapy
      4. Laser photocoagulation
   D. Prognosis: No transformation into melanoma, but note that primary acquired melanosis (PAM; see II.) can occur in dark complexion patients and can simulate CAM. If asymmetric CAM, suspect PAM.

II. Primary Acquired Melanosis
   A. Also termed "conjunctival melanoma in situ" and "intraepithelial melanocytic proliferation with / without atypia"
   B. Clinical features
      1. Flat, patchy pigmentation without cysts
      2. Usually white / European descent
      3. Looks like a flat freckle
   C. Management
      1. Surgical excision using no-touch technique
      2. Cryotherapy
      3. Reconstruction
      4. Topical chemotherapy
         a. Mitomycin C 0.04% q.i.d. for 1 week on, 1 week off, 1 week on, 1 week off
         b. Interferon 1 million units/cc q.i.d. for 3-6 months
   D. Prognosis
      1. Transformation to melanoma at 10 years is 12%, particularly if severe atypia.
      2. Each additional clock hour of PAM contributes 1.7 times risk for transformation to melanoma compared to 1 clock hour of PAM.

III. Secondary Acquired Melanosis
   A. Clinical features: Flat pigmentation at site of exposure
   B. Management: Observation
   C. Prognosis: No risk for melanoma

IV. Nevus
   A. Clinical features
      1. Slightly elevated, multicystic mass, usually at limbus
      2. Pigmented or nonpigmented
      3. Whites > non-whites
   B. Management: Observation or surgical resection
   C. Prognosis: Rare (1/300) risk for transformation to melanoma

V. Melanoma
   A. Clinical features
      1. Incidence is increasing. Study from the United States found rate of conjunctival melanoma significantly increased in white men, but not in white women. In white men, the incidence rate increased 295% over 27 years, especially in men older than 60 years, probably related to solar radiation. Same findings in study from Finland.
      2. Pigmented or nonpigmented mass, commonly associated with PAM
      3. Feeder and intrinsic vessels are prominent.
      4. Growth onto cornea or into fornix or orbit can occur.
   B. Management: Surgical resection
      1. Careful planning of approach is very important.
      2. No-touch technique
      3. Dry ocular surface without BSS
      4. *The first surgery is the most important surgery*, as complete resection without disturbing the tumor or seeding the tumor is tantamount to preventing recurrence and metastasis.
      5. Do not perform incisional biopsy or cut through the melanoma, as this can seed the tumor and lead to multiple recurrences, with need for exenteration.

C. Classification by American Joint Committee on Cancer Classification (AJCC), 7th edition

D. Prognosis

1. Overall exenteration in 15%
2. Overall metastasis in 25%
3. According to AJCC, 5-year rate of metastasis is 11% for T1, 35% for T2, and 42% for T3.

E. Biomarkers

1. BRAF
   a. If mutation, high risk for metastasis
   b. New medications for BRAF mutation include vemurafenib and dabrafenib.
2. TERT
3. PTEN

F. Checkpoint inhibitors

1. New class of medications that unleash T cells to fight cancer
2. Can be used for advanced skin and conjunctival melanoma

VI. Simulators of Melanoma

Several lesions, including extraocular extension of uveal melanoma, mascara deposition, pigmented mycetoma, hemorrhagic cyst, oncocytoma, and others

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Ocular Surface Squamous Neoplasia: What to Do With This Tumor?

Fairooz P Manjandavida MD

Introduction

Ocular surface squamous neoplasia (OSSN) is a blanket term currently used for precancerous and cancerous epithelial lesions of the conjunctiva and cornea that includes the spectrum of dysplasia, conjunctival intraepithelial neoplasia, and malignant squamous cell carcinoma (SCC).[1,2] Previously used terms include "intraepithelial epithelioma," "Bowen disease," and "Bowenoid epithelioma."[3] OSSN is recently broadly classified as conjunctival intraepithelial neoplasia (CIN) and invasive SCC. It is confined to the conjunctival epithelium and accounts for 39% of all premalignant and malignant lesions of the conjunctiva and 4% of all conjunctival lesions.[5] Invasive SCC of the conjunctiva occurs with much lesser frequency than CIN, with incidence that varies from 0.02 to 3.5 per 100,000 population.[6] Clinically, it is often difficult to differentiate between CIN and invasive SCC, but increased thickness and nodularity with feeder vessels are believed to be a sign of malignant transformation. However, there are thick tumors that may remain within the epithelium.

Predisposing factors for the development of OSSN, both environmental and systemic, include exposure to sunlight, HPV type 16 infections, and immunocompromised status.[1,2,4,5] There is a strong systemic association with xeroderma pigmentosum that may present as multiple recurrent lesions requiring long-term follow-up. Papillon- Leferve syndrome, a rare syndrome with palmo-plantar keratoderma, is also associated with OSSN in younger individuals.

Morphological Types

1. Placoid
   - Gelatinous
   - Papilliform
   - Velvety
   - Leukoplakic
2. Nodular
3. Diffuse

OSSN is mostly unilateral, and it is commonly seen in middle-aged and older patients, presenting as redness and ocular irritation. Larger lesions encroaching the cornea may affect the vision. Characteristically, the tumor may appear as a fleshy, nodular, or sessile minimally elevated lesion with overlying keratin, feeder vessels, and intrinsic vascularity.[1,2,5,6] Rose bengal staining is helpful in the diagnosis and assessing the extent of the tumor. Corneal involvement may appear as a subtle, wavy, superficially advancing greyish opacity that may be relatively avascular or may have fine blood vessels. Whereas others may present as papilliform or diffuse gelatinous lesions usually encroaching the cornea, primary corneal dysplasia affects the corneal epithelium with minimal limbal involvement.[7] Primary SCC of the cornea is rare.

Figure 1. This image shows elevated nodular conjunctival-limbal lesion with surface keratin, feeder vessels, and intrinsic vascularity that stains positive with rose-bengal. Corneal encroachment is noted. These are the clinical characteristics features of OSSN.

There are no consistent clinical criteria for distinguishing CIN from invasive SCC. Leukoplakia is usually absent or minimal in CIN; extensive leukoplakia raises the suspicion of malignancy. Nodular lesion causes suspicion of invasive SCC. A diffuse conjunctival OSSN can masquerade as chronic conjunctivitis.[7-9] It is also important to evert the eyelid of patients with OSSN to detect the contiguous or multifocal involvement of the tarsal conjunctiva.

Advanced cases can infiltrate the cornea and sclera to have intraocular extension.[7] Tumors extending into the orbit cause proptosis. Loco-regional lymph node and distant metastasis may occur rarely.[9] The most aggressive variants include spindle cell squamous carcinoma, mucoepidermoid carcinoma, and adenoid SCC.[2]

Diagnosis

OSSN in diagnosed clinically under slit-lamp biomicroscope with characteristic features as enumerated earlier. Anterior segment OCT is used as a diagnostic aid but may not be helpful in delineating the vertical extent in the presence of surface keratin and back-scattering. Recently "optical biopsy," a novel technology of ultra-high-resolution spectral domain OCT, has proven useful in detecting epithelial lesions and in guiding the management of OSSN in the era of topical chemotherapy / immunotherapy.[10] Ultrasound biomicroscopy (UBM) is found to be a useful tool in identifying the intraocular extension in advanced lesions. Orbit imaging with computerized tomography (CT-scan) is advised in tumors with suspected orbital extension and is indicated in those that extend to fornix and caruncle.

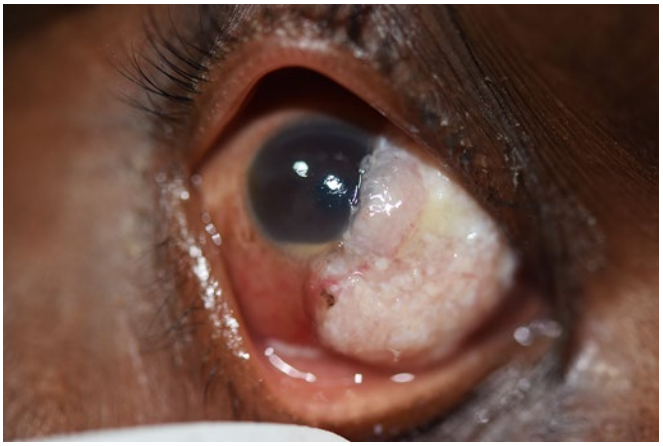

Figure 2. A 42-year-old immunocompromised male with conjunctival mass in right eye with extensive surface keratin presented with hypopyon and intraocular extension.

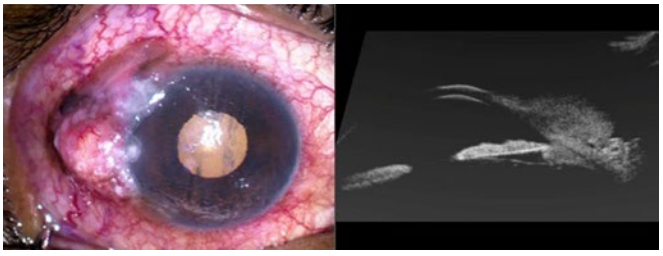

Figure 3. Nodular OSSN with corneal encroachment and scleral fixity shows scleral extension and ciliary body invasion in ultrasound biomicroscopy (UBM).

Treatment

Complete but gentle surgical excision using a technique without touching the tumor, called the "no-touch" technique, is the treatment of choice.[1-3,5,11] The steps of surgical excision include the following:

1. Conjunctival incision is made approximately 4 mm outside the clinically determined tumor margin. The incision incorporates full-thickness conjunctiva and Tenon fascia.
2. Dissection is carried out up to the limbus in the episcleral plane (if there is no episcleral adhesion).
3. Lamellar dissection of tumor-free sclera, 0.2 mm in depth and 2.0 mm outside the adherent conjunctival mass, is performed if the tumor is adherent to the episclera.
4. Absolute alcohol is applied with cotton-tipped applicator to the involved cornea to allow for controlled corneal epitheliectomy 2 mm outside the corneal component.
5. The corneal epithelium is scrolled off to the limbus using a controlled sweeping motion with a Beaver blade.
6. The tumor is removed in 1 piece along the limbus without touching the tumor.
7. Cryotherapy, double-freeze thaw cycle, is applied to the edge of the remaining bulbar conjunctiva and the scleral base if there was episcleral adhesion. Limbal cryotherapy should be limited to 6 clock hours.
8. Excision is followed by direct closure of the conjunctiva or with amniotic membrane graft.

Reported recurrence rate is 15%-52%. Lee et al reported a 17% recurrence after excision of conjunctival dysplasia, 40% after excision of CIN, and 30% for SCC of the conjunctiva.[2] However, with the protocol-based technique described above, the recurrence rate can be limited to less than 5%.

Apart from surgical excision, topical immunotherapy and chemotherapy has recently been considered as a mainstay of treatment in CIN.[12-14]

Indications for Topical Chemotherapy in Noninvasive OSSN

- > 2 quadrants of conjunctival involvement
- > 180° of limbal involvement
- Clear corneal extension encroaching the pupillary axis
- Positive margin after excision
- Patient not fit for surgery

Currently, topical interferon alpha 2b is widely accepted in the management of CIN as immunotherapy for primary treatment, immunoreduction to reduce the size of large tumors to facilitate complete tumor excision, and immunomodulation in immunocompromised patients.[15,16] It is also used in patients with surgical margin positive for tumor cells to prevent recurrence. Topically it is administered as 1 million IU, 4 times daily for 6 to 12 months. Extensive lesions are treated with 3 to 10 IU of monthly intralesional injections until resolution.

Figure 4. Diffuse corneal OSSN with temporal limbal involvement in right eye of 18- year-old immunocompromised female shows complete resolution with 4 months of topical interferon- alpha 2B.

Combined topical immunotherapy and surgical excision provides excellent outcomes, with a reduced recurrence rate.[15] It has the advantage of treating subclinical disease. However, clinical resolution is not immediate, often requiring months and strict patient compliance. It can also be used as a combination of topical and intralesional injection to reduce the treatment duration.

Topical mitomycin C (MMC) has similar indications but is less favored due to surface toxicity.[17-19] There are several protocols, but a dosage of 0.04%, q.i.d., 4 days a week for 4 weeks works best in our experience.

Protocol for Interferon-alpha 2b

- Topical eye drops 1 million IU 4 times a day for 3 to 12 months
- Injection sublesional 3 to 10 million IU once monthly until resolution
- Refrigeration required

Protocol for Topical MMC: Rule of 4

- 0.04% (0.4 mg/ml)
- Four times a day
- Four days a week
- Four weeks
- Two weeks of treatment-free interval
- Refrigeration required

Topical 1% 5-flurouracil (5-FU) is an antimetabolite used in the treatment of OSSN. It is widely available and comparatively inexpensive.[20-25] Various studies have recently reported the effectiveness of 5-FU as a primary modality and postoperative adjuvant to reduce recurrence.[24,25] The advantage of 5-FU over other topical medication is that it does not require refrigeration or cold-chain to be maintained. In developing countries where there is financial restraints and resource limitations, 5-FU can be accepted as a valuable alternative.

Protocol for Topical 5-FU

- 1% eye drops 4 times a day for 4 weeks (1 cycle)
- 2 weeks of treatment-free interval
- Refrigeration not required

Plaque brachytherapy is used to control gross or microscopic residual tumors. It is also indicated as a primary modality or in those with scleral invasion.[26,27] More extensive orbital invasion requires orbital exenteration.

Prognosis

Conjunctival SCC has a good prognosis. With protocol-based management, local recurrence rate is about 5% and regional metastasis is 2%.[22] Prognosis is worse in mucoepidermoid or spindle cell variants and in patients who are immunosuppressed, particularly those with AIDS.

Table 1. Topical Chemotherapeutic Agents for OSS: Summary

Drugs	Type	Mechanism of Action	Dosage	Adverse Effects
Mitomycin C	Alkylating agent	Under aerobic conditions, generates free radicals ↓ Cytotoxicity Lipid peroxidation • Inhibition of DNA and protein synthesis • Inhibits cell migration and production of extracellular matrix	Topical 0.02% to 0.04%	• Conjunctival hyperemia • Blepharospasm • Corneal punctate erosion • Punctal stenosis • Limbal stem cell deficiency
5-fluorouracil	Pyrimidine analogue	• Inhibits thymidylate synthetase • Inhibits production and incorporation of thymidine into DNA • Inhibits RNA synthesis	Topical 1%	• Eyelid erythema • Conjunctival hyperemia • Corneal punctate erosion
Interferon-α2b	Type 1 interferon	• Immune-mediated suppression of IL-10, stimulates IL-2 and IFN-γm RNA • Antiproliferative • Antiviral	Topical or intralesional • 1 million IU/ml • 3 million IU/ml	• Superficial punctate keratopathy • Follicular conjunctivitis **Systemic** • Flu-like syndrome • Fever/ myalgia

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It's a Salmon Patch: What to Do With Lymphoproliferative Lesions

Bita Esmaeli MD FACS

In this segment we will review the differential diagnosis of a "salmon patch" infiltrate as well as tumors and pseudotumors that may mimic this. We will also go over the initial steps in appropriate diagnosis and management of lymphoproliferative lesions of the conjunctiva and briefly review the recent advances in treatment options for the same.

It's Fleshy Tumor: What to Do With Pterygium—An Evidence-Based Approach

Guillermo Amescua MD

NOTES

What Is Going on With This Eye? Is It a Tumor?

Swathi Kaliki MD

Introduction

Ocular surface squamous neoplasia (OSSN) is the most common ocular surface malignancy. Advances in the surgical and nonsurgical management of OSSN have made this malignancy a highly curable tumor.

Various benign and malignant tumors of the ocular surface can mimic OSSN, leading to misdiagnosis and missed diagnosis. Going further, various ocular surface tumors can mimic OSSN, resulting in *over*diagnosis and mistreatment. In this presentation, I will discuss the various case scenarios of misdiagnosis and overdiagnosis of OSSN.

Background Observations

The most common conditions mimicking OSSN and thus leading to misdiagnoses include chronic (blepharo)conjunctivitis, sclerokeratitis, necrotizing scleritis, conjunctival nevus / melanoma, simple limbal stem cell deficiency, and corneal opacity. The conditions resembling OSSN resulting in overdiagnosis include chronic inflammation, actinic keratitis, pterygium, corneal dystrophy, conjunctival leiomyosarcoma, and conjunctival mucoepidermoid carcinoma.

In this presentation, I will discuss the pertinent history of each case and clues to avoid misdiagnosis or overdiagnosis of OSSN.

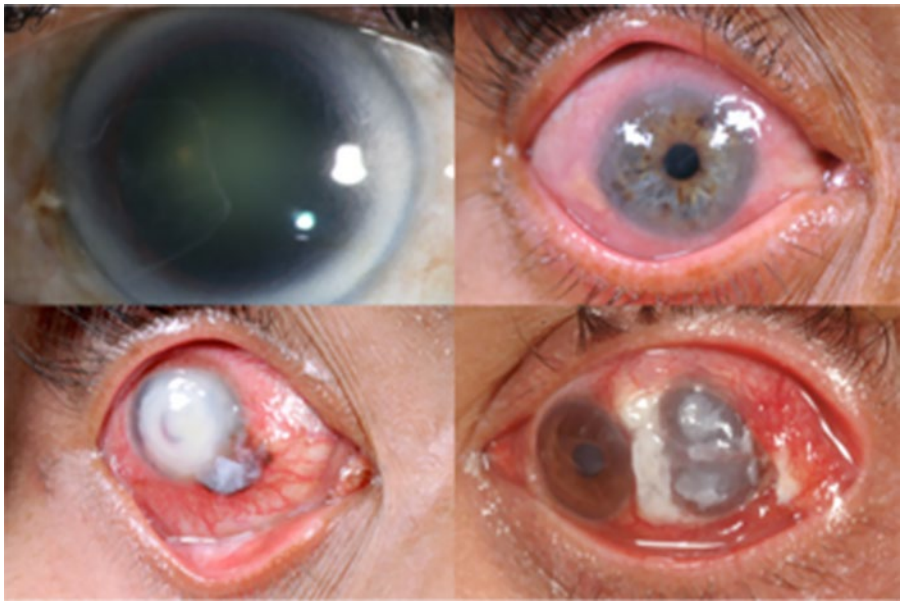

Figure 1.

Conjunctival Lesions in Children

Jacob J Pe'er MD

Most conjunctival lesions in children are benign, while malignant tumors are rare. Epithelial benign tumors, such as squamous papillomas, and nevi, including inflamed nevi, which are common, can be observed or surgically excised. Lymphoproliferative lesions are rare and usually benign but should be excised for diagnosis. Congenital lesions such as hamartomas and choristomas should be handled according to their size and the functional disturbance they cause.

Case: Is It a "Toomah"?

Christopher J Murphy DVM PhD and Sara M Thomasy DVM PhD

Anatomically, the vertebrate eye is a remarkably conservative structure, with all vertebrates adhering to a fundamental design. Similarly, fundamental ocular disease processes affect all vertebrates. Raised conjunctival, limbal, and corneal lesions can be associated with inflammatory as well as neoplastic (and other) disease processes. The best-studied species is *Homo sapiens*, but other mammalian species as well as all other classes of vertebrates (fish, amphibians, reptiles, and birds) can be affected (approx. 51,000 species in aggregate). A small sample of cases will be presented to highlight the similarities and differences between species, as well as some unique considerations in patient handling and management.

Pediatric Corneal Opacity: New Paradigms

Kanwal K Nischal MBBS

Deep phenotyping is becoming more and more important as we discover genotypic variations and possible therapies for congenital eye abnormalities. The first step is to develop a coherent classification system that allows doctors and patients to understand prognoses and outcomes of different interventions. In this talk such a classification will be discussed and the implications of the phenotyping for specific genotyping will be emphasized. While traditionally exonic mutations have been sought when making genetic diagnoses, the role of cis-regulatory elements (CREs) is fast becoming important. This in large part is due to convergent evolutionary biology being used in work on anterior segment developmental anomalies, especially those affecting the cornea.

DREAM Study: Omega 3 Fatty Acids and Dry Eye Disease

Penny Asbell MD FACS

I. Dry Eye RCT Design
   A. Real-world trial design: symptomatic patients despite current treatments
   B. Placebo: who, what, when?
   C. Placebo response in dry eye disease trials
   D. Objectivity of compliance: blood levels most accurate method of compliance in nutritional trial

II. DREAM Results
   A. Main results
   B. Omega 3 at baseline
   C. Baseline data vs. other omega 3 trials
   D. Correlation between symptoms (Ocular Surface Disease Index) and signs
   E. Minimally invasive tests for tear stability and tear production
   F. Inflammatory biomarkers, correlation with signs and symptoms
   G. Novel markers for Sjögren syndrome

Selected Readings

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What's Hot With Cicatrizing Disease?

James Chodosh MD MPH

I. Differential Diagnosis of Cicatricial Conjunctivitis (Common Causes)

   A. Acute onset

      1. Epidemic keratoconjunctivitis (EKC)
      2. Chemical / thermal injury
      3. Stevens-Johnson syndrome / toxic epidermal necrolysis (SJS/TEN)

   B. Chronic onset

      1. Mucous membrane pemphigoid (MMP) and variants, including linear IgA dermatosis, and paraneoplastic pemphigoid
      2. SJS/TEN
      3. Less common causes include sarcoidosis, atopy, postoperative / iatrogenic

II. Diagnosis Is Predominantly by Clinical History and Examination

   Role of skin / conjunctival or other mucosal biopsies to be discussed.

III. Management of Cicatricial Conjunctivitis Depends Largely on the Etiology

   A. In the acute phase, the focus is on prevention:

      1. In EKC: stripping of conjunctival membranes and use of topical corticosteroids
      2. In chemical / thermal injury: use of amniotic membrane and topical corticosteroids
      3. In SJS/TEN: use of amniotic membrane and topical corticosteroids

   B. In the chronic phase, the focus is also on prevention (of worsening).

      1. Medical management: Discussion will include newer biological therapies.
      2. Surgical management of cicatricial conjunctivitis should only be attempted upon resolution of the cause, or if autoimmune (eg, MMP), stabilization and resolution of inflammation.

Simple Limbal Epithelial Transplantation: Indications and Outcomes

Sayan Basu MBBS MS

Introduction

The stem cells responsible for corneal epithelial renewal are located at the limbus. Severe injury or inflammation can irreversibly damage this sensitive region, leading to a potentially blinding condition known as limbal stem cell deficiency (LSCD). Limbal stem cell transplantation (LSCT) from a healthy donor eye is usually successful in restoring a normal corneal surface. The most recent advancement in LSCT is the surgical technique of simple limbal epithelial transplantation (SLET). The main advantages of SLET over earlier techniques of LSCT are that it requires very minimal donor tissue, is relatively easy to replicate, and is much less expensive.

Indications and Surgical Technique

Ocular surface reconstruction using SLET is primarily indicated in cases of LSCD with a wet ocular surface and normal eye lid anatomy and function. Patients with unilateral chronic ocular surface burns are the most suitable candidates for this procedure. Typically, a one clock hour–sized limbal fragment is obtained from the healthy fellow eye and divided into 6 to 10 small pieces, which are then transplanted onto the affected eye over an amniotic membrane overlay graft after removal of the pathological fibrovascular pannus. Complete epithelization of the cornea usually occurs by 7-14 days, and corneal clarity and visual acuity keep improving over time.

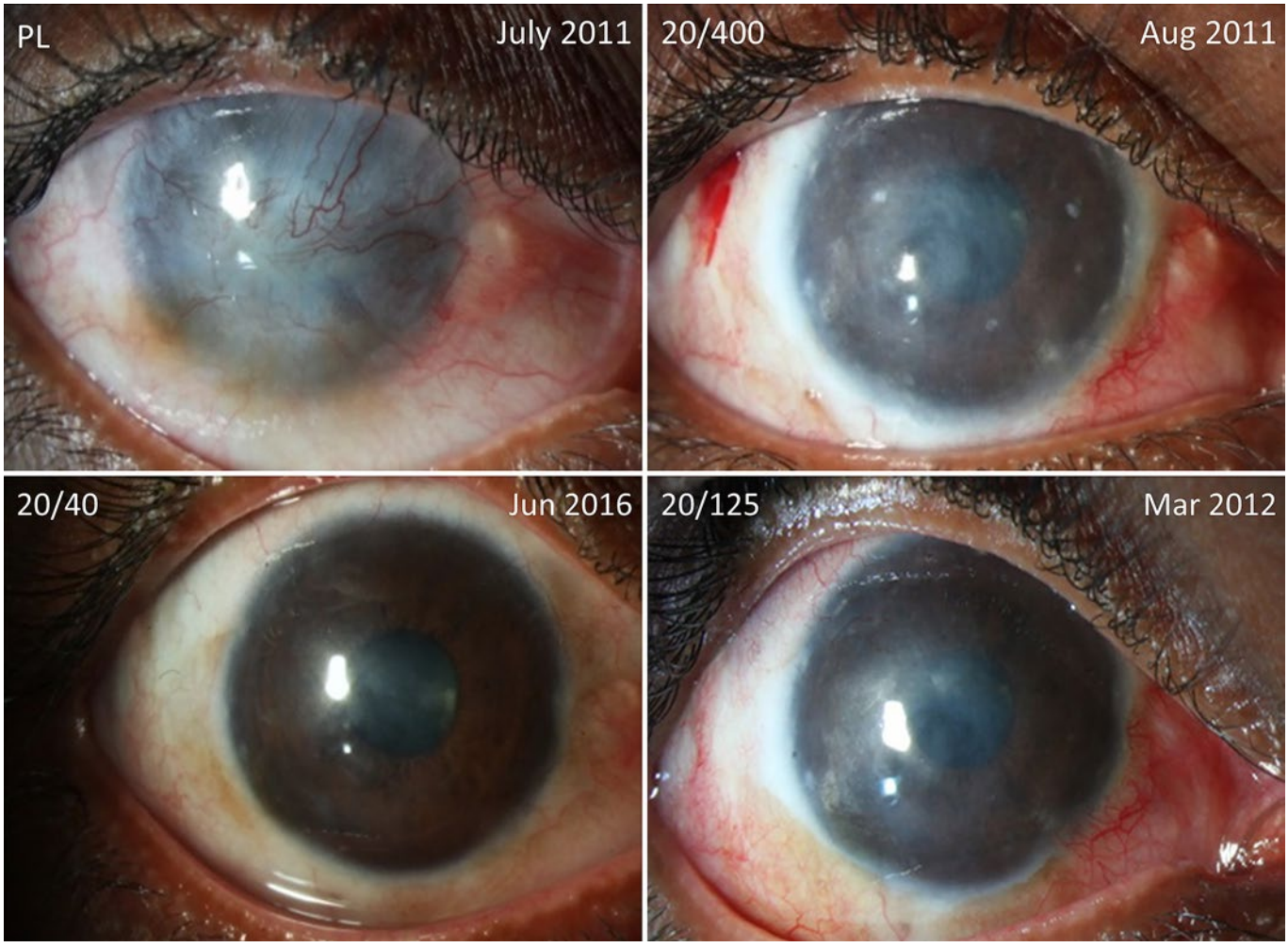

Figure 1.

Outcomes

The first study describing the technique and early postoperative outcomes in 6 patients with unilateral chronic ocular surface burns was published in 2012.[1] Subsequently 2 large case series reporting longer-term outcomes, one on 125 eyes and one on 68 eyes, were published in 2016.[2,3]

The prospective case series of 125 eyes with a minimum of 1 year of follow-up reported a 76% success rate, with survival probabilities of 80% in adults and 72% in children.[2] This study also showed that SLET was easily replicable, and the success rates were similar among cornea fellows in training and experienced ocular surface specialists.

The retrospective, multicenter study on 68 eyes showed the success of SLET in 57 cases (83.8%) with survival probability greater than 80% at 1 year.[3] Several smaller case series with similar success rates and anecdotal case reports of successful results with SLET in unusual indications are also available in literature.[4]

There have also been reports of allogeneic SLET being performed in patients with bilateral LSCD from living-related and cadaveric donors.[4] A recent prospective study found that SLET was successful (77%) even in eyes where other techniques of LSCT have previously failed.[5]

Summary

Patients with severe ocular surface burns and other forms of limbal stem cell damage develop a blinding keratopathy characterized by conjunctivalization of the cornea, neovascularization, or even nonhealing epithelial defects. Traditional approaches of treating LSCD have relied on either transplanting large limbal lenticules, which may be unsafe for the donor eye, or using ex vivo cell expansion, which is safer but very expensive.

With the advent of SLET, it is now possible for anterior segment surgeons to successfully treat patients with LSCD using an easily replicable technique with minimal donor tissue and no additional or sophisticated surgical infrastructure. These attributes can allow SLET to reach hundreds of thousands of corneal blind individuals suffering from LSCD globally, particularly in resource-limited settings of the developing world.

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Fuchs Dystrophy: Future Horizons

Anthony J Aldave MD

I. Molecular
   A. Rho / Rho-kinase pathway inhibition
      1. Mechanism of action
         a. Promotes corneal endothelial cell migration and adhesion
         b. Maintains endothelial cell phenotype (prevents cell state transition)
      2. Patient selection
         a. Combined with injection of ex vivo expanded allogenic human corneal endothelial cells (HCEnC)
         b. Combined with primary descemetorrhexis with or without Descemet membrane transplantation
   B. Mitochondrial protection: elamipretide (ClinicalTrials.gov Identifier: NCT02653391)
      1. Mechanism of action: Mitochondria-targeting peptide that protects against toxic reactive oxygen species and enhances ATP synthesis
      2. Patient selection: Mild to moderate corneal edema
   C. Genetic modulation
      1. Mechanisms of action
         a. Silencing of *TCF4* expression
            i. Targeted gene editing (CRISPR-Cas9)
            ii. Enhanced degradation (RNase-H-activating antisense oligonucleotide)
         b. Modification of *TCF4* pre-mRNA splicing
            i. Oligonucleotide steric blockage (antisense oligonucleotide)
      2. Patient selection: Individuals with pathogenic *TCF4* trinucleotide repeat expansions

II. Surgical
   A. Descemet membrane endothelial keratoplasty (DMEK): Patient selection
      1. Hemi- and quarter-DMEK: mild to moderate central corneal edema
      2. Pull-through insertion techniques: Individuals who are not ideal candidates for DMEK using traditional insertion and unfolding techniques
         a. Aphakia
         b. Aniridia
         c. Presence of an anterior chamber IOL
         d. Prior tube shunt implantation
   B. Primary descemetorrhexis with or without Descemet membrane transplantation: Patient selection
      1. Younger age
      2. Mild central stromal edema (< 625 microns)
      3. Clear peripheral cornea with good endothelial cell density
   C. Cell-based therapies
      1. Ex vivo expanded allogenic human corneal endothelial cells
         a. Cell injection
         b. Cell sheets
      2. Allogenic human mesenchymal stem cells

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Updates from the Cornea Preservation Time Study

Jonathan Lass MD on behalf of the Cornea Preservation Time Study Group

I. Cornea Preservation Time Study (CPTS) Background and Rationale[1]

A. Hypothermic (2°-8°C) corneal donor storage solutions approved by FDA for storage of donor corneas up to 14 days

B. Actual utilization often < 8 days (96% of donor corneas used for keratoplasty in the United States as reported by 19 eye banks in a 2010-2011 survey[1])—surgeon bias, not evidence-based

C. Advantages of extending beyond 7-8 days

II. Study Design

A. Primary objective: To determine the effect of preservation time (PT) on graft success and endothelial cell loss in eyes undergoing Descemet-stripping automated endothelial keratoplasty (DSAEK) for cornea conditions associated with endothelial dysfunction and moderate risk for graft failure, Fuchs dystrophy, and uncomplicated pseudophakic / aphakic corneal edema (PACE)

B. Multicenter, randomized, masked, noninferiority clinical trial

C. Randomized to a donor cornea with preservation time (PT) of 0-7 days (n = 675) or 8-14 days (n = 655)

D. Followed 3 years or until graft failure

III. Outcomes

A. Graft failure defined as regraft for any reason, a cloudy or equivocally cloudy cornea 1 day postoperatively without clearing within 8 weeks, or an initially clear graft that became and remained cloudy for 90 days

B. Endothelial cell density (ECD) captured at donor screening, preoperatively, and at 6, 12, 24, and 36 months; determined from the central endothelium by a central image analysis reading center

IV. Results to Be Covered: Primary Graft Success Results[2]

A. Three-year cumulative probability of graft success

1. 95.3% in the 0-7 days PT group vs. 92% in the 8-14 days PT group

2. Difference of 3.2%; upper limit of the 1-sided 95% CI on the difference was 5.4%, exceeding the prespecified noninferiority limit of 4%.

B. Preplanned secondary analyses

1. Longer PT associated with lower rate of graft success

2. P = .01 [PT analyzed as 4 subgroups]

3. 96.5% (PT of 4 days or less); 94.9% (PT of 5 to 7 days); 93.8% (PT of 8 to 11 days); 89.3% (PT of 12 to 14 days)

C. Conclusions

1. High 3-year success rate in eyes undergoing DSAEK, irrespective of PT

2. However, the study was unable to conclude that the success rate with donor corneas preserved 8 to 14 days was similar to that of corneas preserved 7 days or less with respect to the prespecified noninferiority limit.

3. Although longer PT was associated with a lower success rate, the difference in rates was small when PT was less than 12 days.

a. Primary endothelial cell loss (ECL) results[3]

i. Among eyes with functioning grafts at 3 years, mean (SD) decrease in ECD from baseline: 37% (21%) in the 0-7 days PT group vs. 40% (22%) in the 8-14 days PT group (P = .03)

ii. Preplanned secondary analyses

b. Longer PT was associated with lower ECD.

c. Endothelial cell loss (ECL) comparable from 4 to 13 days

4. Conclusion: Although ECL 3 years after DSAEK is greater with longer PT, the effect of PT on ECL is comparable from 4 to 13 days PT.

V. Preplanned Secondary Objectives of Study

A. To evaluate the effect of donor, recipient, operative, and postoperative factors on graft failure and endothelial cell density 3 years following DSAEK

B. Over 25 donor, recipient, operative, and postoperative parameters were recorded prospectively and analyzed in multivariable factor selection models using P < .01 significance level.

C. Diabetic donor status, recipient diagnosis of PACE, and operative complications increased the risk for graft failure following DSAEK.

D. Diabetic donor status, recipient diagnosis of PACE, and operative complications lower ECD at 3 years.

E. Although most DSAEK cases with graft dislocation had a successful outcome, graft dislocation predicts a significantly increased risk of primary and early graft failure.

F. Longer PT, diabetic donor status, and operative complications were associated with increased risk of graft dislocation.

G. The only factor found to be associated with rejection was recipient age.

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NOTES

Detecting "Dry Eyes": The Utility of Diagnostic Tests Old and New

Christopher J Rapuano MD

I. "Dry Eye Disease" Is a Multifactorial Condition
   A. Hyposecretion of tears
   B. Excessive evaporation of tears
   C. Huge overlap
   D. Signs and symptoms often do not match.

II. Testing
   A. Old
      1. Bulky questionnaires
         a. Ocular Surface Disease Index (OSDI), 12 questions x 5 answers
         b. National Eye Institute Visual Function Questionnaire (NEI VFQ-25), 25 questions x 4 answers
         c. Impact of Dry Eye on Everyday Life (IDEEL), 57 items
      2. Schirmer I and II
      3. Ocular ferning
      4. Tear breakup time (TBUT)
      5. Fluorescein staining
      6. Rose bengal staining
      7. Sjögren blood testing
         a. SS-A
         b. SS-B
         c. ANA
         d. RF
      8. Impression cytology
   B. New
      1. Rapid questionnaires
         a. Standard Patient Evaluation of Eye Dryness (SPEED), 8 questions x 3-4 answers
         b. UNC Dry Eye Management Scale
      2. Tear osmolarity: TearLab
      3. Matrix metalloproteinase-9 (MMP-9) testing: Discovery (TearLab), InflammaDry (Quidel)
      4. Interferometry: LipiView I & II (J&J / Tear Science)
      5. Lissamine green staining
      6. Topographic analysis of tear film stability: Keratograph 5M (Oculus)
      7. Meibomian gland evaluation: LipiView II (J&J / TearScience)
      8. Anterior segment OCT
         a. Quantifies tear meniscus
         b. Evaluates epithelial irregularity
      9. Sjö test (B+L)
         a. Salivary protein-1
         b. Carbonic anhydrase-6
         c. Parotid secretory protein
         d. Possibly early markers for Sjögren syndrome
      10. Eyeprim impression cytology (Europe)

Managing Meibum: Addressing Meibomian Gland Dysfunction in Dry Eye Disease

Roni M Shtein MD

I. Meibomian Gland Dysfunction: The Basics
   A. Anatomy
   B. Physiology
II. Meibomian Gland Dysfunction: Diagnosis
   A. Physical examination
   B. Diagnostic devices
III. Meibomian Gland Dysfunction: Treatment
   A. Eyelid hygiene
   B. Pharmacologic treatments
   C. In-office procedures

Blood, Sweat, and Tears: Topical Hematopoetic Therapies for Dry Eyes

Victor L Perez MD

- Autologous serum eye drops
- Commonly believed that it was first described by Fox et al in 1984 to be used as a tear substitute.
- How are they different than artificial tears?
  - Normal artificial tears serve to lubricate the ocular surface.
  - Autologous serum tears, or ASTs
  - ASTs contain a host of epitheliotrophic factors such as growth factors, immunoglobulins, vitamins, and substance P (Matsumoto et al., 2004 ; Geerling, et al., 2004).
  - ASTs also lack preservatives.
- Indications
  - Severe dry eye (idiopathic, graft versus host disease, etc.)
  - Superior limbic keratoconjunctivitis
  - Recurrent erosions
  - After ocular surface reconstruction
  - Persistent epithelial defects including neurotrophic ulcer
- Relevant literature
- Autologous serum publications for ocular surface
- Adverse effects and downsides
- Platelet-rich plasma (PRP) has been used for over a decade in different clinical areas like orthopedics, oral and maxillofacial surgery, reconstructive surgery, cardiovascular surgery, and plastic surgery, but only recently has PRP been brought to ophthalmology, showing very promising results.
- PRP obtained from total unclogged blood is very rich in platelets and growth factors.
- Platelets are known to secrete some of these factors from alpha granules, such as platelet-derived epidermal growth factor, transforming growth factor β (TGF-β), platelet-derived angiogenesis factor, platelet-derived growth factor, and platelet factor IV.
- Also in 2007, Alio et al demonstrated that the use of autologous PRP promotes the healing of dormant corneal ulcers, even in eyes threatened by corneal perforation, and was accompanied by a reduction in pain and inflammation.
- The advantage of PRP over autologous serum is that PRP has a higher presence of vitamins and growth factors.
- Autologous PRP has a large quantity of growth factors that are released from the platelets; then the growth factors act directly on the ocular surface.
- In the PRP preparation, the platelets are intact and can adhere to the ocular surface and improve the biochemical and biological mechanism.
- Case presentation
- Anitua E, Muruzabal F de la Fuente M, Merayo J, Durán J, Orive G. Plasma rich in growth factors for the treatment of ocular surface diseases. *Curr Eye Res*. 2016; 41(7):875-882.
- PRGF- fibrin clot: regeneration of the ocular surface indications.
- Conclusions
  - The use of ASTs is effective in the treatment of ocular surface disorders.
  - ASTs are safe, and serum from patients with immune disorders can be used.
  - The study and use of platelets preparation and other biologics is the next frontier of biological data.
  - We need to identify these factors.

Sniffing Out New Solutions: Devices and Technology in the Management of Dry Eyes

Stephen C Pflugfelder MD

I. Scleral Contact Lenses

A. The next-generation bandage lens

1. Wear on extended basis with close observation
2. Consider moxifloxacin in lens reservoir
3. Successful treatment of nonhealing epithelial defects and recurrent erosions,[1,2] including epithelial defects refractory to hydrogel lenses

B. Treatment of ocular surface disease

1. Comfort[3]
2. Improved visual acuity[4]

C. Corneal protection and improved outcomes in Stevens-Johnson syndrome[5,6]

D. Reduction of stromal opacity[7]

E. Improved ability to fit eyes with filtering bleb / tube shunt: New custom designs are fit from mold of ocular surface.

II. Nasal Neurostimulation

A. Stimulation of anterior ethmoidal nerve induces reflex tearing.[8-10]

B. Symptom improvement[11]

C. Increased aqueous secretion and tear volume[11,12]

D. Goblet cell degranulation[12]

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Cutting to the Chase: Surgical Options for the Treatment of Ocular Surface Disease

Edward J Holland MD

I. Procedures
   A. Anterior stromal puncture
   B. Superficial keratectomy
   C. Phototherapeutic keratectomy
   D. Amniotic membrane transplantation
   E. Conjunctival surgery
      1. Conjunctival resection
      2. Conjunctival flap
   F. Ocular surface transplantation
      1. Conjunctival limbal autograft (CLAU)
      2. Conjunctival limbal autograft (CLAL)
      3. Keratolimbal allograft (KLAL)
      4. Cultured limbal epithelial transplantation
      5. Simple limbal epithelial transplantation
   G. Keratoprosthesis
      1. Boston KPro
      2. Osteo-odonto keratoprosthesis (OOKP)

A Painful Problem: The Diagnosis and Management of Neuropathic Corneal Pain

Anat Galor MD

I. What Is Neuropathic Corneal Pain?
II. How to Diagnose Neuropathic Corneal Pain
  A. Questionnaires
  B. Quantitative sensory testing
  C. Objective measures
III. How to Manage Neuropathic Corneal Pain
  A. Topical therapies
    1. Anti-inflammatories
    2. Autologous serum tears
    3. Amniotic membrane
    4. Contact lenses
  B. Local therapies
    1. OnabotulinumtoxinA
    2. Nerve blocks
  C. Systemic therapies
    1. Alpha 2 delta (α2δ) ligands
    2. Tricyclic antidepressants
  D. Adjuvant therapies
    1. Electrical stimulation
    2. Desensitization therapy

Case: Not Your Standard Dry Eyes

Sophie Deng MD PhD

Dry eye disease is the one of most common diseases to affect the ocular surface. The etiology is multifactorial, characterized by an instability of the tear film accompanied by ocular symptoms. Other ocular surface diseases, including neurotrophic keratitis, superior limbic keratoconjunctivitis, keratitis secondary to systemic medication, and limbal stem cell deficiency, could coexist with dry eye disease and often cause similar ocular symptoms. These ocular surface diseases might be overlooked or misdiagnosed as merely dry eye disease. In this presentation, representative cases of these ocular surface diseases are presented to illustrate the importance of a detailed ocular history and anterior segment examination in obtaining a correct diagnosis that guides appropriate treatment.

Atypical Keratitis: What Not to Miss

Gerami D Seitzman MD

I. "Typical" Infectious Keratitis
   A. Cornea epithelial defect with inflammation, a positive diagnostic test, treatment with antimicrobials, and resolution of inflammation
   B. Bacterial, fungal, viral infections are often considered typical.

II. "Atypical" Infectious Keratitis
   A. May include corneal suppuration without an epithelial defect, negative diagnostic testing, and/or worsening of condition on antimicrobials
   B. Common "atypical" infections include *Acanthamoebae*, mycobacterial, and microsporidia.
   C. "Atypical keratitis" also occurs when "typical" keratitis behaves unusually.

III. *Acanthamoeba* Keratitis
   A. Early signs include rough keratopathy, pseudodendrites, anterior stromal patchy infiltrates, and radial perineuritis.
   B. Ring infiltrates are late signs.

IV. Microsporidial Keratitis
   A. Superficial keratoconjunctivitis, typically immune compromised
   B. Stromal keratitis, typically immune competent

V. Atypical Mycobacterial
   A. Keratitis is the most common ocular atypical mycobacterial infection.
   B. Vast majority of cases are preceded by a surgery, most commonly LASIK.

VI. Polymicrobial Infections
   A. Simultaneous infections
      1. 20% fungal keratitis coinfected with bacteria
      2. Up to 25% of *Acanthamoeba* keratitis may be culture positive with microbial coisolates.
   B. Sequential infections
      1. HSV/VZV epithelial defect with secondary infection
      2. Unhealthy ocular surface

VII. Toxicity

Can masquerade as persistent infection or secondary infection

   A. Iatrogenic: prolonged fortified antibiotic, preservative toxicity, drug deposits
   B. Anesthetic abuse

VIII. Infections With Intact Cornea Epithelium
   A. Fungal infections
   B. Infectious crystalline keratopathy
   C. Bacteria that can penetrate intact epithelium: *Neisseria gonorrhea*, *Corynebacterium diptheriae*, *Listeria monocytogenes*, *Haemophilus influenzae*

IX. Antibiotic-Resistant Infections
   A. MRSA
   B. Fluoroquinolone resistance

X. Compliance
   A. Expense
   B. Medications only work when they are used.

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Zoster: Give It a Shot

Keith Hugh Baratz MD

Adapted from "Recommendations for Herpes Zoster Vaccine for Patients 50 Years and Older," https://www.aao.org/clinical-statement/recommendations-herpes-zoster-vaccine-patients-50-.

Introduction

Herpes zoster is a serious health problem in the United States. Current estimates of new cases in the US are up to 1.2 million each year, about 20% of which are herpes zoster ophthalmicus (HZO).[1] It is estimated that one in three people over their lifetime will have zoster. Although it is more common and severe in immunocompromised persons, the vast majority, or over 90%, of patients afflicted with zoster are not immunocompromised. While the incidence goes up significantly with age, starting in the 40s, the number of cases is highest in people in their 50s.[2-4] In one Centers for Disease Control and Prevention (CDC) study, the mean age of onset was 52 years.[5]

Risk factors for the development of zoster include increased age, immunocompromised status, female gender, severe physical limitation,[6] heart failure,[7] traumatic brain injury,[8] diabetes,[1] acute kidney failure,[9] and depression.[10]

Disease Complications and Costs

The complications and sequelae of herpes zoster can be severe and long term, even very rarely resulting in death.[11] Thus, the medical costs incurred by herpes zoster and its complications, including direct costs from acute and chronic pain, eye complications, secondary infections and neuropathies, are estimated at $1 billion,[12] with indirect costs from lost work and work productivity adding to that total, especially in younger age groups such as those 50-59 years of age.[13]

Ocular complications of herpes zoster include infectious and inflammatory anterior and posterior segment disease, neurotrophic ocular surface disease, and eyelid malposition and scar. Severe, irreversible vision loss may result from corneal opacification, glaucoma, and retinal disease.[14] Approximately 20% of individuals affected by HZO develop potentially serious ocular disease, such as keratitis, uveitis, glaucoma, or neurotrophic disease. The 10-year probability of developing severe visual loss (20/200 or worse), a serious eyelid malposition, or chronic trichiasis varies between 2% and 9%, depending upon the treatment of the disease. Early recommended treatment with systemic antiviral therapy may decrease the incidence or severity of serious sequelae, but the likelihood of preventing complications is reduced if therapy is delayed, usually considered to be after more than 3 days of initial symptoms[15] or rash. Post-herpetic neuralgia is more likely in older patients, patients with more severe acute pain and rash, and in patients with ophthalmic involvement.[16,17] Systemic complications of zoster include stroke, which is more common after HZO than HZ in other locations,[18-21] temporal arteritis,[22] and possibly heart attack[23,24] and depression.[25]

Evaluation of Current Evidence

Recent evidence appears to indicate that the age of onset of zoster is decreasing, and this effect may be unrelated to zoster vaccination preferentially in the elderly. Two studies reported a significant 5-year decrease in the mean age of onset of zoster from more than 60 years of age to less than 60 years of age.[26,27] Both studies recommended vaccination age may need to be lowered to 50 years of age. The mean age of patients developing HZO-related ocular disease is 63 years.[28]

Effectiveness of Vaccinations and Recommendations of Other Organizations

Zoster Vaccine Live (ZVL, Zostavax™)

A randomized controlled clinical trial demonstrated that the Zoster Vaccine Live (ZVL) (an attenuated live virus vaccine) decreased the incidence of zoster 51% and the occurrence of postherpetic neuralgia by 66% in immunocompetent people age 60 years and older.[29] The vaccine decreased the incidence of zoster more than 60% in people in their 60s, compared to less than 40% in people 70 years and older. However, the effect on disease severity was greater in older persons, resulting in similar reduction in disease burden across age groups. An important limitation of ZVL is its waning effect, and models estimate nearly complete loss of efficacy by 10 years post-vaccination.

On the basis of this study, the Zoster Vaccine Live was approved by the FDA in 2006 and recommended by the CDC in 2008 for immunocompetent people age 60 years and older. CDC also recommended zoster vaccine for people with chronic medical conditions, including those affecting humoral immunity, and people who anticipate becoming immunocompromised. In the US, the low rate of zoster vaccination is a public health problem. As of 2015 CDC data, only 31% of eligible people age 60 years and older had received it.[30]

In 2011, the FDA expanded their approval of the vaccine for immunocompetent people 50-59 years of age, after it was shown to decrease the incidence of zoster by 70% in this age group.[31] The CDC recommendation for the ZVL remains unchanged.

Recombinant Zoster Vaccine (RZV, Shingrix™)

The RZV, also called the Herpes Zoster subunit (HZ/su) vaccine, contains a recombinant varicella zoster virus glycoprotein E surface antigen reconstituted in a novel liposome-based adjuvant system. A clinical trial (ZOE-50) of RZV compared to placebo conducted outside of the US during 2010-2011 published in 2015 demonstrated that this vaccine had an efficacy of ~97% in all age groups of patients.[32] The results of the second part of this trial (ZOE-70) conducted concurrently including participants age 70 years and older were pooled with ZOE-50 and showed ~90% efficacy in vaccine recipients age 70 years and older.[33] The efficacy of this vaccine remained 85% against HZ after 4 years. Local and/or acute systemic reactions interfering with normal activities occurred in over 10% of vaccine recipi-

ents, raising concern about adherence with the 2-dose schedule required for efficacy.[34]

In vitro studies report that the immune response is not inferior in people with a past history of vaccination with ZVL,[35] herpes zoster,[36] or when given at the same time as one influenza vaccine.[37]

FDA approval

RZV was FDA approved in October 2017 for adults age 50 years and older.[38] This vaccine is administered intramuscularly as a 2-dose series 2 to 6 months apart. It is refrigerated and must be discarded if frozen before or after reconstitution. According to the FDA label, acute local and general reactions occur more often in people in their fifties than after age 70 yrs, and general / systemic reactions occur more frequently after the second than the first dose of the 2-dose series.[38]

CDC Recommendations

In January 2018, the Advisory Committee on Immunization Practices of the CDC recommended RZV vaccination of immunocompetent adults 50 years and older, including people with a past history of vaccination with ZVL at least 2 months ago.[39] The CDC states that it is important to counsel patients regarding the possibility of local and systemic acute reactions, and to encourage patients to complete the 2-dose series. With regard to the timing of vaccination with the 2-dose series of RZV in people with a past history of ZVL, the CDC notes one should consider the age at, and time since, ZVL, which is less effective in preventing zoster in people age 70 and above, compared to people in their sixties where vaccination with RZV was studied 5 years after ZVL.[35] CDC recommends RZV as the preferred vaccine over ZVL due to its higher and longer lasting efficacy across all age groups. The CDC issued no recommendations for immunocompromised persons because they were excluded from the clinical trials. According to the CDC, reporting of adverse events, using the Vaccine Adverse Events Reporting System (VAERS) 1-800-822-7967 and Vaccine Safety Datalink, is especially important due to the novel adjuvant RZV contains with high reactogenicity and immunogenicity.

Additional Considerations

People with a history of herpes zoster ophthalmicus may be at risk for recurrent eye disease after vaccination with RZV, as has been reported in a some cases after ZVL.[40,41] It is suggested that HZO patients should be examined by their ophthalmologist within several weeks before and after vaccination against zoster, and adverse events should be reported. The optimal timing of vaccination after an episode of zoster, including HZO, is not specified by the CDC. An episode of zoster stimulates cell-mediated immunity for a period of time, so vaccination is not urgent. It is suggested that vaccination should be delayed after HZO until eye disease is well controlled.

Comparisons Between RZV and ZVL

The CDC recommends RZV as the preferred vaccine over ZVL, although there are no head to head studies comparing the two vaccines. In our opinion, if compliance with the second injection of RZV required for efficacy is doubtful, and concern about acute local and general reactions is a barrier to RZV vaccination, ZVL is an option to consider, especially in immunocompetent adults in their fifties where ZVL reduces HZ by 70% and has fewer systemic reactions.

Conclusion

Both the RZV and the ZVL are FDA approved for individuals age 50 years and older, but the ZVL is limited to use in immunocompetent patients. As of 2018, the CDC now recommends vaccination against zoster with the RZV for immunocompetent adults age 50 years and older. Vaccination starting at age 50 will reduce the burden of this disease, including chronic eye disease. Ophthalmologists should strongly recommend that patients age 50 years and older obtain this vaccination, and should work with primary care physicians, internists, dermatologists, other medical doctors, and health care professionals to strongly recommend vaccination against zoster starting at age 50 years. Given the currently low rate of ZVL immunization in indicated age groups, advocacy by ophthalmologists may play an important role in increasing vaccination rates in the future.

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Viral Endotheliitis: Recognizing and Defeating the Players

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The Take Away

1. HSV, VZV, and CMV are the culprits.
2. There is infectious virus in the aqueous.
3. Virus + inflammation = compromised corneal endothelium.
4. Central disciform is *not* the only corneal presentation.
5. Virus + inflammation = acutely elevated IOP.
6. Treat with more antivirals and less steroids.
7. Aqueous antiviral needs to exceed the viral ID_{50}.

When Medical Therapy Fails, What Next?

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Microbial keratitis is a major cause of corneal blindness, often misdiagnosed and inappropriately treated. Treatment revolves around detection of clinical signs, establishment of an etiological diagnosis, and institution of specific therapy. Medical therapy is usually the first line of treatment. Surgical treatment is called for in eyes with compromised tectonic stability and nonresponse to maximal topical therapy. Various described techniques include application of tissue adhesive, targeted drug delivery in the form of intrastromal and intracameral drug injections, patch grafts, and therapeutic lamellar and full-thickness keratoplasty. The various clinical scenarios for and advantages and disadvantages of each of these methods are described as follows:

Tissue Adhesives

The goal of tissue adhesives is to restore the tectonic integrity of the globe while obviating the need for a definitive corneal procedure.[1] Cyanoacrylate adhesive works best for small corneal perforations and in eyes with significant corneal thinning and melting. Perforations < 3 mm are amenable to gluing . The surgical procedure for the management of corneal perforation involves careful removal of all loose epithelium and necrotic tissue surrounding the perforation site. The perforation site is dried with a surgical sponge, followed by reformation of the anterior chamber with a small amount of air. This is followed by controlled application of a small amount of tissue adhesive after ensuring that the surface is adequately dry. Additional applications may be required adjacent to the existing plug in case the leak persists. A bandage contact lens is applied at the end of the surgical procedure. The antimicrobial agents are continued after the application of the cyanoacrylate glue.

Targeted Drug Delivery

Intrastromal and intracameral injection of antifungal drugs is indicated in eyes with infections not responding to topical therapy, with the presence of endo-exudates, and with infections extending to posterior segment.[2-5] The surgical procedure for intrastromal injections involves delivering the drug in small aliquots, at the level of anterior-mid stroma forming a barrage in the vicinity of the lesion. Repeated injections are, however, usually required for complete response. The antimicrobial agents used for intracameral injections in cases of keratitis are mainly antifungals, like amphotericin B and voriconazole, and also antibacterial agents, such as vancomycin. The dose of amphotericin B for intracameral injection mentioned in the literature varies from 5 to 25 µg/0.1 mL, with 5-10 µg /0.1 mL being the most preferred dose in most studies. Injection of amphotericin B has generally been found to be safe and effective in most of the previous case series. Side effects reported in literature include severe pain lasting for a few hours after the injection and an increase in anterior chamber reaction, which decreases after 48 hours. The anterior chamber reaction may result from drug toxicity or inflamed dilated iris vessels secondary to decompression caused by the paracentesis. Anterior subcapsular cataract, corneal perforation, and raised IOP have also been reported in isolated cases.

An intrastromal injection can be given under peribulbar or topical anesthesia. Under full aseptic conditions, the preloaded drug is administered under operating microscope. With the bevel down, the needle is inserted obliquely from the uninvolved clear area to reach just close flush to the abscess at the mid-stromal level (as the intended level for drug deposit). The drug then is injected, and the amount of hydration of the cornea is used as a guide to assess the area covered. Once the desired amount of hydration is achieved, the plunger is withdrawn slightly to ensure discontinuation of the capillary column and thus prevent back-leakage of the drug. Several divided doses are given around the abscess in order to form a deposit of the drug around the circumference of the lesion. This is done in such a manner that a centripetally directed progressive wave of fluid appears to encompass the abscess along each meridian. Circumferential injection ensures the formation of a barrage of the drug around the entire abscess. The total amount of drug injected intrastromally ranges from 0.05 mL to 0.10 mL. Following intrastromal injection, patients need to continue on prescribed topical antifungal (voriconazole or amphotericin) therapy.

Patch Graft

Tectonic patch grafts are best suited for eyes with large corneal perforations (more than 3 mm) not amenable to tissue adhesives.[6] These effectively restore the integrity of the eye, simultaneously allowing complete removal of infected and necrotic tissue.[7] Usually dermatology punches are used to fashion these grafts. Moderate- to low-quality donor tissue can be used. Irregular astigmatism causing suboptimal visual acuity are the disadvantages.

Therapeutic Lamellar Keratoplasty

Lamellar keratoplasty is used as a tectonic measure in eyes with descemetocele formation or infections sparing the Descemet membrane and the endothelium.[8] Advantages over full-thickness grafts include lesser risk of immunological rejection and endothelial decompensation. Lamellar keratoplasty, however, has the disadvantages of occurrence of intralamellar neovascularization or incomplete removal of pathogens, in the case of deep-seated infections. Eyes with descemetocele formation are managed by careful separation of the overlying corneal stroma using BSS or viscoelastic, thereby baring the Descemet membrane.[9,10]

Therapeutic Penetrating Keratoplasty

Full-thickness keratoplasty is indicated for large central corneal melts, near total corneal infiltrates not responsive to medical therapy, and associated scleral and posterior segment involvement.[11] More recently early therapeutic keratoplasty has been recommended for fungal keratitis.[12] The surgical procedure involves appropriate slit-lamp examination and identifying the

extent of infiltrates to ensure complete removal of infected tissue. The surgery should be carried out under adequate anesthesia and akinesia after administering ocular hypotensives such as intravenous mannitol. General anesthesia is usually preferred over a peribulbar block to reduce positive pressure. Anterior chamber wash can be given using voriconazole and amphotericin B at the end of the surgical procedure. Postoperatively, appropriate antimicrobials are continued, followed by initiation of topical steroids.

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Interface and Wound Infections: Special Considerations for Special Situations

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Bacterial and fungal keratitis are potentially serious and vision-threatening conditions. In general, if managed correctly, routine cases of bacterial keratitis can have reasonable outcomes. Algorithms for diagnosis and management of bacterial keratitis have been well-described, including information about the adjunctive use of topical corticosteroids.[1] The outcomes of fungal keratitis are not as favorable, as these infections can be more difficult to manage, and recent studies have compared different topical and oral antifungals for the treatment of fungal keratitis.[2-4]

Postoperative wound infections present special circumstances that demand different and more aggressive treatment in order to prevent untoward outcomes. In any setting, a corneal wound infection, whether following cataract surgery or keratoplasty, can result in a deep-seated infection resulting from direct implantation of organisms in the corneal stroma. These infections can be hard to treat because topical medications may not penetrate deep enough or adequately enough into the stroma. In addition, the organisms may have a higher chance of getting into the eye, resulting in endophthalmitis. Furthermore, penetrating keratoplasty wound infections also have a chance of resulting in wound dehiscence. Thus aggressive antimicrobial therapy must be instituted in the setting of wound infections. Surgical interventions must also be considered.[5]

Interface infections, like wound infections, can be difficult to treat because the organisms have gained entry via direct implantation and therefore are relatively protected from antimicrobial therapy. In the setting of LASIK, organisms can be implanted directly under the flap, with *Staphylococcus* species and *Mycobacteria* species being common organisms. Aggressive topical therapy along with lifting, scraping, and irrigation of the flap can be effective treatments.[6] Interface infections can also occur after deep anterior lamellar keratoplasty, usually in the setting of incomplete removal of stroma in an active infectious keratitis situation. Penetrating keratoplasty is usually the best option under these circumstances.[7]

Interface infections after endothelial keratoplasty are a newer and a unique circumstance. These infections have usually been determined to be fungal in origin, most commonly *Candida* species.[8-9] It is believed that fungal elements from the donor are sequestered in the interface during Descemet-stripping endothelial keratoplasty (DSEK) and even Descemet membrane endothelial keratoplasty. These infections can appear soon after surgery, or even many weeks afterward. There are no established algorithms for the treatment of these infections, and management is controversial. Some surgeons advocate a watchful waiting using topical and/or oral antifungals, and intrastromal injection of antifungals has also been suggested.[10] Others recommend more aggressive options such as immediate removal of the donor lenticule with anterior chamber wash-out. If this option is employed, it is highly recommended to wait until the eye quiets down prior to reinserting another graft. In more advanced situations, penetrating keratoplasty may be warranted to remove both the source of infection and the surrounding infected tissue. Current research in the United States is focused on prophylaxis against this situation with the addition of antifungals into hypothermic storage media.[11-13]

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Crosslinking and Keratitis: Treatment, or Risk Factor?

Vishal Jhanji MD

Introduction

Microbial keratitis is one of the leading causes of ocular morbidity and visual loss worldwide. Although monotherapy with fluoroquinolone eye drops is sufficient for small corneal ulcers, moderate to severe cases need intensive treatment with fortified antibiotics. Surgical procedures involving epithelial debridement and use of corticosteroid eye drops postoperatively are a risk factor for occurrence of microbial keratitis. Corneal collagen crosslinking has increasingly been used for management of progressive keratoconus. There are reports of occurrence of microbial keratitis after collagen crosslinking. However, more recently, corneal collagen crosslinking has been used an adjuvant treatment for management of cases with infectious keratitis.

Observations

Previous studies have reported variable outcomes regarding the use of collagen crosslinking for microbial keratitis. Overall, it is understood that collagen crosslinking might be useful in anterior and midstromal corneal infections, whereas it doesn't alter the course of the disease in deep-set infections.

In our experience, crosslinking might be a useful adjuvant for mild to moderate cases of bacterial keratitis. In a comparative study, crosslinking did not provide any additional benefit over standard antifungal treatment in cases with fungal keratitis.

This presentation will outline the risks associated with collagen crosslinking, as well as the use of this modality as an adjuvant for treatment of cases with microbial keratitis.

Case Presentation

If It Wasn't for Bad Luck There Would Be No Luck At All!

Charles McGhee PhD FRCOphth FRANZCO

Corneal diseases can occasionally aggregate in a manner that is not explicable by normal chance occurrence—or to quote bluesman Lightnin' Slim: "If it wasn't for bad luck, I wouldn't have no luck at all" (1954). This case report highlights an unusual constellation of corneal and ocular pathology, including congenital and acquired disease, with a "lateral thinking" approach to provide a complex but satisfactory resolution.

Born with a normally developed right eye but a microphthalmic left eye with a congenital cataract, this female patient developed moderate myopia O.D. with BSCVA of 20/20 O.D. and HM O.S. Vision O.D. was further compromised in middle age by severe herpes zoster ophthalmicus keratouveitis. Subsequent loss of corneal sensation and the development of cataract and associated glaucoma O.D. reduced the patient's vision to a level at which she was not able to drive or pursue her professional career, which required use of optical instruments (only HM vision O.S.). Fortunately, an uncomplicated phacoemulsification with IOL restored 20/20 vision O.D.

Five years later a rhegmatogenous retinal detachment occurred in the right eye; this was successfully repaired and the subject regained 20/30 BSCVA, albeit with significant vitreous floaters. Over the next 3 years progressive deterioration of the corneal surface (post-HZO) occurred, with development of band-shaped calcium band keratopathy. Subsequently a severe *Streptococcus viridans* microbial keratitis, though treated successfully, reduced BSCVA to 20/200, and the patient was again unable to drive or pursue her profession. As the patient was effectively uniocular due to the microphthalmos O.S., conservative management was pursued, enabling modest recovery to 20/80 O.D. over the next 3 years.

Seven years after the streptococcal microbial keratitis the patient was referred for a (fifth) opinion in respect to possible options to restore more functional vision O.D. On examination, BSCVA was 20/80 O.D. and HM O.S., and IOP was 24 mmHg and 34 mmHg O.D. and O.S., respectively. The right cornea had virtually no sensation, it was vascularized, variably thinned, and scarred, and it exhibited rough calcium deposits, with suggestion of prior crystalline keratopathy. The left eye was microphthalmic with a small cornea, a quiet anterior chamber, dense cataract, and no view of the posterior segment.

After careful consideration over many months, long discussion, and thoughtful consent, the patient embarked on a series of procedures to restore vision in her vascularized, scarred, anesthetic cornea that ultimately resulted in long-term restoration of 20/30 vision. This short presentation will highlight the somewhat unusual approaches used to turn a lifetime series of "bad luck" to ultimate restoration of vision, driver's license, and professional career.

Suggested Reading

1. McDonald EM, Patel DV, McGhee CN. A prospective study of the clinical characteristics of patients with herpes simplex and varicella zoster keratitis, presenting to a New Zealand emergency eye clinic. *Cornea* 2015; 34(3):279-284.

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Eyegate Pharma: C,O
National Eye Institute: S
Novaliq: C
Shire: C
Sun: C
TearLab Corp.: C
Topivert: C
University of Miami: P

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Allergan: C
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